PassageBio

2025 ANNUAL REPORT

# TO OUR SHAREHOLDERS,

For Passage Bio, 2025 was a year marked by meaningful clinical progress, disciplined execution, and an unwavering commitment to the patients and families who are counting on the important work we do. Our mission remains clear: to develop genetic medicines that could redefine the course of devastating neurodegenerative conditions.

## Addressing an Urgent Unmet Need in FTD

Our lead focus in frontotemporal dementia (FTD) with granulin mutations (*GRN*) represents an area of significant unmet medical need. With no disease-modifying therapies currently approved, people with FTD-*GRN* live, on average, eight years after the onset of symptoms.

Recent market developments in FTD-*GRN* research have increased the urgency for patients and their families. It's why our team is dedicated to advancing PBFT02, a one-time gene therapy designed to target the underlying root cause of this form of FTD.

## Compelling Best-in-Class Potential: Durable PGRN Elevation and Early Biomarker Improvement

We continued to validate the best-in-class potential of PBFT02 by generating compelling early clinical and biomarker data. In FTD, deficiency in progranulin (PGRN), a protein made by the *GRN* gene, may lead to neuronal dysfunction and neurodegeneration. Over the past twelve months, we reported interim data from the ongoing global Phase 1/2 upliFT-D clinical trial showing that treatment with PBFT02 demonstrated durable elevation of cerebrospinal fluid (CSF) PGRN, which support its therapeutic potential to correct the underlying molecular deficiency driving disease progression.

We also saw promising early signals of improvement in a key disease progression biomarker, stabilizing plasma neurofilament light chain levels, as compared to natural history. These encouraging trends suggest that PBFT02 may not only address biochemical pathology but also help slow or stabilize the degenerative processes that define this devastating disease.

## Driving Clinical Execution and Progressing Towards Late-Stage Development

Throughout 2025, we drove strong clinical trial execution worldwide and evolved our program to focus on enrolling patients earlier in their disease where the potential for clinical benefit is greater. We are pleased to have enrolled the first FTD-*GRN* patients in Cohort 3 of the upliFT-D trial, and we recently initiated dosing of PBFT02 in FTD-*C9orf72* patients.

We look forward to continuing enrollment of our upliFT-D clinical trial throughout 2026 across an expanding network of global trial sites. This progress is fundamental to the advancement of PBFT02 and our engagement with regulators on the path forward.

Our regulatory program for PBFT02 is progressing as well, and we plan to gain feedback from global health authorities on a registrational study design in FTD-*GRN* to inform our operational plans for late-stage development.

## Advancing a Differentiated Huntington's Disease Program

In parallel with our FTD program, we advanced a promising preclinical program in Huntington's disease (HD). HD is an autosomal dominant, progressive neurodegenerative disease caused by a mutation in the huntingtin gene, *HTT*, and has no approved disease-modifying therapies. Our differentiated approach is focused on regulating MSH3, a key protein in the DNA repair pathway and a validated target for treating HD.

With the completion of key proof-of-concept studies in 2025, we plan to identify a clinical candidate in the second half of 2026. This program represents an exciting expansion of our pipeline that leverages our gene therapy expertise.

## Looking Ahead

We are energized by our progress in 2025. Every milestone reflects our dedication to patients and families who urgently await new treatment options. We are continually grateful for the support of our shareholders as we advance therapies that have the potential to transform neurodegenerative conditions.

On behalf of all of us at Passage Bio, thank you for your continued belief in our mission.

Sincerely,

**William Chou, M.D.**
President and Chief Executive Officer

# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 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, 2025**

**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 001-39231**

# PASSAGE BIO, INC.
**(Exact Name of Registrant as Specified in Its Charter)**

| **Delaware**<br>**(State or other jurisdiction of incorporation or organization)** | **82-2729751**<br>**(I.R.S. Employer Identification No.)** |
|---|---|
| **One Commerce Square**<br>**2005 Market Street, 39th Floor**<br>**Philadelphia, PA**<br>**(Address of principal executive offices)** | **19103**<br>**(Zip Code)** |

**(267) 866-0311**
**(Registrant's telephone number, including area code)**

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

| Title of each class | Trading Symbol | Name of each exchange on which registered |
|---|---|---|
| Common stock | PASG | The Nasdaq Stock Market LLC (Nasdaq Capital Market) |

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

None

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 issuer (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 Exchange Act). Yes ☐ No ☒

The aggregate market value of the common equity held by non-affiliates of the Registrant on June 30, 2025 (the last business day of the Registrant's second fiscal quarter), based upon the closing price of $8.00 of the Registrant's common stock as reported on The Nasdaq Capital Market, was approximately $25.4 million.

The number of shares of the registrant's common stock outstanding as of February 26, 2026, was 3,207,810.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the Registrant's Definitive Proxy Statement ("Proxy Statement") relating to the 2026 Annual Meeting of Stockholders will be filed with the Commission within 120 days after the end of the Registrant's 2025 fiscal year and is incorporated by reference into Part III of this Report.

**Passage Bio, Inc.**

**ANNUAL REPORT ON FORM 10-K**

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## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "aim," "may," "will," "should," "expect," "forecast," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. All statements other than statements of historical fact contained in this Annual Report, including without limitation statements regarding our plans to develop and commercialize our product candidates, the timing and results of our ongoing or planned preclinical studies and clinical trials, risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, the timing of and our ability to obtain and maintain regulatory approvals, the clinical utility of our product candidates, our commercialization, marketing and manufacturing capabilities and strategy, our expectations about the willingness of healthcare professionals to use our product candidates, the timing, or amount, of receipt of any potential future milestone and royalty payments, the sufficiency of our cash and cash equivalents, general economic, industry and market conditions, including fluctuating interest rates and inflation, changing tariff policies and trade restrictions, any future potential federal government shutdowns, instability in the global banking system, and the plans and objectives of management for future operations and capital expenditures are forward-looking statements.

The forward-looking statements in this Annual Report are only predictions and are based largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of known and unknown risks, uncertainties and assumptions, including those described under the sections in this Annual Report entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Annual Report.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. We intend the forward-looking statements contained in this Annual Report to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act.

## TRADEMARKS AND TRADENAMES

"PASSAGE BIO" is a registered trademark, and the PASSAGE BIO mark, the Passage Bio logo and all product names are our common law trademarks. All other service marks, trademarks and tradenames appearing in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and tradenames referred to in this Annual Report appear without the ® and ™ symbols, but those 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 right of the applicable licensor to these trademarks and tradenames.

**Summary of Risk Factors**

Our business is subject to a number of risks and uncertainties, including those set forth in the section titled "Risk Factors" under Item 1A. Some of these risks are:

- We are a clinical stage genetic medicines company with a history of operating losses, and we may not achieve or sustain profitability. We anticipate that we will continue to incur losses for the foreseeable future. Our limited operating history may make it difficult for you to evaluate our success to date and to assess our future viability;

- We will need to raise additional funding before we can expect to become profitable from any potential future sales of our products;

- PBFT02 is currently our sole clinical stage product candidate and we may not be able to successfully develop and commercialize PBFT02;

- We are early in our development efforts. Our business is dependent on our ability to advance our current and future product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them;

- Certain disorders we seek to treat have low incidence and prevalence and it may be difficult to identify patients with these diseases, which may lead to delays in enrollment for our trials or slower commercial revenue if approved;

- Preclinical and clinical development involve lengthy and expensive processes with uncertain outcomes. We may incur additional expenses or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our current product candidates or any future product candidates;

- Gene therapy is a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval;

- Our product candidates may cause undesirable and unforeseen side effects, which could delay or prevent their advancement into clinical trials or regulatory approval, limit the commercial potential or result in significant negative consequences;

- Gene therapies are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in our development or commercialization programs or otherwise harm our business;

- 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 or technologies that are more advanced or effective than ours;

- We currently rely and expect to continue to rely on third-party manufacturers to produce clinical supply of our product candidates;

- Even if we are able to obtain regulatory approval for and commercialize our product candidates, our products may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business; and

- If we are unable to obtain and maintain patent protection or other necessary rights for our products and technology, or if the scope of the patent protection obtained is not sufficiently broad or our rights under licensed patents 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*

#### Overview

We are a clinical stage genetic medicines company focused on improving the lives of patients with neurodegenerative diseases. Our primary focus is the development and advancement of cutting-edge, one-time gene therapies designed to target critical underlying pathologies in these conditions. We believe we have developed a differentiated approach to developing treatments for central nervous system, or CNS, disorders that allows us to select and advance product candidates with a higher probability of technical and regulatory success.

Our lead clinical product candidate, PBFT02, seeks to elevate progranulin levels to enhance lysosomal function and slow disease progression across a variety of neurodegenerative diseases. PBFT02 is a gene replacement therapy that utilizes an adeno-associated virus serotype 1, or AAV1, capsid to deliver a functional granulin gene, or *GRN*, encoding progranulin, or PGRN, to the brain via intra cisterna magna, or ICM, administration. The lead indication for PBFT02 is frontotemporal dementia, or FTD, caused by progranulin deficiency, or FTD-*GRN*. We believe this clinical product candidate has the potential to provide patients with significantly improved outcomes given the rigorous capsid and transgene selection process, and our chosen route of ICM administration, which provides the potential for enhanced benefits due to widespread vector delivery to the brain and spinal cord and an improved safety profile compared with systemic administration, due to the lower doses required.

We are currently studying PBFT02 in FTD-*GRN*, for which there are currently no approved disease-modifying therapies. In addition to the continued clinical development of PBFT02 to treat FTD-*GRN*, we intend to pursue PBFT02 in additional adult neurodegenerative diseases where we believe increasing PGRN levels could provide benefit. Third-party preclinical studies have shown that increased PGRN levels reduce the pathologic accumulation of TAR DNA binding protein 43, or TDP-43. TDP-43 pathology is a hallmark of multiple neurodegenerative conditions, including FTD due to mutations in the *C9orf72* gene, or FTD-*C9orf72*, approximately 95% of sporadic amyotrophic lateral sclerosis, or ALS, and approximately 50% of sporadic FTD. Additionally, we believe restoration of PGRN has the potential to modulate Alzheimer's disease, or AD, in patients who are carriers of the PGRN-lowering *GRN* rs5848 single nucleotide polymorphism, or SNP. Individuals with this polymorphism have reduced PGRN levels and are at an increased risk for AD. We have received positive regulatory feedback on the clinical pathway to treating FTD-*C9orf72* patients and ALS patients with PBFT02. We have initiated clinical development of PBFT02 in FTD-*C9orf72* patients in the upliFT-D trial for this population.

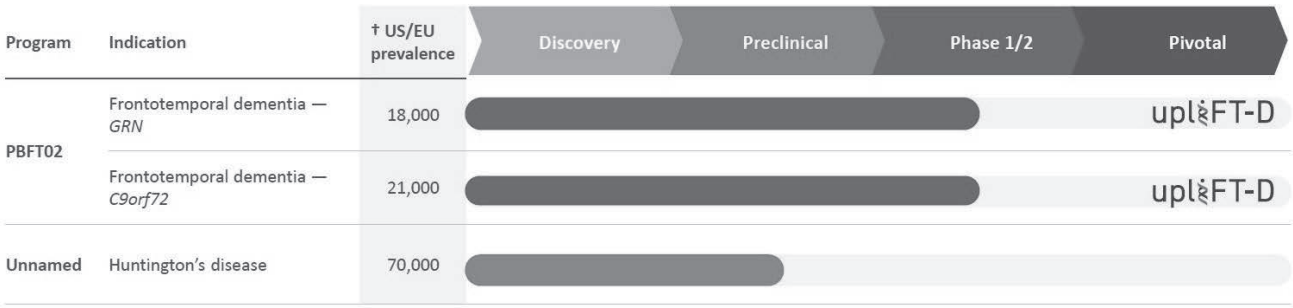
We have an active preclinical research program to develop a genetic medicine to treat Huntington's disease through our research, collaboration and license agreement, or the Gemma Collaboration Agreement, with Gemma Biotherapeutics, Inc., or Gemma. Huntington's disease, or HD, is an adult-onset, progressive neurodegenerative disease characterized by motor, cognitive, and behavioral deterioration, ultimately leading to death within approximately 15 to 20 years after symptom onset. There are currently no disease-modifying therapies approved for the treatment of HD, and we estimate the prevalence of HD in the United States and Europe is approximately 70,000, based on available literature.

We are also party to a series of sublicense agreements, as amended, with Gemma in connection with the outlicensing of three pediatric programs we had previously advanced to clinical stage development, collectively the Outlicensed Programs, and such agreements, the Amended Gemma Sublicenses. In addition, we entered into a Transition Services Agreement, as amended, with Gemma. We refer to the Amended Gemma Sublicenses, the Transition Services Agreement, and the Gemma Collaboration Agreement, collectively, as the Outlicense Transaction Agreements.

Prior to the execution of the Outlicense Transaction Agreements, we advanced our preclinical programs through our research collaboration with the Trustees of the University of Pennsylvania's, or Penn's, Gene Therapy Program, or GTP. This collaboration provided access to differentiated scientific expertise for the conduct of rigorous preclinical studies to generate promising product candidates. Gemma is comprised of a core research team from GTP and is continuing the same approach to preclinical development to support the continued development of our preclinical Huntington's disease program.

## Our Pipeline

We have a gene therapy pipeline with the potential to address multiple neurodegenerative diseases. Our development programs consist of:




*† US/EU prevalence per third-party sources*

In addition to the indications above, we believe amyotrophic lateral sclerosis, or ALS, and Alzheimer's disease, or AD, represent future potential pipeline expansion opportunities for PBFT02.

### *PBFT02 for the Treatment of FTD-GRN*

We are currently developing PBFT02, a gene replacement therapy which utilizes an AAV1 capsid to deliver a functional copy of *GRN* encoding for PGRN, for the treatment of FTD-*GRN*. FTD-*GRN* is an inheritable form of FTD caused by reductions in PGRN production due to mutations in the *GRN* gene. PGRN is a complex and highly conserved protein with multiple roles in cell homeostasis, neurodevelopment, and inflammation. In FTD-*GRN*, PGRN deficiency results in lysosomal dysfunction, neuroinflammation, and neurodegeneration.

Currently, there are no disease-modifying therapies approved for the treatment of FTD-*GRN*, and we estimate the prevalence of FTD-*GRN* in the United States and Europe is approximately 18,000, based on available literature. Supported by findings in preclinical studies, we believe that PBFT02 may provide FTD-*GRN* patients with significantly improved outcomes. We selected the AAV1 capsid and ICM administration for PBFT02 because this approach led to extensive and robust vector delivery throughout the brain and spinal cord of non-human primates, or NHPs, and due to the higher PGRN levels in cerebrospinal fluid, or CSF, achieved using AAV1 as compared with other serotypes tested. ICM administration of AAV1 to NHPs resulted in elevated CSF levels of human PGRN when compared with CSF levels in healthy human subjects, and in excess of levels achieved in NHPs with AAVhu68 or AAV5. We have an active Investigational New Drug, or IND, application from the U.S. Food and Drug Administration, or the FDA, and approved clinical trial authorizations, or CTAs, in multiple countries for PBFT02. We are conducting our upliFT-D trial, an international, multi-center, open-label, single-arm Phase 1/2 clinical trial of PBFT02 in patients with a diagnosis of symptomatic FTD-*GRN*.

In June 2025, we reported biomarker data from patients in our upliFT-D trial. Dose 1 of PBFT02 (3.3e10 genome copies/g estimated brain weight, or 4.5e13 total genome copies) resulted in robust and durable increases in CSF PGRN levels, with concentrations increasing from below 3.0 ng/mL at baseline to a mean of 12.4 ng/mL at one month (n=6), 19.4 ng/mL at six months (n=6), 25.9 ng/mL at 12 months (n=4), and 23.8 ng/mL at 18 months (n=2). These levels of CSF PGRN are higher than the range found in healthy adult controls of 3.3 to 8.2 ng/mL (mean=4.8 ng/mL; n=61). CSF PGRN levels for the first patient treated with Dose 2 of PBFT02 (1.6e10 genome copies/g estimated brain weight, or 2.2e13 total genome copies) increased substantially from 1.5 ng/mL at baseline to 7.6 ng/mL at one month, approaching the upper limit of the range found in healthy adult controls. In contrast, following PBFT02 administration, plasma PGRN levels were unaltered, remaining similar to baseline concentrations and below mean levels found in healthy adult controls. Dose 1 of PBFT02 resulted in an average 4% increase in plasma neurofilament light chain, or NfL, levels, a biomarker associated with disease progression, compared to baseline at 12 months post-treatment (n=4). This change in plasma NfL after PBFT02 administration contrasts with an expected increase in plasma NfL levels of approximately

28% and 29% per year among untreated, symptomatic FTD-*GRN* patients, based on analysis of the ALLFTD natural history data and published natural history data (Saracino 2021), respectively.

As of our June 2025 data disclosure, interim safety highlights from PBFT02 in FTD-*GRN* patients (n=8) included:

- Seven patients experienced a collective total of 26 treatment emergent adverse events, or TEAEs, considered related to PBFT02.
- Two patients experienced a total of three serious TEAE considered related to PBFT02. These included venous sinus thrombosis (2 patients) and hepatoxicity (1 patient). These serious TEAE all occurred at Dose 1, were asymptomatic and responded to treatment.
- One patient experienced one serious TEAE of pulmonary embolism in the setting of a concurrent systemic infection six weeks after receiving PBFT02, considered unrelated to PBFT02.
- No evidence of thrombotic angiopathy, dorsal root ganglion toxicity as measured by nerve conduction studies, and no complications during ICM administration were observed across any of the eight treated patients.

We completed the dosing of Cohorts 1 and 2 in the upliFT-D trial in July 2025. Cohort 1 consists of 5 patients who received Dose 1 of PBFT02, and Cohort 2 consists of 4 patients, split equally between Dose 1 and Dose 2 of PBFT02. Cohorts 1 and 2 included participants with a global Clinical Dementia Rating, or CDR, plus National Alzheimer's Coordinating Center with Frontotemporal Lobar Degeneration, or NACC FTLD, score of 1 or 2 at baseline. The global CDR rating is scored from 0 (normal/asymptomatic) to 3 (severe).

In advance of enrolling Cohort 3, which we expect to consist of 10 FTD-*GRN* patients receiving Dose 2 of PBFT02, we amended the upliFT-D clinical trial protocol to introduce a short course of low dose prophylactic anticoagulation. We also amended the protocol to exclude patients with a global CDR score of 2 (moderate) at baseline and include only patients with global CDR scores of 0.5 (prodromal) or 1 (mild) at baseline. As of March 2026, we are enrolling patients in Cohort 3 across our global trial sites.

In September 2025, we completed a Type D Chemistry, Manufacturing, and Controls meeting with the FDA and aligned on key elements of the analytical plan to establish comparability of product manufactured with our high-productivity, suspension-based PBFT02 manufacturing process to the current product being used in our ongoing clinical trial.

We expect to deliver on the following related to our upliFT-D trial for PBFT02 for the treatment of FTD-*GRN*:

- Report updated interim safety and biomarker data from Dose 2 in FTD patients in the first half of 2026; and,
- Seek regulatory feedback on registrational trial design in FTD-*GRN* in the first half of 2026.

***PBFT02 for the Treatment of FTD-C9orf72 and ALS***

We are also evaluating PBFT02 for the treatment of additional adult neurodegenerative diseases where we believe elevated PGRN levels could provide benefits. This approach stems from PGRN's pleiotropic cellular effects including the regulation of microglial activation and lysosomal function, and in particular its potential to ameliorate TDP-43 pathology. TDP-43 is a ribonucleic acid / deoxyribonucleic acid, or RNA/DNA, binding protein that normally resides in the nucleus where it regulates gene expression, RNA splicing, RNA trafficking, and mRNA turnover. Cytoplasmic TDP-43 pathology is a hallmark of multiple neurodegenerative conditions including FTD-*GRN*, FTD-*C9orf72*, approximately 95% of sporadic ALS, and approximately 50% of sporadic FTD. In these disorders, hyperphosphorylated TDP-43 accumulates in the cytoplasm of cell bodies and dendritic processes of neurons and glia. Experimental evidence suggests that loss of TDP-43's normal nuclear function contributes to neurodegenerative processes.

The potential for benefit of increased PGRN in disorders with TDP-43 pathology has been demonstrated by third-party preclinical studies in mice and zebrafish which showed that increased PGRN levels reduced TDP-43 pathology and associated toxicities. We anticipate that elevating neuronal PGRN levels in diseases with TDP-43 pathology may provide significant benefits to patients. We have initiated preclinical studies to extend these initial observations. Based on available literature, we estimate the prevalence of FTD-*C9orf72* in the United States and Europe is approximately 21,000. There are no disease modifying therapies approved for the treatment of FTD-*C9orf72*.

We received positive regulatory feedback on the clinical pathway to treating FTD-*C9orf72* with PBFT02 in the ongoing upliFT-D trial, and Cohorts 4 and 5 of upliFT-D will consist of three to five symptomatic FTD patients with *C9orf72* gene mutations who will initially receive Dose 2 PBFT02. We are enrolling and have initiated dosing patients in Cohort 4 across our global trial sites.

Similarly, we received positive regulatory feedback on the clinical pathway to treating ALS with PBFT02 which we believe represents a future pipeline opportunity.

***PBFT02 for the Treatment of AD***

We also believe that elevating PGRN levels has the potential to improve the course of AD in patients who carry the *GRN* rs5848 single nucleotide polymorphism, or *GRN* SNP. The *GRN* SNP has an allele frequency of approximately 30% and is associated with reduced PGRN levels. Its presence has been shown to confer an increased risk for AD onset. Within symptomatic AD patients, *GRN* SNP carriers not only have lower levels of PGRN, but also higher levels of CSF tau, which correlates with increased AD pathology in the brain and more rapid disease progression. Third party preclinical studies in animal models have demonstrated that low levels of PGRN may exacerbate AD pathology and, conversely, high levels of PGRN may reduce AD pathology. We believe this represents a future pipeline opportunity for PBFT02.

***Clinical Supply***

Through our partners, we have manufactured the PBFT02 clinical supply to support completion of the ongoing Phase 1/2 clinical trial in FTD-*GRN* and FTD-*C9orf72*, and initiation of a registrational trial in FTD-*GRN*.

***Active Research Programs***

We have an active preclinical research program through the Gemma Collaboration Agreement to develop a genetic medicine to treat HD.

HD is an autosomal dominant disorder caused by a mutation in the huntingtin gene, or *HTT*, in which a CAG trinucleotide repeat tract in the DNA is expanded. This leads to the expression of mutant huntingtin protein. *HTT* CAG repeat tracts are unstable and can continue to elongate over time, termed somatic instability. In neurons, CAG expansion occurs at different rates in different cells, and CAG expansion to above a certain threshold leads to neuronal dysfunction and death. DNA repair proteins such as MSH3 play a key role in driving somatic instability in HD, by erroneously incorporating extra CAG repeats into *HTT* DNA in certain circumstances. Published literature has shown that reducing somatic instability by decreasing MSH3 expression reduced disease pathology in HD mice. Further, published human genetic studies have shown that certain genetic MSH3 variants which reduce somatic instability are associated with delayed disease onset and slowed progression in HD patients.

Our approach is to reduce somatic instability and thereby slow neurodegeneration in HD by suppressing MSH3 expression in the brain, via AAV-mediated delivery of a miRNA gene. We expect to declare a clinical candidate for this program in the second half of 2026.

Beyond this program, through the Gemma Collaboration Agreement, we also have the option to license programs for four additional new indications in CNS diseases.

**Our Strategy**

Our primary focus is the development and advancement of cutting-edge, one-time therapies designed to target the underlying pathology of neurodegenerative diseases.

To achieve our vision, we have assembled a world-class team whose members have decades of collective experience in drug development and commercialization. We leverage this experience as we strive to develop

treatments that benefit patients with neurodegenerative conditions and their families. Patients are considered in every decision we make.

Key elements of our strategy include:

- **Focus on neurodegenerative indications for which we can have a transformative impact on patients' lives.** We believe that genetic medicines have the potential to significantly change the course of neurodegenerative diseases and to transform patients' lives, by providing patients with one-time disease modifying treatments for life-threatening conditions with limited or no approved treatment options.

- **Advance PBFT02 for the treatment of FTD-*GRN*.** Based on the initial clinical data for PBFT02 in FTD-*GRN*, we are prioritizing the execution of the ongoing upliFT-D trial, with the goal of advancing this program to the registrational phase. We believe this product candidate has the potential to provide FTD-*GRN* patients improved clinical outcomes, given our initial observations of robust and durable elevations in CSF PGRN levels and early evidence of reductions in plasma NfL, a disease progression biomarker, in patients after PBFT02 administration.

- **Broaden the application of PBFT02 by exploring its potential in additional neurodegenerative indications.** Based on initial clinical data for PBFT02 in FTD-*GRN* and evidence supporting progranulin's role in neurodegeneration, we have expanded our upliFT-D trial to include FTD-*C9orf72* cohorts and are exploring the therapeutic potential of PBFT02 in other diseases, including ALS and AD. We believe that our approach of advancing one genetic medicine candidate to treat multiple indications is a cost-effective strategy due to shared research and development costs, streamlined regulatory processes, and the opportunity for diversified revenue streams.

- **Extend existing, and establish new, relationships with patients and patient advocacy groups.** Patients are at the core of what we do. We have been engaging with patients, their families, and their advocacy groups since our inception and have acquired an intimate understanding of how we can positively impact their lives. These relationships deeply inform us as we develop and ultimately seek to commercialize our product candidates. We also have agreements with third-party providers to offer genetic counseling to adults who have been diagnosed with FTD at no cost to the patient.

- **Build upon our strong manufacturing and analytical foundation.** We believe the quality, reliability and scalability of our genetic medicine manufacturing techniques and expertise will be a critical advantage to our long-term success. We have combined broad in-house expertise with an outsourced model for execution. Our internal manufacturing and quality experts oversee external manufacturing and supply chain operations provided by third-party strategic relationships, such as Catalent Maryland, a unit of Catalent, Inc. acquired by Novo Holdings A/S, or Catalent. We believe Catalent is capable of producing enough supply to support our planned clinical trials of our current clinical product candidate, and its initial commercial launch if approved.

- **Selectively enter new research and development relationships.** We will selectively enter new research collaborations and explore other potential collaborations to build or advance our pipeline, contingent on the prioritization of operating expenses. We will look to nurture our genetic medicine technology capabilities by keeping abreast of advances in next-generation capsid development, promoter selection, transgene design, gene silencing and gene editing, which will help us to engineer optimal product profiles to address diseases with substantial unmet clinical needs.

**Genetic Medicine Background**

Each person's genetic material, or genome, consists of DNA in sequences of genetic code called genes. The DNA in the human genome contains approximately three billion nucleotide base pairs, and small changes, or mutations, routinely occur in the base pairs. A mutation in a single gene can alter the amount or activity of the protein expressed by the gene, causing deformities and disease. Currently, there are estimated to be over 10,000 diseases caused by a genetic abnormality in a single gene, which are also known as monogenic diseases. One gene therapy approach is to introduce into cells a new, fully functional version of a defective or missing gene. This approach is the basis for our FTD-*GRN*

program. In addition, gene therapy can also be applied to correct dysfunctional biological pathways that are not necessarily inherited or associated with one defective gene, by reducing the expression of pathological proteins or increasing the production of corrective biological targets. This is the basis for our programs that target conditions such as FTD-*C9orf72* and HD.

The development of molecular therapeutics to modulate human gene expression and correct disease-causing genetic defects had its advent several decades ago, and with advances in science and a deeper understanding of human genetics it has expanded to include a broad range of genetic medicines with the potential to modulate gene expression through diverse molecular mechanisms.

These transformative genetic medicines include gene therapy (delivery of an external gene to replace the normal function of a defective gene), gene silencing (delivery of a DNA or RNA-based therapeutic that modulates the transcription or translation of an injurious gene product), gene editing (delivery of a DNA or RNA-based therapeutic that corrects the expression of targeted genes) and combinations of these therapeutic modalities. We believe that this expanded molecular biological tool box will provide new therapeutics with the potential to deliver highly potent and safe interventions across a diverse set of CNS diseases, offering several advantages, including:

- **Potential to treat most diseases of genetic etiology.** Theoretically, it should be possible to design and deliver a genetic medicine to correct the expression of any human protein whose presence, absence or activity causes disease.
- **Potential to target mechanisms that have not been effectively or safely modulated by traditional small molecule or protein-based therapeutics.** The inherent specificity of genetic medicines for unique nucleic acid sequences can provide a high therapeutic index resulting from high potency and the potential to deliver adequate doses while avoiding off-target safety liabilities.
- **Efficient delivery of transformative therapeutics.** Because genetic medicines are designed to deliver a long-standing effect following a single administration, a single dose of these therapeutics has the potential to provide clinical benefits for many years.

Genetic medicines can be designed to mitigate challenges faced by other approaches in the development of therapeutics for the CNS. CNS disorders are among the most devastating in their impact on patients and their families. These disorders are generally life-threatening to patients. There is a significant need for genetic medicines that can target these disorders. Our lead clinical program, upliFT-D, is focused on a rare, monogenic CNS disorder, FTD-*GRN*, because it offers a compelling opportunity for the effective application of a genetic medicine, by correcting the progranulin deficiency that results from disease-causing mutations in the *GRN* gene. We are also exploring the potential for our progranulin gene therapy candidate, PBFT02, to target other degenerative disorders, such as FTD-*C9orf72*, ALS, and AD, where increasing progranulin levels in the central nervous system could provide benefit.

**Our Approach**

The field of genetic medicine is rapidly expanding and we believe we have developed a differentiated approach to developing treatments for CNS disorders that allows us to select and advance product candidates with a higher-probability of technical and regulatory success. Our gene therapy product candidates use AAV, a small, non-pathogenic virus that is genetically engineered to function as a delivery vehicle, or vector. In our current clinical program, the AAV is administered to a patient to introduce a healthy copy of a gene, or the transgene, to the cells in a process referred to as transduction. Our current approaches use AAVs to deliver a wild type transgene to either (i) restore expression of a fully functional version of a mutated gene or to (ii) overexpress a gene product. The components of an AAV gene therapy vector include the therapeutic gene that makes up the DNA payload, or the transgene, the outer viral shell that encloses the DNA payload, or the capsid, and any promoters added to the vector to boost expression of the transgene. The AAV is often described by the serotype, or strain, of the vector. The core tenets of our approach include a rigorous process for selecting product candidates, mitigation of early development risk through relationships with leading researchers and academic institutions, and mitigation of clinical development risk through deep relationships with patient advocacy groups, key opinion leaders and practitioners. Together,

these relationships allow us to directly benefit from decades of collective experience, the latest technologies and contemporary perspectives from patients.

In selecting our product candidates, we are focusing initially on optimizing transduction and expression of transgenes in the indication-specific target tissues. This involves prioritizing the following principles: selection of the route of administration to maximize transgene biodistribution; selection of capsid, transgene and promoter to optimize efficiency of transduction and expression; leveraging biological mechanisms such as cross-correction to maximize availability of transgene product to target cells; and the effective use of biomarkers to assess treatment effects on transduction, transgene expression and on disease pathophysiology.

- **Optimal route of administration:** Identifying the optimal route of administration for AAV gene therapy is critical to achieving safe and effective levels of transgene expression in the targeted location in the CNS. The optimal route of administration for CNS treatments should also leverage the immuno-privileged aspects of the CNS to reduce the potential for deleterious effects of neutralizing antibodies, or NAbs, on the biodistribution of AAV capsids. We evaluate preclinical trial outcomes and other data to decide the preferred route of administration on a program-by-program basis. For our clinical stage product candidate, we believe that ICM administration is the optimal route of administration as compared to other potential delivery mechanisms due to its potential to provide widespread biodistribution to the brain and spinal cord. Further, when compared with systemic and other intra-thecal administration routes, we can achieve comparable protein expression at lower dosages, and thereby also lower the potential for toxicities. The potential for an impact from NAbs is also reduced.

- **Capsid, transgene, and promoter selection:** For each clinical program, we conduct rigorous studies to select the capsid, transgene, and promoter to use for our product candidate. We identify the optimal AAV gene therapy for each of our indications depending on the target indication, our goal of CNS and/or peripheral nervous system transduction, and the target brain regions and cell types. Typically, we compare multiple capsids in NHPs to identify the capsid best suited for each program.

- **Cross-correction:** Our existing clinical-stage product candidate exploits the cross-correction mechanism by which secreted gene product from transduced cells is taken up by non-transduced cells. We believe this cross-correction mechanism can help overcome the limits of vector biodistribution and CNS transduction inefficiency that are characteristic of other genetic medicine approaches, and will ultimately drive clinical benefit.

- **Effective use of biomarkers:** Our development program targets must have measurable, predictive biomarkers to inform early and efficient clinical development decisions. These include biomarkers to confirm achievement of target levels of transduction and gene expression, one or more downstream pharmacodynamic biomarkers to demonstrate positive functional effects on pathways involved in disease etiology, and disease activity and progression biomarkers to demonstrate effects on disease course.

We have a strategic research collaboration with Gemma, which provides us with access to differentiated discovery technology and expertise and informs the basis of our product candidate selections and subsequent preclinical development through to IND status. Our collaboration with Gemma, and previously with GTP, allows us to choose programs that have been, or will be, validated through extensive testing in preclinical disease models. These activities include developing payload constructs, evaluating efficacy in cells and in relevant animal models of disease, selecting the optimum capsid and route of administration for the targeted indication, and evaluating transduction efficiency, biodistribution, safety and tolerability of lead candidates in NHPs. We believe that the gene therapy preclinical expertise provided previously by GTP, and now by Gemma, improves the probability of technical and regulatory success of our clinical programs for PBFT02 indications, for our Huntington's disease preclinical program, and for future pipeline programs.

**Our Lead Program – PBFT02 for the treatment of FTD-*GRN***

FTD is one of the more common causes of early-onset dementia, occurring in patients with a median age of 55 years. FTD presents as a rapidly progressive clinical syndrome and causes impairment in behavior, language, and executive function. Changes in personal and social conduct occur in early stages of the disease, including loss of inhibition, apathy,

social withdrawal, hyperorality and ritualistic compulsive behaviors. These symptoms are severely disabling and may lead to misdiagnosis as a psychological or emotionally based problem, or, in the elderly, be mistaken for withdrawal or eccentricity. FTD progresses to immobility and loss of speech and expression. Survival averages eight years after onset of symptoms.

In approximately 5% to 10% of individuals with FTD, the disease is caused by mutations in the *GRN* gene, causing a deficiency of progranulin. PGRN is a complex and highly conserved protein that binds to multiple cell membrane receptors to generate diverse intracellular effects, including anti-inflammatory effects, growth factor and regenerative activity, and importantly, improvement in lysosomal activity. In FTD-*GRN*, PGRN deficiency leads to lysosomal and microglial dysfunction, TDP-43 pathology, and ultimately neurodegeneration.

There are no disease modifying therapies approved for the treatment of FTD. Anti-depressants have been shown to manage some behavioral symptoms. Based on the available literature, we estimate the prevalence of FTD-*GRN* in the United States and Europe is approximately 18,000.

We are developing PBFT02 to treat patients affected with FTD-*GRN*, via a single ICM administration. PBFT02 is a gene replacement therapy that utilizes an AAV1 viral vector to deliver a modified DNA encoding the *GRN* gene to a patient's cells. The goal of this vector construct and delivery approach is to provide higher levels of PGRN to the CNS to overcome the progranulin deficiency in *GRN* mutation carriers, who have reduced CNS PGRN, resulting in CSF levels ranging from 30% to 50% of those observed in normal, mutation non-carriers.

We selected the AAV1 capsid and ICM administration route due to the widespread and robust expression of the human PGRN transgene observed throughout the brain and spinal cord in NHP studies. ICM AAV1 administration in NHPs resulted in superior levels of human PGRN in CSF compared with other AAV vectors, exceeding PGRN levels observed in NHPs that received AAV5 or AAVhu68 serotypes by greater than five fold.

***Indication Selection***

The development of PBFT02 in FTD-*GRN* is facilitated by the following:

- **Cross-correction:** Following treatment with PBFT02, overexpressing PGRN in a subset of cells in the CNS could provide a source of secreted protein that could be taken up by surrounding cells, resulting in the potential for cross-correction and broad restoration of neuronal lysosomal function across the entire brain.

- **Biomarkers:** There are known biomarkers in FTD-*GRN* that are measurable and available to assist in drug development.

    - *Pharmacodynamic biomarker.* PGRN is a secreted protein that can be measured in CSF and plasma, and it has been shown to be reduced in the CSF of human *GRN* mutation carriers.

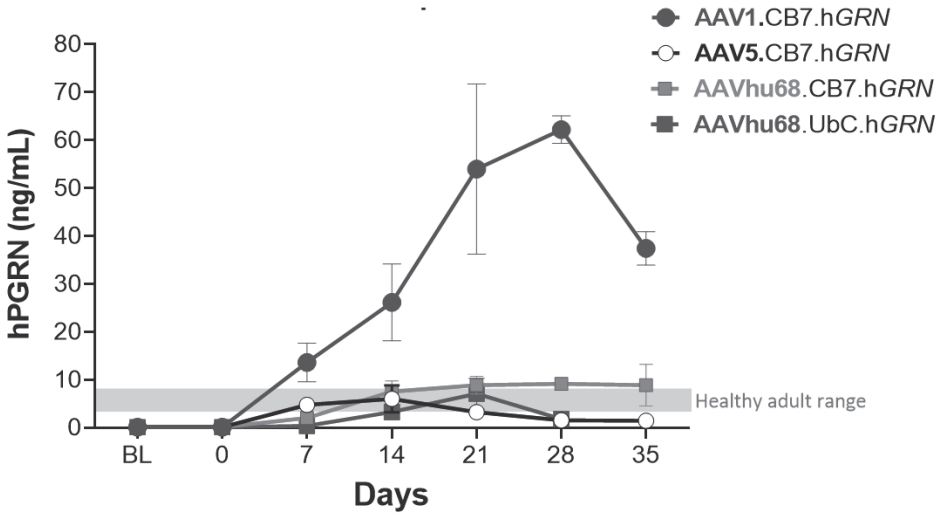
    - *Disease progression biomarkers.* We expect to be able to use recent progress in the identification of clinical disease progression biomarkers for FTD, including plasma and CSF biomarkers, and neuroimaging, to facilitate clinical development by enabling early detection of treatment effects on disease pathophysiology.

- **Preclinical Validation:** In our preclinical studies in *Grn* knockout mice, or $Grn^{-/-}$ mice, intracerebroventricular, or ICV, administration of PBFT02 resulted in increased levels of PGRN in the CNS and CSF, with reduced lysosomal storage pathology and neuroinflammation. ICM administration in NHPs, which do not have the disease phenotype, resulted in robust increases in PGRN levels in CNS and CSF.

*Preclinical Studies*

PBFT02 was selected as our development candidate following preclinical proof of concept studies in adult NHPs, which evaluated the expression of human PGRN protein in the CSF after ICM administration of four different vector constructs. The AAV1.hPGRN vector construct produced elevated levels of PGRN that were greater than five times higher than the AAVhu68.hPGRN and AAV5.hPGRN vectors tested, as shown below.

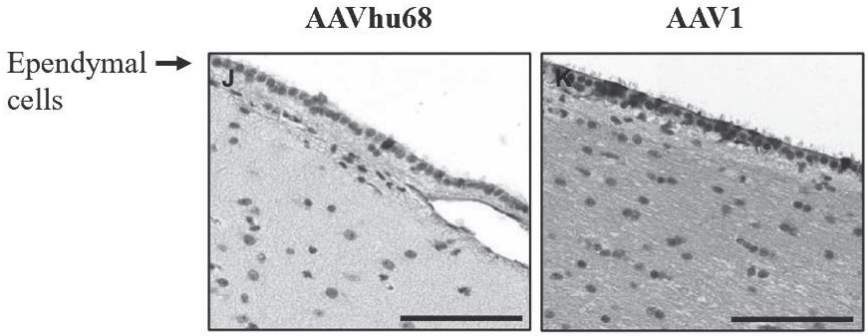
**Comparison of Vector Serotypes: Production of Human PGRN-protein in CSF of NHPs Following ICM-Administration of Different AAVs with Human *GRN* Gene Payload**




*Two adult rhesus macaques per treatment received ICM AAV.hPGRN High dose, 3.0e13 GC / 3.3e11 GC/g brain) on study day 0. The decline in hPGRN after peak levels in NHPs correlated with the appearance of antibodies against the human transgene product. Shading: Healthy adult sample range of PGRN levels in CSF (n = 61) (Passage Bio data).*

In a separate NHP study, rhesus macaques were necropsied 28 days after administration of AAV1 and AAVhu68 vectors expressing a green fluorescent protein, or GFP, reporter gene, to examine differential transduction. Ependymal cell transduction was evaluated by immunohistochemistry in multiple brain regions. As shown in the figure below, transduction of the ependymal cells (as shown by density of darkened ependymal cells) was substantially higher in the animal treated with AAV1 (48%, n=1) as compared to the animals treated with AAVhu68 (1-2%, n=2). In all other CNS cell types, AAV1 and AAVhu68 demonstrated similar transduction efficiency.

**Ependymal Cell Transduction in NHPs Following ICM Delivery of AAV1 or AAVhu68 Vectors Expressing GFP**

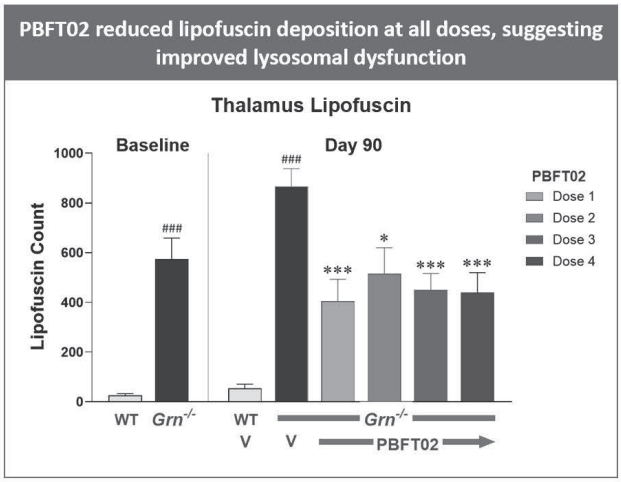


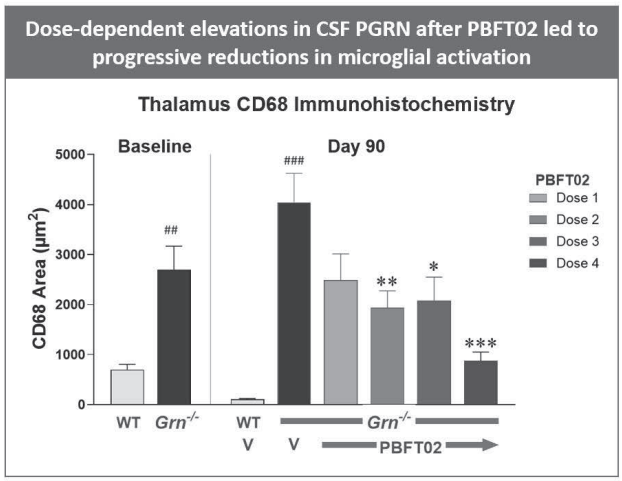

*Representative sections showing GFP immunohistochemistry in ependymal cell layers, from rhesus macaques following ICM administration of AAVhu68.GFP or AAV1.GFP. Scale bars = 5 mm*

Based on the results from the NHP vector comparison studies, we selected AAV1 as the capsid for our PBFT02 product.

The efficacy of the AAV1 vector was assayed in a dose-ranging study in PGRN-deficient *Grn*$^{-/-}$ mice. PBFT02 was administered via ICV delivery at one of four ascending doses or vehicle to adult mice at an age when lipofuscin deposition (a marker of lysosomal dysfunction), lysosomal enzyme abnormalities, and neuroinflammation were present in brain regions involved in FTD-*GRN* pathophysiology. In this study, human PGRN expression in the CSF increased in a dose-related manner following PBFT02 administration. Transgene expression led to improvements in histopathologic and enzymatic changes in key brain regions in the mice, including the cerebral cortex, hippocampus, and thalamus. The improvements included a reduction in the accumulation of lipofuscin and reduced neuroinflammation (as shown in the thalamus in the figure below), and elevated lysosomal hexosaminidase activity.

**PBFT02 Improved Lysosomal Dysfunction and Inflammation in a Mouse Model of Granulin Deficiency**



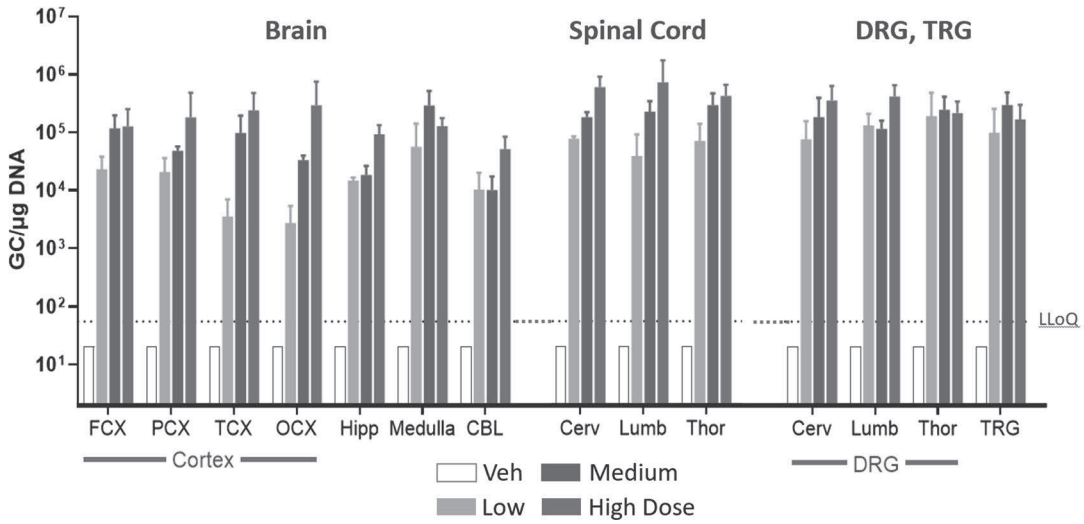




*Markers of lysosomal dysfunction (lipofuscin autofluorescence) and inflammation (CD68 immunohistochemistry) in the thalamus of Grn$^{-/-}$ mice 90 days after ICV PBFT02 administration. Staining in brain sections of PBFT02-treated Grn$^{-/-}$ mice was compared with vehicle-treated WT and Grn$^{-/-}$ mice. Both markers were elevated in Grn$^{-/-}$ mice at the time of treatment (baseline). Data are mean +/- standard error of the mean, or SEM. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001, one-way ANOVA followed by Tukey's multiple comparison test. Abbreviations: -/-, gene knockout; ANOVA, analysis of variance; CSF, cerebrospinal fluid; ICV, intra-cerebroventricular; SEM, standard error of the mean; V, vehicle; WT, wild type.*

*NHP Toxicology Study*

A 90-day GLP compliant toxicology study was conducted in NHPs to assess the safety, tolerability, biodistribution and excretion profile of PBFT02 following ICM administration at three dose levels. No blood or CSF abnormalities related to PBFT02 administration were observed except for asymptomatic, mild, and transient increases in CSF leukocytes in the majority of animals. PBFT02 was shown to be well-tolerated at all doses evaluated and no adverse effects were detected on body weight or clinical, neurological, or behavioral signs. Vector distributed to the CSF and high levels of gene transfer were detected in the brain, spinal cord and dorsal root ganglia, or DRG, at day 90. The quantity of vector genomes detected in CNS tissues was generally dose-related, as shown in the figure below.

**Vector Biodistribution 90 Days After ICM Administration of PBFT02 to NHPs**

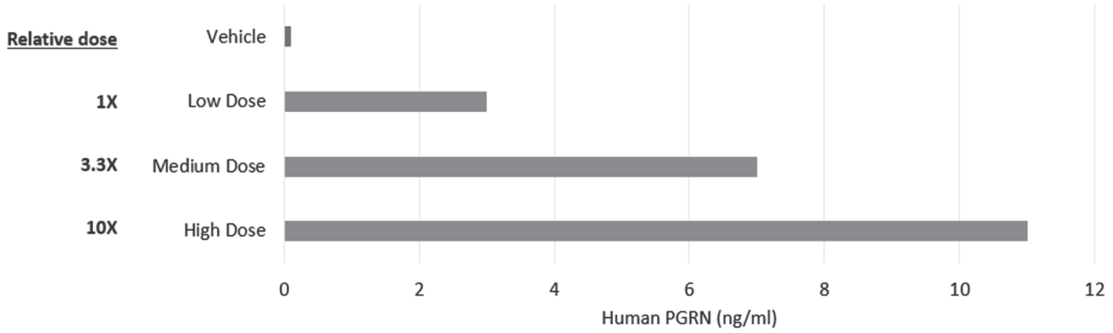



*Tissues were collected at necropsy from adult NHPs 90 days after a single ICM administration of PBFT02 at doses indicated (n=3/group) and from vehicle- (ITFFB-) treated NHPs (n=2) as a control. Each bar represents mean PBFT02 vector genomes detected per µg of DNA. Error bars represent the SEM. Dashed line represents limit of detection of assay. Abbreviations: Cerv, cervical; DRG, dorsal root ganglion; FCX, frontal cortex; Hipp, hippocampus; Lumb, lumbar; PCX, parietal cortex; OCX, occipital cortex; TCX, temporal cortex; Thor, thoracic; TRG, trigeminal root ganglion.*

PBFT02 was also shown to reach significant concentrations in the peripheral blood, liver and spleen. PBFT02 vector DNA was detectable in urine and feces five days post-administration and was undetectable within 60 days.

Human PGRN was detectable in CSF and serum in all animals by 7 to 14 days after PBFT02 administration, showing dose-related levels of human PGRN that peaked between days 14 to 28. Expression declined from day 14, correlating with the appearance of antibodies against the human transgene product which are not expected to develop in haploinsufficient patients with FTD-*GRN*.

**Dose-Related Increases in CSF Progranulin in NHPs Following ICM PBFT02 Administration**




*Adult rhesus macaques received ICM PBFT02 (n = 3/dose) or vehicle (n =2) on trial day 0. CSF sampled 14 days post-dose.*

Mild to minimal grade transient degeneration of DRG, trigeminal root ganglia, or TRG, and associated sensory nerve axonopathy, were observed in NHPs after all PBFT02 dose groups. These histopathologic observations were not linked with any clinical or neurological abnormalities in any animals up to 90 days post-dose. One PBFT02-treated animal exhibited a peripheral nerve conduction impairment in the median nerve, evident from bilateral reductions in sensory nerve action potential, or SNAP, amplitudes on day 28 and day 90, that appeared to be treatment related, as severe axon loss and endoneurial fibrosis were detected at necropsy. PBFT02-induced SNAP changes and sensory neuron degeneration were not associated with any clinical or neurological abnormalities in any animals up to 90 days post-dose.

***Clinical Development***

Our clinical development plan is to treat FTD-*GRN* and FTD-*C9orf72* patients with a single dose of PBFT02 via ICM administration.

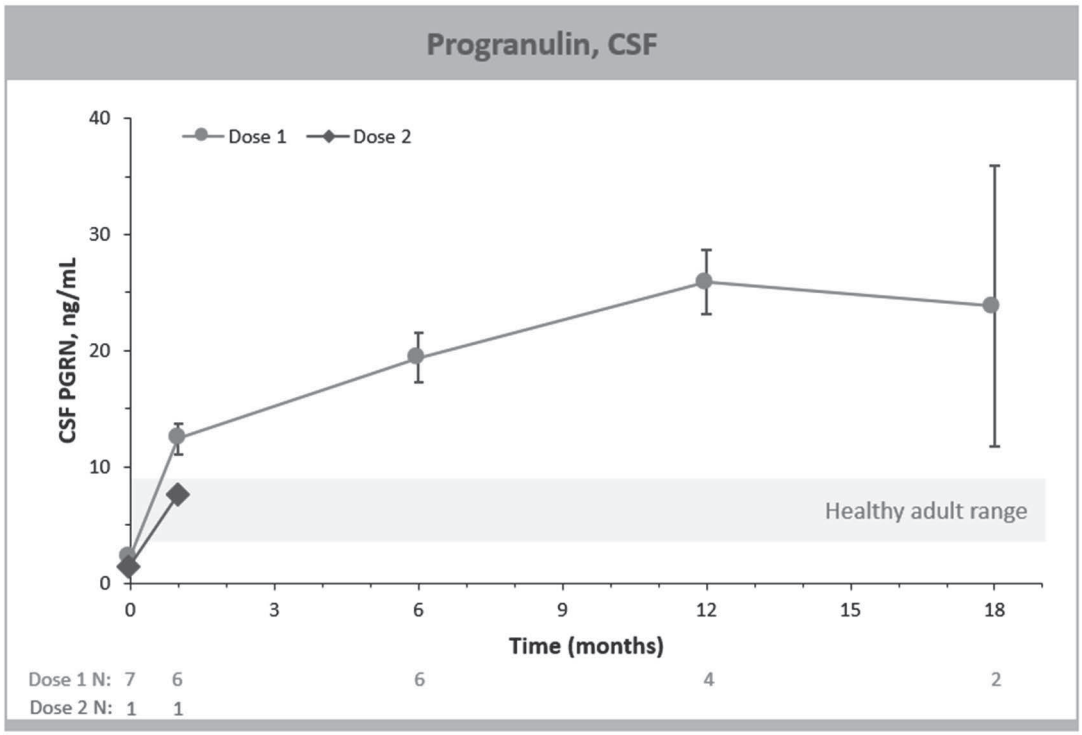
We initiated our upliFT-D trial, an international, multi-center, open-label, single-arm Phase 1/2 clinical trial of PBFT02 in patients with a diagnosis of symptomatic FTD-*GRN*. The FTD-*GRN* portion of the trial is a three-cohort dose-escalation trial, with three to ten subjects per cohort. Dose 1 (3.3e10 genome copies/gm brain weight, or 4.50e13 total genome copies) was administered to five patients in Cohort 1 and the first two patients in Cohort 2. With the third patient in Cohort 2, we introduced Dose 2, which is 50% lower than Dose 1 and exceeds the minimum effective dose determined in the *Grn*$^{-/-}$ mouse model. Dose 2 was administered to the remaining patients in Cohort 2, is expected to be administered to all patients in Cohort 3, and to all patients in Cohort 4 (FTD-*C9orf72*). Patients in Cohorts 1 and 2 had a global CDR score of 1 or 2. All patients in Cohorts 3, 4 and 5 will have a global CDR score of 0.5 or 1. The primary endpoint of the trial is to assess safety and tolerability over 60 months. Additional endpoints are to assess change from baseline to 24 months on biomarkers, including CSF and plasma PGRN levels, biomarkers of lysosomal function, neurodegeneration and disease progression, changes in brain volume by MRI, and change in clinical outcomes as measured by the CDR plus NACC FTLD, and other neurocognitive assessments. Interim analyses are planned for certain biomarkers starting at one month post dosing and for clinical outcomes beginning at one year post dosing. Upon completion of a cohort, the Independent Data Monitoring Committee, or IDMC, will review available biomarker and safety data from each subject in the cohort. All subjects will be evaluated over two years for safety and efficacy, followed by an additional 36 months of long-term follow-up.

***Clinical Development Results***

*Biomarkers*

In June 2025, we reported interim biomarker data from eight patients in our upliFT-D trial. Dose 1 of PBFT02 resulted in robust and durable increases in CSF PGRN levels, with concentrations increasing from below 3.0 ng/mL at baseline to a mean of 12.4 ng/mL at one month (n=6), 19.4 ng/mL at six months (n=6), 25.9 ng/mL at 12 months (n=4), and 23.8 ng/mL at 18 months (n=2). These levels of CSF PGRN are higher than the range found in healthy adult controls of 3.3 to 8.2 ng/mL (mean=4.8 ng/mL; n=61). CSF PGRN levels for the first patient treated with Dose 2 of PBFT02 (1.6e10 genome copies/g estimated brain weight, or 2.2e13 total genome copies) increased substantially from 1.5 ng/mL at baseline to 7.6 ng/mL at one month, approaching the upper limit of the range found in healthy adult controls. In contrast, following PBFT02 administration, plasma PGRN levels were unaltered, remaining similar to baseline concentrations and below mean levels found in healthy adult controls (data not shown).

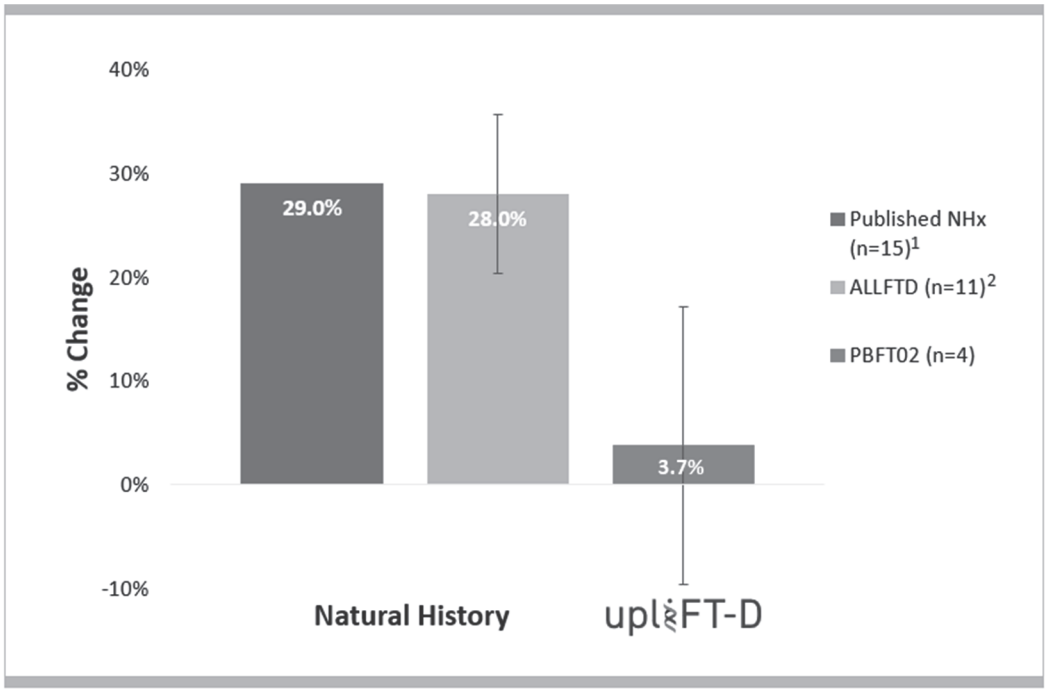
**CSF Progranulin Levels Following Administration of PBFT02**




*Shading: Healthy adult sample range for CSF PGRN (range: 3.28 – 8.15 ng/mL, mean: 4.76 ng/mL, n = 61) (Passage Bio data)*
*Dose 1: 4.5e13 GC; Dose 2: 2.2e13 GC*
***CSF**, cerebrospinal fluid; **M**, month*

Dose 1 of PBFT02 resulted in an average 4% increase in plasma neurofilament light chain, or NfL, levels, a biomarker associated with disease progression, compared to baseline at 12 months post-treatment (n=4). This change in plasma NfL after PBFT02 administration contrasts with an expected increase in plasma NfL levels of approximately 28% and 29% per year among untreated symptomatic FTD-*GRN* patients, based on analysis of the ALLFTD natural history data and published natural history data (Saracino 2021), respectively.

**Plasma NfL Annual Rate of Change**




*[1]Natural history: 15 symptomatic FTD-GRN patients; average time since diagnosis 2.9 years (Saracino et al, 2021).*
*[2]Passage Bio analysis of ALLFTD natural history sample comprised of individuals with a pathogenic GRN mutation and a CDR+NACC FTLD global score between 0.5 and 2, inclusive. In upliFT-D FTD-GRN cohort, average time since diagnosis in PBFT02 patients 2.3 years (n=4). NfL, neurofilament light chain; NHx, natural history.*

*Safety and Tolerability*

Seven patients experienced a collective total of 26 TEAEs considered related to PBFT02. Two of those patients experienced a total of three serious TAEs considered related to PBFT02, including venous sinus thrombosis experienced by two patients and hepatoxicity experienced by one patient. These serious TEAE all occurred at Dose 1, were asymptomatic, and responded to treatment. One patient experienced one serious TEAE, considered unrelated to PBFT02, of pulmonary embolism in the setting of a concurrent systemic infection six weeks after receiving PBFT02. There has been no evidence of thrombotic angiopathy, dorsal root ganglion toxicity as measured by nerve conduction studies, and no complications during ICM administration were observed across any of the treated patients.

***Clinical Development Plan Guidance***

We expect to report updated interim safety and biomarker data in the first half of 2026.

As our clinical data matures, we are planning for continued interactions with regulatory authorities to align on design of the registrational trial and appropriate pathway to submission of a Biologics License Application, or BLA, and regulatory approval for commercialization in the United States and internationally. We expect to seek regulatory feedback on registrational trial design in FTD-*GRN* in the first half of 2026.

**Regulatory Designations and Clinical Trial Approvals for PBFT02**

We have an active IND from the FDA and approved CTAs in multiple countries for PBFT02, which allows us to proceed with our upliFT-D trial, an international, multi-center, open-label, single-arm Phase 1/2 clinical trial of PBFT02 in patients with a diagnosis of symptomatic FTD-*GRN* and FTD-*C9orf72*.

The FDA has granted Orphan Drug Designation to PBFT02 for FTD, which would include the treatment of FTD genetic subtypes like FTD-*GRN* and FTD-*C9orf72*, and Fast Track Designation to PBFT02 for the treatment of FTD-*GRN.* Similarly, the European Commission granted Orphan designation for PBFT02 for FTD, which includes FTD-*GRN* and FTD-*C9orf72*.

**Manufacturing**

Gene therapy manufacturing is a critical factor in the successful development and commercialization of novel genetic medicines. We have a well-established relationship with Catalent for process development, manufacturing, supply chain, and analytical testing. Additionally, we plan to expand our outsourced analytical testing capabilities to support future program development needs.

For our current clinical drug product, we utilize a production platform approach with HEK293 mammalian cells as the substrate, triple plasmid transient transfection and single-use fixed-bed iCELLis® bioreactor system for the manufacture of our AAV product candidates. We have completed internal process development and the scale-up of a high-productivity, GMP-ready suspension-based manufacturing process for PBFT02 at 200-liter scale. This process is substantially more efficient than the current adherent-based process, with improved yield and the potential of a lower cost of goods. In September 2025, we completed a Type D CMC meeting with the FDA and reached alignment on the analytical plan to support comparability between product manufactured using our high-productivity, suspension-based PBFT02 process and the product used in our upliFT-D clinical trial. In addition, we have developed a potency assay for the release of PBFT02 for late-stage clinical studies and commercialization, and received initial positive feedback from the FDA on the suitability of the potency assay and our plans to implement the assay in our comparability protocol and lot release ahead of late-stage clinical development. These two achievements position the PBFT02 program for late-stage development.

We have a collaboration agreement with Catalent that governs our relationship with Catalent for the supply of current Good Manufacturing Practices, or cGMP, capacity. Access to cGMP manufacturing capacity gives us the ability to meet production requirements for our current and future clinical trials. We also have an amended and restated development services and clinical supply agreement, and together with the amended and restated collaboration agreement, the Amended Catalent Agreements, with Catalent to support clinical scale manufacturing for our gene therapy product candidates. The Amended Catalent Agreements establish a limited exclusive relationship between us and Catalent for the manufacture of bulk drug substance and drug product for PBFT02 and PBGM01 programs. The limited exclusive relationship under the Amended Catalent Agreements converts to a non-exclusive relationship (i) in the event Catalent fails to meet certain performance standards and (ii) following certain conditional events related to the divestiture by us of either PBFT02 or PBGM01, in which case, if such events occur, we would pay Catalent certain fees. In the event of certain transactions, we may terminate the Amended Catalent Agreements for convenience with respect to such products, in which case, we would pay Catalent a certain termination fee.

The outlicense and completed transition of our program in GM1 gangliosidosis, or GM1, to Gemma under the Outlicense Transaction Agreements, is deemed by Catalent to be a divestiture under the Amended Catalent Agreements. As such, we are required to make payment of $0.9 million to Catalent.

**Other Active Research Programs**

We have an active preclinical research program to develop a genetic medicine to treat Huntington's disease through our Gemma Collaboration Agreement (which was previously conducted by Penn under the Penn Agreement) for which we are exploring multiple potential treatment targets for HD. HD is an adult-onset, progressive neurodegenerative disease characterized by motor, cognitive, and behavioral deterioration, ultimately leading to death within approximately 15 to 20 years after symptom onset. There are currently no disease-modifying therapies approved for the treatment of HD and we estimate the prevalence of HD in the United States and Europe is approximately 70,000, based on available literature.

HD is an autosomal dominant disorder caused by a mutation in the huntingtin gene, or *HTT*, in which a CAG trinucleotide repeat tract in the DNA is expanded. This leads to the expression of mutant huntingtin protein. *HTT* CAG

repeat tracts are unstable and can continue to elongate over time, termed somatic instability. In neurons, CAG expansion occurs at different rates in different cells, and CAG expansion to above a certain threshold leads to neuronal dysfunction and death. DNA repair proteins such as MSH3 play a key role in driving somatic instability in HD, by erroneously incorporating extra CAG repeats into *HTT* DNA in certain circumstances. Published literature has shown that reducing somatic instability by decreasing MSH3 expression reduced disease pathology in HD mice. Further, published human genetic studies have shown that certain genetic MSH3 variants which reduce somatic instability are associated with delayed disease onset and slowed progression in HD patients.

Our approach is to reduce somatic instability and thereby slow neurodegeneration in HD by suppressing MSH3 expression in the brain, via AAV-mediated delivery of a miRNA gene. We expect to declare a clinical candidate for this program in the second half of 2026.

Beyond this program, as a result of the Gemma Collaboration Agreement, we also have the option to license programs for four additional CNS indications.

**Competition**

The biotechnology and pharmaceutical industries, including the genetic medicines field, are characterized by rapidly changing technologies, competition, and a strong emphasis on intellectual property. We are aware of several companies focused on developing gene therapies in various indications as well as several companies addressing methods for modifying genes and regulating gene expression. We may also face competition from large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions with genetic medicine and other therapeutic approaches.

For the treatment of FTD, there are no approved disease-modifying therapies. We consider our most direct competitor with respect to PBFT02 for the treatment of FTD-*GRN* to be AviadoBio Ltd, which began enrolling their Phase 1/2 gene therapy trial in patients with FTD-*GRN* in 2023. AviadoBio Ltd entered into an exclusive option and licensing agreement with Astellas Pharma Inc. in October 2024. Additional companies, including Kyowa Kirin Co., Ltd. and QurAlis Corporation, are conducting preclinical research using genetic medicine approaches to treat patients with FTD-*GRN*. Denali Therapeutics Inc., in partnership with Takeda Pharmaceutical Company Limited, is conducting a Phase 1/2 clinical trial for their recombinant progranulin protein. Vesper Bio ApS completed a Phase 1/2 trial for a small molecule sortilin antagonist in asymptomatic patients with a *GRN* mutation. We are also aware of other therapeutic approaches in preclinical development that may target FTD-*GRN* patients, including the small molecule progranulin enhancer program by Arkuda Therapeutics, who entered into an exclusive option and asset purchase agreement with Johnson & Johnson Innovative Medicine in the first quarter 2024. With respect to PBFT02 for the treatment of FTD-*C9orf72*, Transposon Therapeutics, Inc., conducted a Phase 2 trial with a small molecule autophagy modulator for FTD-*C9orf72*. There are other approaches in preclinical development for the treatment of FTD-*C9orf72*. In addition to the *GRN* and *C9orf72* targeted therapies, there are numerous programs targeting the TDP-43 pathway and other targets for the treatment of FTD.

For the treatment of Huntington's disease, there are no approved disease-modifying therapies. There are multiple clinical-stage trials evaluating potential disease modifying therapies with mechanisms of action including targeting *HTT* lowering. We consider our most direct competitors to be those directly targeting somatic instability via modulating DNA repair. There are four companies with preclinical gene therapy programs targeting the DNA repair protein MSH3 including Evox Therapeutics Ltd, Latus Bio, Inc., uniQure N.V., and Voyager Therapeutics, Inc. Multiple other companies are exploring different approaches to target MSH3 in preclinical research. Approaches targeting other DNA repair proteins, such as upregulation of FAN1, are also in preclinical development. Numerous companies are exploring other targets for the treatment of HD.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical, and other resources than we do, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. 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 product candidates that we may develop. Competitors also may obtain FDA or other regulatory approval for their products 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, if ever. Additionally, new or advanced technologies developed by our competitors may render our current or future product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

**License Agreements**

*University of Pennsylvania*

As a result of the Outlicense Transaction Agreements, we restructured our research, collaboration and licensing agreement with Penn, as amended, previously the Penn Agreement and now referred to as the Penn License Agreement. Pursuant to the Penn License Agreement, as of July 31, 2024, we (i) terminated the funding of discovery research programs; (ii) terminated the research and exploratory research programs; (iii) terminated the remaining eight options we had for future CNS indications; (iv) terminated the transaction fee payable to Penn in the event of certain corporate transactions; and (v) retained our current exclusive and non-exclusive licenses to our programs in FTD, GM1, Krabbe disease, or Krabbe, and metachromatic leukodystrophy, or MLD, and certain platform technologies resulting from the discovery programs that we funded.

For our licensed programs in FTD, GM1, Krabbe and MLD, the Penn License Agreement requires that we make payments of up to $16.5 million per product candidate. Each payment will be due upon the achievement of specific development milestone events by such licensed product for a first indication, reduced development milestone payments for the second and third indications and no development milestone payments for subsequent indications. In addition, on a product-by-product basis, we are obligated to make up to $55.0 million in sales milestone payments on each licensed product based on annual worldwide net sales of the licensed product in excess of defined thresholds. Pursuant to the Amended Gemma Sublicenses, Gemma is responsible for the payments to Penn related to the Outlicensed Programs.

Upon successful commercialization of a product using the licensed technology, we are obligated to pay to Penn, on a licensed product-by-licensed product and country-by-country basis, tiered royalties (subject to customary reductions) in the mid-single digits percentage on annual worldwide net sales of such licensed product. In addition, other than the Amended Gemma Sublicenses, we are obligated to pay to Penn a percentage of sublicensing income, ranging from the mid-single digits to low double digits, for sublicenses under the Penn License Agreement. The agreement will expire on a licensed product-by-licensed product and country-by-country basis upon the later of (i) the expiration of the last valid claim of the licensed patent rights that covers the exploitation of such licensed product in such country, and (ii) the expiration of the royalty period. Pursuant to the Amended Gemma Sublicenses, Gemma is responsible for the payments to Penn related to the Outlicensed Programs.

*Gemma - Research, Collaboration and License Agreement*

In connection with the transfer of the Outlicensed Programs, on July 31, 2024, we entered into the Gemma Collaboration Agreement. Pursuant to the Gemma Collaboration Agreement, (i) Gemma will conduct certain preclinical and IND-enabling work for our active research program in Huntington’s disease and a currently paused research program in TLE, which were previously being conducted by Penn under the Penn Agreement and (ii) Gemma will grant us options to conduct mutually agreed research programs in four new CNS indications.

The Gemma Collaboration Agreement requires that we make payments of up to (i) $16.5 million per product candidate in the aggregate for Huntington’s disease and any future CNS indications available to us under our four options and (ii) $39.0 million per product candidate in the aggregate arising from the research program for TLE. Each payment will be due upon the achievement of specific development milestone events by such licensed product for a first indication, reduced development milestone payments for the second and third indications and no development milestone payments for subsequent indications. In addition, on a product-by-product basis, we are obligated to make up to $55.0 million in sales milestone payments on each licensed product based on annual worldwide net sales of the licensed product in excess of defined thresholds.

Upon successful commercialization of a product using the licensed technology, we are obligated to pay to Gemma, on a licensed product-by-licensed product and country-by-country basis, tiered royalties (subject to customary reductions) in the mid-single digits percentage on annual worldwide net sales of such licensed product. In addition, we are obligated to pay to Gemma a percentage of sublicensing income, ranging from the mid-single digits to low double digits, for sublicenses under the Gemma Collaboration Agreement. The agreement will expire on a licensed product-by-licensed product and country-by-country basis upon the later of (i) the expiration of the last valid claim of the licensed patent rights that covers the exploitation of such licensed product in such country, and (ii) the expiration of the royalty period.

If we were to exercise any of the four options, we would owe Gemma a non-refundable aggregate fee of $1.0 million per product indication, with $0.5 million due upfront and another $0.5 million fee owed upon a further developmental milestone.

*Gemma - Sublicense Agreements and Transition Services Agreement*

In connection with the transfer of the Outlicensed Programs to Gemma, in July 2024, we entered into the Gemma Sublicenses. On May 7, 2025, we agreed to amend each of the Gemma Sublicenses to revise certain financial terms related to the Outlicensed Programs, or the Amended Gemma Sublicenses. Pursuant to the Amended Gemma Sublicenses, we are entitled to receive (i) an aggregate total of $15.0 million in initial payments for licenses and clinical product supply, of which $7.5 million was previously received, $2.5 million of which was due in May 2025, and $5.0 million of which is due in March 2026; (ii) an additional $5.0 million contingent on Gemma completing certain business milestones; (iii) up to an additional $114.0 million in development and commercial milestone payments; and (iv) single digit royalties as a percentage of annual worldwide net sales in exchange for sublicenses to relevant intellectual property, transfer of regulatory dossiers and transfer of clinical trial materials and product supply related to the Outlicensed Programs. In addition, Gemma is responsible for all payments to Penn related to the Outlicensed Programs under the Penn License Agreement.

In addition, we entered into the Transition Services Agreement, as amended by the First Amendment to the Transition Services Agreement, dated January 31, 2025, pursuant to which, we provided transitional services at cost to Gemma through May 31, 2025, and are entitled to reimbursement for transitional services performed retroactively from March 1, 2024, related to the transfer of the Outlicensed Programs. As of December 31, 2025, we have collected $7.5 million in initial payments and $4.8 million in transition services payments under these agreements. In addition, we have applied $1.5 million in amounts owed to Gemma for the Huntington's disease program against amounts due to us for transition services.

**Intellectual Property**

Our commercial success depends in part on our ability to obtain and maintain proprietary and/or intellectual property protection in the United States and other countries for our current product candidate and future products, as well as our core technologies, including our manufacturing know-how. We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business by seeking, maintaining, and defending our intellectual property, whether developed internally or licensed from third parties. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of gene therapy. Additionally, we intend to rely on regulatory protection afforded through rare drug designations, data exclusivity and market exclusivity as well as patent term extensions, or PTE, and patent term adjustments, or PTA, where available.

Currently, our patent protection consists of patents and patent applications that (i) we have in-licensed from Penn under the Penn Agreement for product candidates in our licensed indications and (ii) we solely own based on the internally developed processes for manufacturing or analyzing our product candidate as well as use of the product candidate in relation to certain neurodegenerative diseases, and (iii) we co-own, with Penn, related to product candidates for the treatment of Huntington's disease.

The in-licensed patent applications are directed to new AAV capsids and certain defined variants, to recombinant AAV viruses, or rAAVs, capable of delivering certain genes into human cells to treat monogenic diseases of the CNS, as well as to methods of treating those monogenic diseases with rAAV.

Our in-licensed patent portfolio currently includes two patent families with claims directed to rAAV for use in treating FTD. The first patent family includes patents issued in the U.S., Japan, and Saudia Arabia, and applications pending in 13 jurisdictions, including the U.S., Argentina, Brazil, Canada, China, Europe, Israel, Japan, and Korea. The patent applications and any patents that may issue from applications in this family are expected to expire on February 21, 2040, absent any term adjustments or extensions. The second patent family includes applications in 16 jurisdictions, including the U.S., Argentina, Taiwan, Brazil, Canada, China, Europe, Israel, Japan and Korea. Any patents that may issue from applications in this family are expected to expire on August 26, 2041, absent any term adjustments or extensions.

The in-licensed patent portfolio further includes seven patent families with pending or issued claims directed to rAAV and its use in the treatment of GM1, Krabbe, or MLD. The patent families have been sublicensed to Gemma under our sublicense agreements with Gemma in connection with the outlicense of PBGM01 for the treatment of GM1, PBKR03 for the treatment of Krabbe, and PBML04 for the treatment of MLD.

We have options under the Penn Agreement and the Gemma Collaboration Agreement to add additional intellectual property to our existing license, as described in the section “License Agreements”.

Our patent portfolio, which we solely own, includes one patent family with claims directed to the method of purifying rAAV. This patent family includes applications pending in 12 jurisdictions, including the U.S., Brazil, Canada, China, Europe, Israel, Japan, and Korea. Any patents that may issue from applications in this family are expected to expire on October 6, 2043, absent any term adjustments or extensions.

The company-owned patent portfolio further includes a patent family directed to the use of rAAV for the treatment of FTD and other neurodegenerative diseases as well as a patent family directed to an assay for testing the potency of the rAAV. The first patent family includes a patent cooperation treaty, or PCT, application and a Taiwanese application. Any patents that may issue from applications in this family are expected to expire on March 3, 2045, absent any term adjustments or extensions. The second patent family includes a PCT application. Any patents that may issue from applications in this family are expected to expire on June 5, 2045, absent any term adjustments or extensions.

The terms of individual patents may vary based on the countries in which they are obtained. Generally, patents issued from applications filed in the United States are effective for 20 years from the earliest effective non-provisional filing date. This term may be extended with a patent term adjustment to account for delays caused by the U.S. Patent and Trademark Office, or USPTO. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of an FDA regulatory review period. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The duration of patents outside of the United States varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective national filing date.

In addition to patents and patent applications that we license, we rely on trade secrets and know-how to develop and maintain our competitive position. For example, significant aspects of our AAV manufacturing capabilities and gene therapy technology are based upon trade secrets and know-how. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, and obtain and maintain control and/or ownership of certain technologies, in part, through confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how, including by implementing measures intended to maintain the physical security of our premises and the physical and electronic security of our information technology systems.

Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. With respect to our owned or licensed intellectual property, we cannot be sure that patents will issue with respect to any of the pending patent applications to which we own or license rights or with respect to any patent applications that we or our licensors may file in the future, nor can we be sure that any of our licensed patents or any patents that may be issued in the future to us or our licensors will be commercially

useful in protecting our product candidates and methods of manufacturing the same. Moreover, we may be unable to obtain patent protection for certain of our product candidates generally, as well as with respect to certain indications. See the section entitled "Risk Factors—Risks Related to Our Intellectual Property" for a more comprehensive description of risks related to our intellectual property.

**Government Regulation and Product Approval**

The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

***FDA Approval Process***

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Biological products used for the prevention, treatment, or cure of a disease or condition of a human being are subject to regulation under the FDC Act, except the section of the FDC Act which governs the approval of New Drug Applications, or NDAs. Biological products, such as gene therapy products, are approved for marketing under provisions of the Public Health Service Act, or PHSA, via a BLA. However, the application process and requirements for approval of BLAs are very similar to those for NDAs. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as clinical hold, FDA refusal to file NDA/BLAs and/or to approve pending NDAs or BLAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Biological product development for a new product or certain changes to an approved product in the United States typically involves preclinical laboratory and animal tests, the submission to the FDA of an IND which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including Good Laboratory Practices, an international standard meant to ensure the presence of a standard quality system under which laboratory work and non-clinical studies are conducted, recorded and archived. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term preclinical tests, such as tests of reproductive toxicity and carcinogenicity in animals, may continue after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational biologic to subjects, including healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with Good Clinical Practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. subjects and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA regulations or presents an unacceptable risk to the clinical trial subjects. The trial protocol and informed consent information for subjects in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB

may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions if it believes that the subjects are subject to unacceptable risk.

Clinical trials to support BLAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the biologic into subjects, the product is tested to assess safety, dosage tolerance, metabolism, pharmacokinetics, pharmacological actions, side effects associated with drug exposure, and to obtain early evidence of a treatment effect if possible. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug or biologic for a particular indication, determine optimal dose and regimen, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, generally Phase 3 trials are undertaken to obtain additional information about clinical effects and confirm efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug or biologic and to provide adequate information for the labeling of the product. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the safety and efficacy of the drug or biologic. In rare instances, a single Phase 3 trial may be sufficient when either (1) the trial is a large, multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible or (2) the single trial is supported by confirmatory evidence.

In addition, the manufacturer of an investigational drug in a Phase 2 or Phase 3 clinical trial for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access to such investigational drug.

After completion of the required clinical testing, a BLA is prepared and submitted to the FDA. FDA approval of the BLA is required before marketing and distribution of the product may begin in the United States. The BLA must include the results of preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting a BLA is substantial. The submission of most BLAs is additionally subject to a substantial application user fee. Under an approved BLA, the applicant is also subject to an annual program fee. These fees typically increase annually. A BLA for a drug that has been designated as an orphan drug is not subject to an application fee, unless the BLA includes an indication for other than a rare disease or condition. The FDA has 60 days from its receipt of a BLA to determine whether to file the application based on the Agency's determination that it is adequately organized and sufficiently complete to permit substantive review. Once the FDA files the submission, the FDA begins an in-depth review. The FDA has agreed to certain performance goals to complete the review of BLAs. Most applications are classified as Standard Review products that are reviewed within ten months of the date the FDA files the BLA; applications classified as Priority Review are reviewed within six months of the date the FDA accepts the BLA for filing. A BLA can be classified for Priority Review when the FDA determines the biologic product has the potential to treat a serious or life-threatening condition and, if approved, would be a significant improvement in safety or effectiveness compared to available therapies. The review process for both standard and priority reviews may be extended by the FDA for three or more additional months to consider certain late-submitted information, or information intended to clarify information already provided in the BLA submission.

The FDA may also refer applications for novel biologic products, or biologic products that present difficult questions of safety or efficacy, to be reviewed by an advisory committee—typically a panel that includes clinicians, statisticians and other experts—for review, evaluation, and a recommendation as to whether the BLA should be approved. The FDA is not bound by the recommendation of the advisory committee, but generally follows such recommendations. Before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the biologic product is manufactured. The FDA will not approve the product unless compliance with cGMPs is satisfactory and the BLA contains data that provide substantial evidence that the biologic is safe, pure, potent and effective in the claimed indication.

After the FDA evaluates the BLA and completes any clinical and manufacturing site inspections, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in

the BLA submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application for approval. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. An approval letter authorizes commercial marketing and distribution of the biologic with specific prescribing information for specific indications. As a condition of BLA approval, the FDA may require a Risk Evaluation and Mitigation Strategy, or REMS, to help ensure that the benefits of the biologic outweigh the potential risks to patients. A REMS can include medication guides, communication plans for healthcare professionals, and elements to assure a product's safe use, or ETASU. An ETASU can include, but is not limited to, special training or certification for prescribing or dispensing the product, dispensing the product only under certain circumstances, special monitoring, and the use of patient-specific registries. The requirement for a REMS can materially affect the potential market and profitability of the product. Moreover, the FDA may require substantial post-approval testing and surveillance to monitor the product's safety or efficacy.

Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. Changes to some of the conditions established in an approved BLA, including changes in indications, product labeling, manufacturing processes or facilities, require submission and FDA approval of a new BLA or BLA supplement before the change can be implemented. A BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing BLA supplements as it does in reviewing BLAs.

***Additional Standard for Gene Therapy Products***

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving the use of gene therapy. The FDA has issued various guidance documents regarding gene therapies, which outline additional factors that the FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical assessment of gene therapies; the chemistry, manufacturing, and controls, or CMC, 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 delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. For instance, the FDA usually recommends that sponsors observe all surviving subjects who receive treatment using gene therapies that are based on adeno-associated virus vectors in clinical trials for potential gene therapy-related delayed adverse events for a minimum 5-year period. The FDA does not require the long-term tracking to be complete prior to its review of the BLA.

***Orphan Drug Designation***

Under the Orphan Drug Act, the FDA may grant Orphan Drug Designation to biological products intended to treat a rare disease or condition—a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a product available in the United States for such disease or condition will be recovered from sales of the product. Orphan Drug Designation must be requested before submitting a BLA. After the FDA grants Orphan Drug Designation, the identity of the biological product and its potential orphan disease use are disclosed publicly by the FDA. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first BLA applicant to receive FDA licensure for a particular active moiety to treat a particular disease with FDA Orphan Drug Designation is entitled to a seven-year exclusive marketing period in the United States for that product in the approved indication. For large molecule drugs, including gene therapies, sameness is determined based on the principal molecular structural features of a product. As applied to gene therapies, the FDA has recently issued final guidance in which it stated it generally intends to consider certain key features, such as the transgenes expressed by the gene therapy and the vectors used to deliver the transgene, to be principal molecular structural features. With regard to vectors, the FDA generally intends to consider whether two vectors from the same viral class are the same or different on a case-by-case basis. The FDA does not intend to consider minor differences between transgenes and vectors to be different principal molecular structural features. When two gene therapy products express the same transgene and have or use the same vector, determining whether two gene therapies are the same drug may also depend on additional features of the final gene therapy product that can contribute to the therapeutic effect, such as

regulatory elements and the cell type that is transduced (for genetically modified cells). In such cases, the FDA generally intends to determine whether two gene therapy products are different on a case-by-case basis. During the seven-year marketing exclusivity period, the FDA may not approve any other applications to market a biological product containing the same principal molecular structural features for the same indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. A product can be considered clinically superior if it is safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biological product for the same disease or condition, or the same biological product for a different disease or condition. Among the other benefits of Orphan Drug Designation are tax credits for certain research and a waiver of the BLA user fee.

***Fast Track Designation and Priority Review***

The FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Such Fast Track Designation may be granted for products that are intended to treat a serious or life-threatening disease or condition for which there is no effective treatment and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast Track Designation applies to both the product and the specific indication for which it is being studied. Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review.

Priority review may be granted for products that are intended to treat a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an application designated for priority review in an effort to facilitate the review.

***Disclosure of Clinical Trial Information***

Sponsors of clinical trials of FDA-regulated products, including biological products, are required to register and disclose certain clinical trial information on the website www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of a clinical trial are then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of clinical trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of clinical development programs as well as clinical trial design.

***Additional Controls for Biologics***

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend biologics licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases within the United States.

After a BLA is approved, the product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the lot manufacturing history and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products, such as viral vaccines, before allowing the manufacturer to release the lots for distribution. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products. As with drugs, after approval of a BLA, biologics manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

***Biosimilars***

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products shown to be highly similar to or interchangeable with an FDA-licensed reference biological product. Biosimilarity sufficient to reference a prior FDA-approved product requires that there be no differences in route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity must be shown through analytical trials, animal studies, and, in some cases, a clinical trial or trials. A biosimilar product may be deemed interchangeable with a previously approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. The first biosimilar product was approved by the FDA in 2015, and the first interchangeable product was approved in 2021.

A reference biologic is granted 12 years of exclusivity from the time of first licensure, or BLA approval, of the reference product during which no application for a biosimilar may be licensed, and no application for a biosimilar can be submitted for four years from the date of licensure of the reference product. The first biologic product submitted under the biosimilar abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against a finding of interchangeability for other biologics for the same condition of use for the lesser of (i) one year after first commercial marketing of the first interchangeable biosimilar, (ii) 18 months after the first interchangeable biosimilar is approved if no patent litigation ensues, (iii) 18 months after resolution of a lawsuit over the asserted patents of the reference biologic in favor of the first interchangeable biosimilar applicant, or (iv) 42 months after the first interchangeable biosimilar's application has been approved if a patent lawsuit is ongoing within the 42-month period.

***Post-Approval Requirements***

Once a BLA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. Biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic safety summary reports are required following FDA approval of a BLA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, biological product manufacture, packaging, and labeling procedures must continue to conform to cGMPs after approval. Biologic manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects a biologic product's manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with required regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

***Other U.S. Healthcare Laws and Compliance Requirements***

In the United States, biotechnology company activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare & Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services, or HHS (e.g., the Office of Inspector General and the Office for Civil Rights), the U.S. Department of Justice, or DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. The laws biotechnology companies may have to comply with include the anti-fraud and abuse provisions of the Social Security Act, the

federal false claims laws, the privacy and security provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended, as applicable.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering, recommending or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti- Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and/or formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. In addition, the statutory exceptions and regulatory safe harbors are subject to change.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (discussed below).

The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Federal false claims laws, including the federal civil False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the U.S. government. In addition, manufacturers can be held liable under the civil False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of the product for unapproved, and thus generally non-reimbursable, uses and purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes.

HIPAA created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Data privacy and security regulations by both the federal government and the states in which business is conducted may also be applicable. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. HIPAA requires covered entities to limit the use and disclosure of protected health information to specifically authorized situations, and requires covered entities to implement security measures to protect health information that they maintain in electronic form. Among other things, HITECH made HIPAA's security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, certain types of advanced practice nurses, and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Commercial distribution of products requires compliance with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. In addition, several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. Certain local jurisdictions also require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Sales and marketing activities are also potentially subject to federal and state consumer protection and unfair competition laws. Violation of any of the federal and state healthcare laws described above or any other governmental regulations may result in penalties, including without limitation, significant civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, imprisonment, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, refusal to enter into government contracts, oversight monitoring, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings.

***Coverage, Pricing and Reimbursement***

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which regulatory approval is obtained. In the United States and markets in other countries, sales of any products for which regulatory approval is obtained for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication.

Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Expensive pharmaco-economic studies may need to be conducted in order to demonstrate the medical necessity and cost-effectiveness of product candidates, in addition to the costs required to obtain the FDA approvals. Product candidates may not be considered medically necessary or cost-effective. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product and a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare and Medicaid Services, or CMS. CMS decides whether and to what extent our products will be covered and reimbursed under Medicare. Although private third-party payors tend to follow Medicare practices, no uniform or consistent policy of coverage and reimbursement for drug products exists among third-party payors. Adequate third-party reimbursement may not be available to enable the maintenance of price levels sufficient to realize an appropriate return on investment in product development.

Different pricing and reimbursement schemes exist in other countries. In the European Union, or EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates for which regulatory approval is received for commercial sale may suffer if the government and other third-party payors fail to provide coverage and adequate reimbursement. In addition, emphasis on managed care in the United States has increased and is expected to continue to increase the pressure on healthcare pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which regulatory approval is received, less favorable coverage policies and reimbursement rates may be implemented in the future.

***Healthcare Reform***

Healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government rebate programs and additional downward pressure on pharmaceutical product prices. Several healthcare reform proposals culminated in the enactment of the Inflation Reduction Act of 2022, or IRA, which, among other things, eliminated, beginning in 2025, the coverage gap under Medicare Part D by significantly lowering the enrollee maximum out-of-pocket cost and requiring manufacturers to subsidize, through a newly established manufacturer discount program, 10% of Part D enrollees' prescription costs for brand drugs below the out-of-pocket maximum, and 20% once the out-of-pocket maximum has been reached. The IRA also requires HHS to directly negotiate the selling price of a statutorily specified number of drugs and biologics each year that CMS reimburses under Medicare Part B and Part D. The negotiated price may not exceed a statutory ceiling price. Only high-expenditure single-source biologics that have been approved for at least 11 years (seven years for single-source drugs) are eligible to be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. For 2026, the first year in which negotiated prices became effective, CMS selected 10 high-cost Medicare Part D products in 2023, negotiations began in 2024, and the negotiated maximum fair price has been announced. In addition, CMS selected and announced the negotiated maximum fair price for 15 additional Medicare Part D drugs, which will become effective in 2027. For 2028, CMS selected an additional 15 drugs, comprised of drugs covered under Medicare Part D and, for the first time, drugs payable under Medicare Part B. For 2029 and subsequent years, 20 Part B or Part D drugs will be selected.

Currently, a drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded from the IRA's price negotiation requirements, but loses that exclusion if it has designations for more than one rare disease or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. However, as a result of a statutory amendment enacted in July 2025, beginning with the 2028 negotiated price applicability year, a drug may be designated for more than one rare disease or condition and still be excluded from price negotiation, as long as the only approved indications are for such rare diseases or conditions. The IRA also imposes rebates on Medicare Part B and Part D drugs whose prices have increased at a rate greater than the rate of inflation, and in November 2024, CMS finalized regulations for the Medicare Part B and Part D inflation rebates. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, some significant, including civil monetary penalties. These provisions may be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high-expenditure single-source drugs and biologics have been challenged in multiple lawsuits. Thus, while it is unclear how the IRA will be implemented, it will likely have a significant impact on the pharmaceutical industry and the pricing of our products and product candidates. It is unclear to what extent other statutory, regulatory, and administrative initiatives will be enacted and implemented in the future.

**Employees and Human Capital Resources**

As of December 31, 2025, we had 24 full-time employees. Of these employees, 7 held Ph.D., Pharm.D. or M.D. degrees, and 13 were engaged in research, development and technical operations. All of our employees are based in the United States. None of our employees are represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is good. From time to time, we also retain independent contractors to support our organization.

***Our Mission and Our Employees***

At Passage Bio, our mission is to improve the lives of patients with neurodegenerative diseases, while also building strong relationships with the communities we serve. We embrace collaboration, discipline and efficiency, while welcoming fresh ideas and stimulating personal development. We align our core values with our mission statement, which is outlined below:

- Put Patients First
    - We place the health and safety of our patients at the center of every decision we make
    - We value the voice of our patient communities; we listen and we learn
    - We are driven to improve patients' lives; they are relying on us

- Commit to Excellence
    - We apply leading-edge science and technology to develop gene therapies for our patients
    - We strive to be the best in everything we do
    - We embrace diversity and inclusion as essential to the success of our company
    - We have an unrelenting focus on quality

- Make an Impact
    - We act with a sense of urgency; patients are waiting
    - We are nimble and adaptable in driving toward our goals
    - We approach every day with courage and tenacity

- Act with Integrity
    - We communicate openly, honestly and respectfully with each other
    - We make decisions based on what's right
    - We are accountable for our actions
    - We care about our community and strive to be good citizens

- Succeed Together
    - We are all part of the solution and help each other be successful
    - We innovate by challenging the status quo, taking appropriate risk and encouraging diversity of thought
    - We value and foster collaboration, both internally and with our external partners
    - We work hard and find ways to make it fun

***Our Working Environment***

We are committed to creating and maintaining a workplace where all our employees can thrive in an environment that values differences, provides equal opportunities and embraces different backgrounds and perspectives. We treat all individuals with respect and dignity and provide all our employees with fair treatment based on merit. We emphasize working together to develop innovative solutions in support of our mission. We believe our working environment allows us to attract and retain the best employees and develop the best solutions. It is an integral part of our business strategy.

***Our Compensation and Benefits***

We view our employees as one of our most valuable assets in serving our mission. We compete in the highly competitive biotechnology industry, and attracting, retaining and developing a diverse group of talented employees is crucial to our strategy and our ability to compete effectively. We are committed to the development and retention of our workforce to support our research, clinical operations, manufacturing and regulatory efforts. There currently is a shortage of skilled individuals with substantial experience discovering, developing and manufacturing genetic medicines, which is likely to continue. As a result, competition for these individuals is intense and the turnover rate can be high. We face substantial competition among numerous companies and academic institutions for individuals with these skills.

Given the highly competitive nature of our industry and the importance of recruitment and retention to our success, we strive to provide our employees with what we believe is a very competitive and comprehensive total rewards package of compensation, benefits and services. This package includes competitive market pay, healthcare benefits for employees and family members, life insurance benefits, short and long-term disability benefits, generous paid time off benefits, parental leave, bereavement leave, flexible work schedules, a 5% employer match of employee contributions to our sponsored retirement plans, and an annual stipend for employees to spend on professional development. Additionally, we also offer every full-time employee the benefit of equity ownership in our Company through our equity plans.

The compensation and benefits program is governed by our board of director's Compensation Committee. Specifically, the Compensation Committee, with advice from an independent executive compensation consulting firm, determines compensation for the chief executive officer and other executive officers, which includes an evaluation of market rates for all components of compensation.

Our Compensation Committee and an independent executive compensation consulting firm also evaluate and recommend the framework of compensation and benefit plans, as it relates to discretionary non-equity incentive plans and equity incentive plans, for non-executive officers. For non-executive officers, we utilize a third-party resource to evaluate market rates for base compensation.

**Reverse Stock Split**

On May 28, 2025, our stockholders provided authorization for our Board of Directors to effect a reverse stock split to regain compliance with Nasdaq's listing requirements. On July 14, 2025, we effected a 1-for-20 reverse stock split of our common stock, or the Reverse Stock Split. No fractional shares were issued in connection with the Reverse Stock Split. Stockholders who were otherwise entitled to receive fractional shares received the number of shares of Common Stock as rounded up to the nearest whole share. All share and per share amounts in this Annual Report, including the stock options, restricted stock units, and employee stock purchase plan activity, as well as other share information in this Report have been adjusted retroactively to reflect the Reverse Stock Split for all periods presented.

**Legal Proceedings**

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business.

We are the defendant in litigation with a former employee, who filed a lawsuit in the Court of Common Pleas of Philadelphia County asserting claims for breach of contract and violation of the Pennsylvania Wage Payment and Collection Law. The plaintiff, who was terminated from their employment in 2019, contended that we entered into a binding settlement agreement in February 2020 under which he was to receive shares of company stock and additional compensation. Specifically, he contended that before the announcement of our initial public offering in February 2020, he was promised 150,000 shares of stock as part of the settlement, and that those shares were not subject to the reverse stock split that was implemented for all shareholders. We responded that the shares offered in settlement negotiations in 2020 were to be subject to the reverse split, and that had the settlement been finalized, the plaintiff would have been entitled to 33,836 shares (1,692 shares adjusted for the Reverse Stock Split effected in 2025). A trial in this case was held in October 2024. The jury found that an agreement was reached, but it agreed with us that any shares to be awarded to the plaintiff were subject to the reverse split. The jury awarded damages in an amount that was roughly equal to what we contended had been offered to the plaintiff before the initial public offering. Both sides then challenged the verdict, and on December 12, 2024, the judge who presided over the trial delivered a judgment in our favor, finding that no binding agreement was reached and that the plaintiff was not entitled to recover any damages. On December 23, 2024, the plaintiff filed an appeal with the Superior Court of Pennsylvania. On September 25, 2025, the appellate court affirmed the entry of judgment in favor of the Company and on October 7, 2025, the plaintiff filed an Application for Reargument to the Superior Court of Pennsylvania. In December 2025, the Superior Court of Pennsylvania denied the Application for Reargument. In December 2025, the plaintiff petitioned for review of their appeal to the Pennsylvania Supreme Court which is currently pending. We intend to continue to defend against this claim.

Other than the above, we are not presently a party to any legal proceedings that, in the opinion of management, would, if decided against us, have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm, and other factors.

**Corporate Information**

We were incorporated under the laws of the State of Delaware in July 2017 under the name Passage Bio, Inc. Our principal executive office is located at One Commerce Square, 2005 Market Street, 39th Floor, Philadelphia, Pennsylvania, 19103, and our telephone number is (267) 866-0311. Our website address is www.passagebio.com. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated by reference into, this Annual Report.

**Available Information**

We file annual, quarterly and current reports, proxy statements and other documents with the Securities and Exchange Commission, or SEC, under the Securities Exchange Act of 1934, as amended, or Exchange Act. The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding issuers, including us, that file electronically with the SEC. The public can obtain any documents that we file with the SEC at www.sec.gov. Copies of each of our filings with the SEC can also be viewed and downloaded free of charge at our website, https://investors.passagebio.com/, after the reports and amendments are electronically filed with or furnished to the SEC.

**Item 1A.** ***Risk Factors***

## RISK FACTORS

*Investing in our common stock involves a high degree of risk. Before making your decision to invest in shares of our common stock, you should carefully consider the risks and uncertainties described below, together with the other information contained in this annual report, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations". The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us. We cannot assure you that any of the events discussed below will not occur. These events could have a material and adverse impact on our business, financial condition, results of operations and prospects. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment.*

### Risks Related to Our Financial Position and Need for Additional Capital

***We are a clinical stage genetic medicines company with a history of operating losses, and we may not achieve or sustain profitability. We anticipate that we will continue to incur losses for the foreseeable future. Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.***

We are a clinical stage genetic medicines company with a limited operating history on which to base your investment decision. Biotechnology product development is a highly speculative undertaking and involves a substantial degree of risk. Our operations to date have been limited primarily to staffing our company, business planning, raising capital, entering into collaboration and vendor agreements for conducting preclinical research and clinical development activities for our product candidates, and performing clinical development activities and manufacturing clinical supply. All of our product candidates are in the clinical development stage, have been outlicensed to a third party, or are in the preclinical or discovery stage. We have no products approved for commercial sale and have not generated any revenue from commercial product sales, and we will continue to incur significant research and development and other expenses related to our clinical development and ongoing operations. We have generally funded our operations to date through proceeds from sales of convertible preferred stock and public offerings, and do not expect to receive revenue from commercial product sales, for many years, if ever.

We have incurred net losses since our inception in 2017. We incurred net losses of $45.5 million and $64.8 million for the years ended December 31, 2025 and 2024, respectively. As of December 31, 2025, we had an accumulated deficit of $704.8 million. Substantially all of our operating losses have resulted from expenses incurred in connection with our research and development programs, acquiring the rights to our product candidates, and from general and administrative expenses associated with our operations. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future as we intend to continue to conduct research and development, clinical testing, regulatory compliance activities, manufacturing activities, and, if any of our product candidates is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in us incurring significant losses for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We expect that it will be several years, if ever, before we have a commercialized product. We anticipate that our expenses will increase substantially if, and as, we:

- advance our product candidates from the preclinical or discovery stage to the clinical development stage;
- advance our clinical product candidates into later stage clinical development;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- hire additional clinical, quality control, regulatory, manufacturing, scientific and administrative personnel;
- expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development, manufacturing and commercialization efforts;
- develop our internal manufacturing capabilities;

- maintain, expand and protect our intellectual property portfolio; and
- incur additional legal, accounting or other expenses in operating our business, including the additional costs associated with operating as a public company.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors.

***We have never generated revenue from product sales and may never achieve or maintain profitability.***

We have no products approved for commercial sale and have not generated any revenue from commercial product sales. To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities can include completing preclinical studies and initiating and completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, obtaining coverage and adequate reimbursement from government and third-party payors, marketing, distributing, and selling those products that are approved and satisfying any post marketing requirements. 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. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability.

Even 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 you to lose all or part of your investment.

***We will need to raise additional funding before we can expect to become profitable from any potential future sales of our products. This additional financing 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 our product development efforts or other operations.***

We will require substantial future capital in order to complete planned and future preclinical and clinical development for our portfolio of product candidates and potentially commercialize these product candidates, if approved. If our product portfolio progresses into later stage clinical trials, or our current preclinical product candidates progress into the clinical trial stage, we expect our spending levels to significantly increase in connection with our continued clinical trial activities and production of our clinical product candidates' supply. 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. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Our ability to raise additional funds also depends on general financial, economic and market conditions as well as other factors, including financial institutions that may experience insolvency or financial distress over which we may have no or limited control. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate certain of our licensing activities, our research and development programs or other operations.

Our operations have consumed significant amounts of cash since inception. As of December 31, 2025, our cash and cash equivalents were $46.3 million. We expect that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements through the end of the first quarter of 2027. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect.

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

- the scope, timing, progress and results of discovery, preclinical development, laboratory testing and clinical trials for our product candidates;

- the expenses of manufacturing our product candidates for clinical trials and in preparation for marketing approval and commercialization;
- the extent to which we enter into collaborations or other arrangements with additional third parties in order to further develop our product candidates;
- the expenses of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the expenses and fees associated with the discovery, acquisition or in-license of additional product candidates or technologies;
- our ability to establish collaborations on favorable terms, if at all;
- the expenses required to scale up our clinical, regulatory and manufacturing capabilities;
- the expenses of future commercialization activities, if any, including establishing sales, marketing, manufacturing and distribution capabilities, for any of our product candidates for which we receive marketing approval;
- the availability of coverage and adequate reimbursement from government and third-party payors for our product candidates for which we receive marketing approval; and
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval.

Accordingly, we will need to continue to rely on additional financing to achieve our business objectives, which may not be available to us on acceptable terms, or at all. For example, we are party to the Sales Agreement with Cowen relating to the sale and issuance, from time to time, of shares of our common stock in at-the-market equity offerings with an aggregate offering price up to $125.0 million, or the ATM Facility. However, our ability to raise capital under the ATM Facility or other registration statements may be limited by, among other things, SEC rules and regulations impacting the eligibility of smaller companies to use Form S-3 for primary offerings of securities. Based on our public float as of the date of the filing of this Annual Report on Form 10-K, we are only permitted to utilize a shelf registration statement, including the registration statement under which the ATM Facility is operated, subject to Instruction I.B.6 to Form S-3, which is referred to as the "baby shelf" rule. For so long as our public float is less than $75.0 million, we may not sell more than the equivalent of one-third of our public float during any 12 consecutive months pursuant to the baby shelf rules. Although alternative public and private transaction structures may be available, these may require additional time and cost, may impose operational restrictions on us, and may not be available on attractive terms.

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. If adequate funds are not available to us on a timely basis or on terms acceptable to us, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more product candidates or discovery stage programs or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize any product candidates, if approved.

***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 substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or securities convertible into equity, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. 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, selling or licensing our assets, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or 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 or on terms acceptable to us, we may be required

to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

**Risks Related to Product Development and Regulatory Approval**

***PBFT02 is currently our sole clinical stage product candidate and we may not be able to successfully develop and commercialize PBFT02.***

We are currently dependent on the potential development of a single clinical product candidate, PBFT02. We are still developing our sole clinical product candidate, and PBFT02 cannot be marketed or sold in the United States or in foreign markets until regulatory approval has been obtained from the FDA or applicable foreign regulatory agencies. The process of obtaining regulatory approval is expensive and time consuming. The FDA and foreign regulatory authorities may never approve PBFT02 for sale and marketing, and even if PBFT02 is ultimately approved, regulatory approval may be delayed or limited in the United States or in other jurisdictions. Even if we are authorized to sell and market PBFT02 in one or more markets, there is no assurance that we will be able to successfully market PBFT02 or that PBFT02 will achieve market acceptance sufficient to generate profits. If we are unable to successfully develop and commercialize PBFT02 due to failure to obtain regulatory approval for PBFT02, to successfully market PBFT02 or, to generate profits from the sale of PBFT02 due to other risk factors outlined in this report, it would have material adverse effects on our business, financial condition, and results of operations.

***We are early in our development efforts. Our business is dependent on our ability to advance our current and future product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them. If we are unable, or experience significant delays in doing so, our business will be materially harmed.***

We are early in our clinical development efforts and our clinical product candidate is in early phase clinical trials. Additionally, we have a portfolio of programs that are in different stages of preclinical development and some may never advance to clinical stage development. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product.

Each of our programs and product candidates will require additional preclinical and/or clinical development, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building a commercial organization or successfully outsourcing commercialization, substantial investment and significant marketing efforts before we generate any revenue from product sales. Our product candidates must be authorized for marketing by the FDA, or certain other ex-U.S. regulatory agencies before we may commercialize our product candidates.

The clinical and commercial success of our product candidates will depend on several factors, including the following:

- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies, biocompatibility studies and minimally efficacious dose studies in animals, where applicable;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for our product candidates;
- successful enrollment and completion of clinical trials, including under the international current Good Clinical Practices, or cGCPs, and current Good Laboratory Practices, or GLPs;
- positive results from our current and future clinical programs that support a finding of safety and effectiveness and an acceptable benefit-risk profile of our product candidates in the intended populations;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers or our own facilities for clinical supply and, where applicable, commercial manufacturing capabilities;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;

- commercial launch of our product candidates, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our product candidates, including method of administration, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies;
- establishment and maintenance of healthcare coverage and adequate reimbursement and patients' willingness to pay out-of-pocket in the absence of such coverage and adequate reimbursement;
- establishment of a physician training system and network for administration of our product candidates by administration into the ICM;
- enforcement and defense of intellectual property rights and claims; and
- maintenance of a continued acceptable safety, tolerability and efficacy profile of our product candidates following approval.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

***Preclinical and clinical development involve lengthy and expensive processes with uncertain outcomes. We may incur additional expenses or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our current product candidates or any future product candidates.***

All of our product candidates are in clinical or preclinical development and their risk of failure is high. We also rely on third parties, such as Gemma, for our preclinical and IND-enabling studies. It is impossible to predict when or if any of our product candidates will receive regulatory approval. To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive preclinical studies and lengthy, complex and expensive clinical trials that our product candidates are safe and effective in humans. Clinical testing can take many years to complete, and its outcome is inherently uncertain. We will rely on contract laboratories and other third parties, or our CROs, for the clinical development of our clinical product candidates. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials or early cohorts of our clinical trials of our product candidates, including early biomarker data, may not be predictive of the results of later-stage clinical trials or later cohorts of our clinical trials. Early clinical trials and in particular initial cohorts of early clinical trials often enroll significantly fewer patients than later stage clinical trials or later cohorts of the same clinical trial and may not be as predictive as larger trials. We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful or come to agreement on other aspects of clinical trial design. Moreover, a clinical trial can fail at any stage of testing. Differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products. A number of companies in the biotechnology industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or to unfavorable safety profiles, notwithstanding promising results in earlier trials. There is typically a high rate of failure of product candidates proceeding through clinical trials. Most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our future clinical trials will ultimately be successful or support clinical development of our current or any of our future product candidates.

We, or our collaborators, may experience delays in initiating or completing clinical trials. We, or our collaborators, also may experience numerous unforeseen events during, or as a result of, any future clinical trials that we could conduct that could delay or prevent our ability to receive marketing approval or commercialize our clinical product candidates or any future product candidates, including:

- regulators, such as the FDA, may place our clinical trials on clinical hold;
- institutional review boards, or IRBs, the FDA or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- delays in reaching, or failure to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- novel therapies, such as gene therapies with less well-characterized safety profiles, may require slower or more staggered early clinical trial enrollment to adequately assess safety data;
- clinical trials of any product candidates may fail to show safety or efficacy, produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or subjects may drop out of these clinical trials or fail to return for post-treatment follow up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs, or ethics committees may require that we or our investigators suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our trials are being exposed to unacceptable health risks;
- expenses of clinical trials of any of our product candidates may be greater than we anticipate;
- the quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be inadequate to initiate or complete a given clinical trial;
- our inability to manufacture sufficient quantities of our product candidates for use in clinical trials;
- reports from clinical testing of other therapies may raise safety or efficacy concerns about our product candidates;
- our failure to establish an appropriate safety profile for a product candidate based on clinical or preclinical data for such product candidate as well as data emerging from other molecules in the same class as our product candidate; and
- the FDA or ex-U.S. regulatory agencies may require us to submit additional data such as long-term toxicology studies or impose other requirements before permitting us to initiate a clinical trial.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including: the size and nature of the patient population; the number and location of clinical sites we enroll; the proximity of patients to clinical sites; the eligibility and exclusion criteria for the trial; the design of the clinical trial; the inability to obtain and maintain patient consents; the risk that enrolled participants will drop out before completion; and competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs or therapeutic biologics that may be approved for the indications being investigated by us. Furthermore, we expect to rely on our collaborators, CROs and clinical trial sites to ensure the proper and timely conduct of our future clinical trials, including the patient enrollment process, and we have limited influence over their performance. Additionally, we could encounter delays if treating physicians encounter unresolved ethical issues associated with enrolling patients in future clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. For example, treating physicians with eligible patients for our upliFT-D trial may instead elect to use alternative treatment approaches from our competitors, if such competitors are to receive regulatory approval in advance of our program, in lieu of enrolling in our clinical trial.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, or the FDA or other regulatory authorities, or if a clinical trial is recommended for suspension or termination by the Independent Data Monitoring Committee for such trial. A suspension or termination may be imposed due to a number of factors, including: failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols; inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold; unforeseen safety issues or adverse side effects; failure to demonstrate a benefit from using a product or treatment; failure to establish or achieve clinically meaningful trial endpoints; changes in governmental regulations or administrative actions; or lack of adequate funding to continue the clinical trial. Clinical studies may also be delayed or terminated as a result of ambiguous or negative interim results.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

Our product development expenses will increase if we experience delays in clinical testing or marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition and results of operations significantly.

***Success in early preclinical studies or clinical trials may not be indicative of results obtained in later preclinical studies and clinical trials.***

Conducting preclinical testing is a lengthy, time-consuming and expensive process. The length of time of such testing may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. Delays associated with programs for which we are conducting preclinical testing and studies may cause us to incur additional operating expenses. We may experience unexpected or adverse results in our ongoing or future clinical trials. We will be required to demonstrate through adequately designed and executed clinical trials that our product candidates are safe and effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. Our current clinical trial for PBFT02 in FTD-*GRN* patients has relatively small cohorts and results experienced to date may not be indicative of future success. If safety issues arise, we may be delayed or prevented from expanding into subsequent phases of our trial. Earlier gene therapy clinical trials conducted by others also utilized AAV vectors. However, these studies should not be relied upon as evidence that our planned clinical trials will succeed. Trial designs and results from previous trials are not necessarily predictive of our future clinical trial designs or results, and initial positive results we may observe may not be confirmed upon full analysis of the complete trial data. In addition, the positive results we have observed for our product candidates in preclinical animal models may not be predictive of our future clinical trials in humans. Our product candidates may also fail to show the desired safety and efficacy in later stages of clinical development even if they successfully advance through initial clinical trials.

***Preliminary, topline or interim data from our clinical trials that we or our partners announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we have made, and may continue to make, public preliminary, topline or interim data from our clinical trials, including preliminary biomarker data. Preliminary or topline data from clinical trials remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary or topline data that were previously made public. Interim data from clinical trials that we may complete are also subject to the risk that one or more of the clinical outcomes may materially change as subject enrollment continues and more data become available. As a result, preliminary, topline and interim data should be viewed with caution until the final data are available. Adverse differences between preliminary, topline or interim data and final data could significantly harm our reputation and business prospects.

***If we do not achieve our projected development goals in the time-frames we announce and expect, the commercialization of our products may be delayed.***

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, manufacturing and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of preclinical studies and clinical trials, the release of data from such studies and the submission of regulatory filings, including IND submissions. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are, and will be, based on a variety of assumptions.

The actual timing of these milestones can vary significantly compared to our estimates, in some cases for reasons beyond our control. We may experience numerous unforeseen events during, or as a result of, any future clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates.

***Gene therapy is a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. Currently, only a limited number of gene therapy products have been approved in the United States and in foreign countries.***

Our current product candidates are based on gene therapy technology and our future success depends on the successful development of this novel therapeutic approach. The regulatory requirements that govern any novel gene therapy product candidates we develop are not entirely clear and are subject to change. The clinical trial requirements of the FDA and ex-U.S. regulatory agencies 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 potential products. The regulatory approval process for novel product candidates such as ours may be more expensive and take longer than for other, better known or extensively studied product candidates. Further, as we are developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA or comparable foreign regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. To date, only a limited number of gene therapy products have been approved in the United States and foreign countries, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States or other jurisdictions. Further, approvals by ex-U.S. regulatory agencies may not be indicative of what the FDA may require for approval, or vice versa.

***Our product candidates may cause undesirable and unforeseen side effects, which could delay or prevent their advancement into clinical trials or regulatory approval, limit the commercial potential or result in significant negative consequences.***

While new AAV vectors have been developed to reduce side effects previously reported in third-party gene therapy treatments, gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material.

For example, two patients in our upliFT-D trial have experienced a total of three SAEs related to PBFT02. Subsequent to the SAEs, we amended the upliFT-D trial protocol to both increase the steroid regimen and to introduce a short course of low dose prophylactic anticoagulation. Additional possible adverse side effects could occur that may require changes to the protocol in the future. Further, adverse side effects could substantially limit the effectiveness of the treatment. For example, in previous third-party clinical trials involving AAV vectors for gene therapy, some subjects experienced the development of a T-cell immune response, whereby after the vector is within the target cells, the cellular immune response system triggers the removal of transduced cells by activated T-cells. Other recent clinical trials involving high doses of AAV vectors have also resulted in liver damage and death. Further, following administration of any AAV vector, patients are likely to develop neutralizing antibodies specific to the vector administered. Other preclinical studies have suggested that high dosages of AAV administration may result in toxicity due to degeneration of the dorsal root ganglia. Preliminary results of our NHP toxicology studies for our PBFT02 product candidate have demonstrated trigeminal ganglia and dorsal root ganglia toxicity. Based on these results, and if our vectors demonstrate a similar effect in other programs, we may decide or be required to perform additional preclinical studies or to halt or delay further clinical development of our product candidates.

In addition to side effects caused by the product candidate, the administration process or related procedures also can cause adverse side effects. Our current clinical product candidate utilizes ICM administration. While this method of administration has been available for decades, its use for therapies is relatively new, no therapies are currently approved using ICM administration, and it may be perceived as having greater risk than more common methods of administration, such as intravenous injection. If any such adverse events occur, our clinical trials could be suspended or terminated. If we cannot demonstrate that any adverse events were not caused by the drug or administration process or related procedures, the FDA or ex-U.S. regulatory authorities could order us to cease further development of, or deny approval

of, our product candidates for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to not initiate, delay, suspend or terminate any future 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 Risk Evaluation and Mitigation Strategies, or REMS, to ensure that the benefits of the product outweigh its risks, which 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. Furthermore, 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 in the labeling;
- 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 occurrences may harm our business, financial condition and prospects significantly.

***Adverse public perception of genetic medicines may negatively impact regulatory approval of, and/or demand for, our potential products.***

Regulatory approval of and/or demand for our potential products will depend in part on public acceptance of the use of genetic medicine for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that genetic medicines are unsafe, unethical or immoral, and consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, their patients being willing to receive, and third-party payors being willing to cover and reimburse for treatments that involve the use of product candidates we may develop.

There have been several significant adverse side effects reported in genetic medicine treatments in the past. For example, in 1999, there was public backlash against gene therapy following the death of a clinical trial subject in a gene therapy clinical trial that utilized an adenovirus vector. It was later discovered that adenoviruses could generate an extreme immune system reaction that can be life threatening. Dr. James Wilson, who has also served as a consultant to us as a Scientific Advisor, was a co-investigator of the 1999 trial while he was Director of the Institute for Human Gene Therapy of Penn. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy by us or our competitors, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception and potential regulatory delays in the clinical testing or approval of our product candidates.

***As an organization, we have limited experience designing and implementing clinical trials and we have never conducted pivotal clinical trials. Failure to adequately design a trial, or incorrect assumptions about the design of the trial, could adversely affect the ability to initiate the trial, enroll patients, complete the trial, or obtain regulatory approval on the basis of the trial results, as well as lead to increased or unexpected costs.***

The design and implementation of clinical trials is a complex process. As an organization, we have limited experience designing and implementing clinical trials, and we may not successfully or cost effectively design and implement clinical trials that achieve our desired clinical endpoints efficiently, or at all. A clinical trial that is not well designed may delay or even prevent initiation of the trial, can lead to increased difficulty in enrolling patients, may make it more difficult to obtain regulatory approval for the product candidate on the basis of the trial results, or, even if a product candidate is approved, could make it more difficult to commercialize the product successfully or obtain reimbursement

from third-party payors. Additionally, a trial that is not well designed could be inefficient or more expensive than it otherwise would have been, or we may incorrectly estimate the related expenses to implement the clinical trial, which could lead to a shortfall in funding.

***Certain disorders we seek to treat have low incidence and prevalence, and it may be difficult to identify patients with these disorders, which may lead to delays in enrollment for our trials or slower commercial revenue if approved.***

Genetically defined disorders generally, and especially those for which certain of our current product candidates are targeted, have low incidence and prevalence. For example, we estimate the prevalence of FTD-*GRN* deficiency in the United States and Europe is approximately 18,000. This could be a significant obstacle to the timely recruitment and enrollment of a sufficient number of eligible patients into our trial. Further, we expect to rely in part on our relationships with patient advocacy groups to assist in identifying eligible patients, and any deterioration of those relationships could impede our ability to successfully enroll patients. Patient enrollment may be affected by other factors including:

- the severity of the disease under investigation;
- design of the trial protocol;
- the eligibility criteria for the trial;
- the perceived risks, benefits and convenience of administration of the product candidate being studied;
- our efforts to facilitate timely enrollment in clinical trials;
- the availability of other clinical trials being conducted for the same indication;
- the patient referral practices of physicians; and
- the proximity and availability of clinical trial sites to prospective patients.

Our inability to enroll a sufficient number of patients with these diseases for our planned clinical trials, including FTD-*GRN*, would result in significant delays and could require us to not initiate or abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Additionally, our projections of the number of people who have these disorders, including FTD-*GRN*, are based on estimates, including third-party analyses commissioned by us. The total addressable market opportunity for our product candidates will ultimately depend upon, among other things, the final approved product labeling for each of our product candidates, if our product candidates are approved for sale in our target indications, acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients globally may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. Our products may potentially be dosed on a one-time basis, which means that patients who enroll in our clinical trials may not be eligible to receive our products on a commercial basis if they are approved, leading to lower revenue potential.

***Even if we complete the necessary clinical trials, we cannot predict when, or if, we will receive regulatory approval to commercialize a product candidate and the approval may be for a more narrow indication than we seek.***

Prior to commercialization, our product candidates must be approved by the FDA pursuant to a BLA in the United States and by similar ex-U.S. regulatory authorities. The process of obtaining marketing approvals, both in the United States and abroad, is expensive and takes many years, 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. 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. Our company does not have experience in submitting and supporting the applications necessary to gain marketing approvals. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. 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. Regulatory authorities 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.

Approval of our product candidates may be delayed or refused for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials, including the methods for collecting and analyzing data, the statistical analysis plan, and the lack of a concurrent control arm or a decision to use external or historical controls;
- the FDA or comparable foreign regulatory authorities may not agree that the efficacy endpoints used in our clinical trials are appropriate to establish clinical benefit in the intended populations;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications;
- development of products for ultra rare diseases may involve the use of natural history data as an external control. We may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that the control arm(s) are adequate to establish the safety and/or effectiveness of our product candidates;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities a durable response to our product candidates;
- we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or comparable foreign regulatory authorities may not agree that we have sufficiently developed, validated or implemented the assays and methods proposed as part of our potency strategy and our approach to testing product candidates for routine lot release, or they may disagree with our approach to assuring the potency of product candidates and determining whether product lots are suitable for release;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- the facilities of the third-party manufacturers with which we contract may not be adequate to support approval of our product candidates;
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval; and
- even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

In addition, three decisions from the U.S. Supreme Court in July 2024 may lead to an increase in litigation against regulatory agencies that could create uncertainty and thus negatively impact our business. The first decision overturned established precedent that required courts to defer to regulatory agencies' interpretations of ambiguous statutory language. The second decision overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. The third decision extended the statute of limitations within which entities may challenge agency actions. These cases may result in increased litigation by industry against regulatory agencies and impact how such agencies choose to pursue enforcement and compliance actions. However, the specific, lasting effects of these decisions, which may vary within different judicial districts and circuits, is unknown. We also cannot predict the extent to which FDA and SEC regulations, policies, and decisions may become subject to increasing legal challenges, delays, and changes.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or REMS. These regulatory authorities may require precautions or contra indications with respect to conditions of use or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the product labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially and adversely affect our business, financial condition, results of operations and prospects.

Further, the regulatory authorities may require concurrent approval of a companion diagnostic device. For our product candidates, it may be necessary to use FDA-cleared or FDA-approved diagnostic tests to diagnose patients or to assure the safe and effective use of product candidates in trial subjects. The FDA refers to such tests as in vitro companion diagnostic devices. The FDA has issued guidance describing the agency's current thinking about the development and regulation of in vitro companion diagnostic devices. The final guidance articulates a policy position that, when an in vitro diagnostic device is essential to the safe and effective use of a therapeutic product, the FDA generally will require approval or clearance of the diagnostic device at the same time that the FDA approves the therapeutic product. At this point, it is unclear how the FDA will apply this policy to our current or future gene therapy product candidates. Should the FDA deem genetic tests used for diagnosing patients for our therapies to be in vitro companion diagnostics requiring FDA clearance or approval, we may face significant delays or obstacles in obtaining approval of a BLA for our product candidates.

***The FDA and ex-U.S. regulatory agencies have demonstrated caution in their regulation of gene therapy treatments. Ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of our product candidates, which may be difficult to predict.***

The FDA and ex-U.S. regulatory agencies at both the federal and state level in the United States, U.S. congressional committees, and foreign governments, have expressed interest in further regulating the biotechnology industry, including gene therapy and genetic testing. Any such further regulation may delay or prevent commercialization of some or all of our product candidates.

Regulatory requirements in the United States and abroad governing gene therapy products have changed frequently and may continue to change in the future. In addition to the FDA, the Institutional Biosafety Committee and IRB of each institution at which we conduct our planned clinical trials, would need to review the proposed clinical trial to assess the safety of the trial. Within the FDA, the Office of Therapeutic Products, within the Center for Biologics Evaluation and Research, or CBER, consolidates the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee advises CBER on its review. Adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our product candidates.

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 or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our 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. If we fail to do so, we may be required to delay or discontinue development of such 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 an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

***Disruptions at the FDA or other comparable foreign regulatory authorities may slow the time necessary for new products to be reviewed and/or approved, which would adversely affect our business. In addition, there is substantial uncertainty regarding new initiatives under the current administration and how these might impact the FDA, its implementation of laws, regulations, policies and guidance and its personnel. Similar initiatives may also be directed toward other government agencies. These initiatives could prevent, limit or delay development and regulatory approval of our product candidates, which would adversely affect our business.***

Disruptions at the FDA or other comparable foreign regulatory authorities may slow the time necessary for new products to be reviewed and/or approved, which would adversely affect our business. Changes in FDA staffing could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. If any legislation, executive orders, or lapses in agency funding impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Similar consequences may occur as a result of any future shutdown of the federal government. For example, on October 1, 2025, the U.S. government shut down, and similar to its previous shutdowns, certain regulatory agencies, such as the FDA, had to furlough critical employees and stop critical activities. Whenever a government shutdown occurs or becomes prolonged, or if geopolitical or global health concerns prevent the FDA from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, any ongoing government shutdown could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

FDA-regulated industries, such as ours, face uncertainty with regard to the regulatory environment we will face under the current administration as we proceed with research and development and potential future commercialization. Some of these efforts have manifested to date as efforts to reduce the size of the federal government, including large-scale reductions in force at the FDA. The loss of key personnel at the FDA, including those in leadership positions, is likely to impact operations at the FDA, which could result in, among other things, delays or limitations on our ability to obtain guidance, or changes to previous guidance obtained, from the FDA on our product candidates in development, longer review times and delays in obtaining the regulatory approvals for our product candidates. Moreover, the current administration has recently proposed action to freeze or reduce the budget of the National Institutes of Health as related to its funding for medical research, which could decrease the ability of facilities that rely on NIH funding to enroll and conduct clinical trials or increase the costs to us of conducting clinical trials. There remains general uncertainty regarding future activities. New executive orders, regulations, policies or guidance could be issued or promulgated that adversely affects us or creates a more challenging or costly environment to pursue the development of new therapeutic products. Alternatively, state governments may attempt to address or react to changes at the federal level with changes to their own regulatory frameworks in a manner that is adverse to our operations. If we become negatively impacted by future governmental orders, regulations, policies or guidance, there could be a material adverse effect on us and our business.

***Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad and will limit our ability to realize their full market potential.***

In order to eventually market any of our product candidates in any particular foreign jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a jurisdiction by jurisdiction basis regarding safety and efficacy. Approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. 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, or EU. Addressing each specific country requirement and obtaining approval to commence a clinical trial in these countries could result in delays in starting, conducting, or completing a clinical trial. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets and expect to rely on third-party consultants. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be unrealized.

***We may not be successful in our efforts to build a pipeline of additional product candidates.***

Our business model is centered on developing therapies for patients with CNS disorders by establishing focused selection criteria to select, develop and advance product candidates that we believe will have a higher probability of technical and regulatory success through development into commercialization. We may not be able to continue to identify and develop new product candidates in addition to the pipeline of product candidates that we have established through our collaboration with GTP. As a result of the Outlicense Transaction Agreements, we no longer have a collaboration with GTP and instead have a collaboration with Gemma. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

**Risks Related to Our Reliance on Third Parties**

***We currently rely on our collaboration with Gemma for many aspects of our preclinical research and development programs, including for discovering, preclinically developing and conducting IND-enabling studies for our preclinical product candidates and our near-term future pipeline of product candidates. Failure or delay of Gemma to fulfill all or part of its obligations to us under the agreement, a breakdown in collaboration between the parties or a complete or partial loss of this relationship could materially harm our business.***

As part of the Outlicense Transaction Agreements, we entered into the Gemma Collaboration Agreement with Gemma to discover and develop certain AAV vector-based therapeutics, and the products developed under such collaboration currently represent all of our product pipeline and research programs. We currently rely on Gemma for preclinical research and development capabilities for new product candidates. Pursuant to the Gemma Collaboration Agreement, Gemma is responsible for discovery, preclinical development activities, including IND-enabling non-clinical studies and research grade manufacturing and other collaborative activities set forth in the plan for the funded research. Either party has the right in certain circumstances to terminate the collaboration pursuant to the terms of the Gemma Collaboration Agreement. If Gemma delays or fails to perform its obligations under the Gemma Collaboration Agreement, disagrees with our interpretation of the terms of the collaboration or our discovery plan or terminates our existing agreement, our future pipeline of product candidates could be significantly adversely affected and our prospects will be materially harmed.

The term of the research funding portion of the Gemma Collaboration Agreement, under which we have the ability to acquire exclusive rights to additional gene therapy products for CNS indications, expires in July 2029. If we seek to extend or alter the terms of our collaboration, we will need to negotiate a new or amended agreement, which may not be available to us on equally favorable terms, if at all. Gemma has also entered into collaborations with third parties, including certain of our competitors, addressing targets and disease indications outside the scope of our collaboration. As a result, Gemma may have competing interests with respect to their priorities and resources. We may have disagreements with Gemma with respect to the interpretation of the Gemma Collaboration Agreement, use of resources or otherwise that could cause our relationship with Gemma to deteriorate. As a result, Gemma may reduce their focus on, and resources allocated to, our programs, potentially delaying or terminating our ability to advance product candidates through preclinical studies. Additionally, Gemma could face operational and financial challenges that could impact its ability to execute under the Gemma Collaboration Agreement.

Further, under the Penn License Agreement and the Gemma Collaboration Agreement, Gemma and Penn are primarily responsible for prosecuting and maintaining our licensed intellectual property, and either of them may fail to properly prosecute, maintain or defend such intellectual property. In such event, if we are unable to otherwise maintain or defend such intellectual property, we could face the potential invalidation of the intellectual property or be subjected to litigation or arbitration, any of which would be time-consuming and expensive. To enforce the licensed intellectual property rights under the Penn License Agreement or the Gemma Collaboration Agreement, we will need to coordinate with Penn and Gemma, respectively, which could slow down or hamper our ability to enforce our licensed intellectual property rights. In such an event, we could face increased competition that could materially and adversely affect our business.

***We rely on third parties to conduct our preclinical studies and clinical trials and rely on them to perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.***

Although we have recruited a team that has experience with clinical trials, as a company, we have limited experience in conducting clinical trials. Moreover, we currently rely on third-parties, now primarily Gemma, for our discovery and certain of our preclinical research, and will continue to rely upon medical institutions, clinical investigators, and CROs to conduct clinical trials for our product candidates. We expect to rely heavily on these parties for execution of preclinical and clinical trials for our product candidates and control only certain aspects of their activities. If these parties reduce the levels of efforts and resources to our product candidate activities, prioritize work with a competitor of ours or if a dispute were to arise between us and these parties, they may not meet our expected deadlines or provide us with sufficient materials for our regulatory filings. Nevertheless, we will be responsible for ensuring that each of our preclinical and clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards and our reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our preclinical studies and clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

We, Gemma, and our CROs will be required to comply with regulations, including cGCPs for conducting, monitoring, recording and reporting the results of preclinical and clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any drugs in clinical development. The FDA enforces cGCP regulations through periodic inspections of clinical trial sponsors, principal investigators, and trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our future clinical trials will comply with cGCPs. In addition, our clinical trials must be conducted with product candidates produced in accordance with the requirements in the current Good Manufacturing Practices, or cGMP, regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action.

Although we currently design and intend to continue designing our planned clinical trials for our product candidates, for the foreseeable future CROs will conduct all of our planned clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less day-to-day control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any preclinical studies or

clinical trials with which such CROs are associated with may be extended, delayed or terminated. In such cases, 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 in the subject indication could be harmed, our costs could increase and our ability to generate revenue could be delayed.

***We rely on third parties to conduct our clinical trials. If those third parties do not perform as contractually required, fail to satisfy legal or regulatory requirements, miss expected deadlines or terminate the relationship, our development program could be delayed with potentially material and adverse effects on our business, financial condition, results of operations and prospects.***

We rely on third-party clinical investigators, CROs, clinical data management organizations and consultants to assist or provide the design, conduct, supervision and monitoring of clinical trials of our product candidates. Because we rely and intend to rely on these third parties and will not have the ability to conduct all clinical trials independently, we will have less control over the timing, quality and other aspects of clinical trials than we would have had we conducted them on our own. These investigators, CROs and consultants will not be our employees and we will have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. The third parties with which we may contract might not be diligent, careful or timely in conducting our clinical trials, resulting in the clinical trials being delayed or unsuccessful.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we will be responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the general investigational plan and protocols for the trial as well as applicable legal and regulatory requirements. The FDA generally requires preclinical studies to be conducted in accordance with GLPs and clinical trials to be conducted in accordance with cGCPs, including for designing, conducting, recording and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control will not relieve us of these responsibilities and requirements. Any adverse development or delay in our preclinical studies or clinical trials as a result of our reliance on third parties could have a material and adverse effect on our business, financial condition, results of operations and prospects.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into alternative arrangements or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially adversely impact our ability to meet our desired clinical development timelines.

***We have outlicensed our lysosomal pediatric products to Gemma, a genetic medicines company, and we may in the future enter into collaborations with other third parties for the discovery, development and commercialization of our product candidates. If any of our current or future collaborators cease development efforts under our collaboration agreements, or if any of those agreements are terminated, these collaborations may fail to lead to commercial products and we may never receive milestone payments or future royalties under these agreements.***

Gemma is a newly-formed company with a limited history of operations. If Gemma is not successful in continuing the development and commercialization of the lysosomal pediatric products that we have licensed to them, we will not receive any downstream economic benefit and the products will revert back to us.

We may in the future enter into third-party collaborations for research, development and commercialization of other therapeutic technologies or product candidates. Biotechnology companies are our likely future collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements.

With Gemma and any future collaboration agreements, we expect to have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Moreover, our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Our current and potential future collaborations involving our product candidates may pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on preclinical studies or clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation, indemnification obligations and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources; collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- if a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated; and
- collaboration agreements may restrict our right to independently pursue new product candidates.

As a result of the foregoing, our current and any future collaboration agreements may not lead to development or commercialization of our product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated. Any failure to successfully develop or commercialize our product candidates pursuant to our current or any future collaboration agreements could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Moreover, to the extent that any of our existing or future collaborators were to terminate a collaboration agreement, we may be forced to independently develop our product candidates and research programs, including funding preclinical studies or clinical trials, assuming marketing and distribution costs and maintaining and defending intellectual property rights, or, in certain instances, abandon product candidates altogether, any of which could result in a change to our business plan and have a material adverse effect on our business, financial condition, results of operations and prospects.

***We may not be successful in finding additional collaborators for continuing development of certain of our product candidates or successfully commercializing or competing in the market for certain indications.***

We may decide to pursue collaborations with additional pharmaceutical and biotechnology companies for the development and potential commercialization of some of our product candidates. We face significant competition in seeking appropriate collaborators. Any new collaboration may be on terms that are not optimal for us, and we may not be able to maintain any new collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product candidate do not meet expectations or the collaborator terminates the collaboration. In addition, a significant number of recent business combinations among large pharmaceutical companies has resulted in a reduced number of potential future collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of 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 drugs, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. 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.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, 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 increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

***We may have conflicts with our collaborators that could delay or prevent the development or commercialization of our product candidates.***

We may have conflicts with our collaborators, including Penn and Gemma, such as conflicts concerning the interpretation of preclinical or clinical data, the achievement of milestones, the interpretation of contractual obligations, payments for services, development obligations or the ownership of intellectual property developed during our collaboration. If any conflicts arise with any of our collaborators, such collaborator may act in a manner that is adverse to our best interests. Any such disagreement could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating revenues: unwillingness on the part of a collaborator to pay us milestone payments or royalties we believe are due to us under a collaboration, which could require us to raise additional capital; uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations; unwillingness by the collaborator to cooperate in the development or manufacture of the product, including providing us with product data or materials; unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities; initiating of litigation or alternative dispute resolution options by either party to resolve the dispute; or attempts by either party to terminate the relevant agreement.

***We may in the future seek to engage in strategic transactions to acquire or in-license new products, product candidates or technologies. If we are unable to successfully complete, or realize the benefits from, such transactions it may adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expenses and present significant distractions to our management.***

From time to time, we may consider strategic transactions, such as additional collaborations, acquisitions of companies, asset purchases, joint ventures and in-licensing of new products, product candidates or technologies that we believe will complement or augment our existing business. If we acquire assets with promising markets or technologies, we may not be able to realize the benefit of acquiring such assets if we are not able to successfully integrate them with our existing technologies. We may encounter numerous difficulties in developing, testing, manufacturing and marketing any new products resulting from a strategic acquisition that delay or prevent us from realizing their expected benefits or enhancing our business.

We cannot assure you that following any such strategic transaction, we will achieve the expected synergies to justify the transaction. For example, such transactions may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions would entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the transaction or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and would have a material and adverse effect on our business, financial condition, results of operations and prospects. Conversely, any failure to enter any strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market.

**Risks Related to Manufacturing**

***Gene therapies are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in our development or commercialization programs or otherwise harm our business.***

We currently rely on third parties to develop, manufacture and test clinical supplies of our product candidates, including the materials used to administer our product candidates. For our initial clinical trials, we rely on the manufacturing facility of Catalent Maryland, a unit of Catalent, Inc. acquired by Novo Holdings A/S, or Catalent, for supply of our product candidates. We have limited experience as a company in developing manufacturing facilities. If or when we decide to construct our own manufacturing facility for long-term commercial market supply, we may face delays in building out a plant, constructing new facilities, transferring technology to the facilities or hiring experts to staff and operate the facilities and, accordingly, our production capacity could be limited. We use external contract testing labs and analytical development and process development services to support our pipeline. The manufacturing processes used to produce our product candidates are complex, novel and have not been validated for commercial use. Many factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

Our product candidates require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product is consistent from lot-to-lot or will perform in the intended manner. For example, we have recently developed a potency

assay for release of PBFT02 for late-stage clinical studies and commercialization. While we have received initial positive feedback from the FDA on the suitability of our proposed potency assay, there can be no assurance that this assay will be approved by the FDA or ensure product potency, that we will be successful in our attempts to qualify our assay to support late-stage clinical studies, or that the assay will be deemed acceptable by the FDA. Accordingly, we employ multiple steps to control the manufacturing process to assure that the process works consistently and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, low lot yields, product recalls, product liability claims or insufficient inventory. As a result, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet the FDA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA and ex-U.S. regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or ex-U.S. regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures, low lot yields or product recalls. Lot failures, low lot yields or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

We, or our third-party collaborators, also may encounter problems hiring and retaining the experienced scientific, quality-control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our, or our third-party collaborators', manufacturing process or facilities could result in delays in our planned clinical trials and increased costs, and could make us a less attractive collaborator for potential partners, including larger biotechnology companies and academic research institutions, which could limit our access to additional attractive development programs. It could also require us to find alternative manufacturing processes, which may be unavailable to us on attractive terms, or at all. Problems in our manufacturing process could restrict our ability to meet potential future market demand for our products.

***Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.***

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

***We currently rely, and expect to continue to rely, on third party manufacturers and third party testing laboratories to produce and test clinical supply of our product candidates, and we have not entered into binding agreements with any such parties to support commercialization. The competition for gene therapy contract development, manufacturing, and testing services is intense, and capacity is limited. In addition, these manufacturers and testing laboratories do not have experience producing or testing our product candidates at commercial scale and may be unable to obtain necessary regulatory approvals or to manufacture and test our product candidates with the quality, quantities, analytical consistency, or timelines required to support commercialization.***

We currently rely, and expect to continue to rely, on third parties for the production, release and stability testing, and quality control of our clinical trial materials, including the materials used to administer our product candidates. Because all manufacturing and testing activities are outsourced, we can control only certain aspects of their operations. The landscape for gene therapy contract development, manufacturing, and testing is highly competitive, and third party

manufacturers and testing laboratories are in high demand. Reliance on these third party manufacturers and testing labs may expose us to risks different than if we manufactured and tested product candidates ourselves, including but not limited to increased competition from other biotechnology companies for manufacturing slots, testing capacity, and specialized analytical expertise.

For example, we currently rely on Catalent for our clinical supply manufacturing and on third party laboratories for lot release testing, stability testing, and specialized assays needed to support regulatory submissions. While we have secured an agreement with Catalent to manufacture clinical supply of our product candidates, we have not yet secured manufacturing or testing capabilities for commercial quantities of our product candidates. We may be unable to negotiate binding agreements with manufacturers or testing laboratories to support potential commercialization activities on commercially reasonable terms, or at all. In addition, under our current agreements with Catalent, (i) we no longer have exclusive access to the dedicated clean room suite and may not be able to secure future capacity to meet our requirements for future clinical and commercial supply, and (ii) we have an exclusive obligation to manufacture certain products with Catalent and therefore may be unable to work with other third party manufacturers. As a result, we may be unable to continue to develop and commercialize our products or product candidates.

Before any of our third party manufacturers or third party testing laboratories can begin to commercially manufacture or test our product candidates, they must demonstrate to regulatory authorities that the planned chemistry, manufacturing and controls—including all analytical testing, release assays, and validation processes—meet applicable regulatory requirements. Manufacturing and testing of product candidates for clinical and commercial purposes must comply with cGMP and applicable ex U.S. regulatory requirements. These requirements govern quality control and documentation policies and procedures for both manufacturers and contract testing laboratories. Complying with cGMP and ex U.S. regulatory requirements will require substantial time, money, and effort in production, assay development, method validation, recordkeeping, and quality control to ensure that our product candidates meet applicable specifications and other requirements.

Our third party manufacturers and testing laboratories must also demonstrate to the FDA and ex U.S. regulators that they can manufacture and test our product candidates in accordance with cGMP as part of pre approval inspections. Failure by any manufacturer or testing lab to pass a pre approval inspection may significantly delay our ability to proceed with clinical trials in the respective jurisdiction or to obtain FDA or ex U.S. regulatory approval. If any of our third party manufacturers or testing labs fail to comply with these requirements, we could be subject to regulatory action that limits the jurisdictions in which we may sell our products. As a result, our business, financial condition, and results of operations may be materially harmed.

In addition, third party manufacturers or testing laboratories may fail to comply with cGMP or similar regulatory requirements outside the United States. Failure by us, our manufacturers, or our testing labs to comply with these requirements could result in sanctions 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. Such events could significantly and adversely impact the availability of both manufactured product and testing capacity, limiting supplies of our product candidates.

Even if third party manufacturers and testing laboratories comply with applicable regulatory requirements, we cannot assure that they will be able to successfully manufacture or test additional product candidates at a larger scale, in a timely or economical manner, or at all. Analytical testing for gene therapy products is complex, and scaling up testing capacity, transferring methods to alternative labs, or validating new assays may introduce delays or assay variability. If third party manufacturers or testing labs are unable to successfully increase our manufacturing or testing scale or capacity, the development, testing, and clinical trials of our product candidates may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

***Our third-party manufacturers and suppliers use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time-consuming or costly.***

Our third-party manufacturers and suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. The operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state, and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

***Any contamination in our third parties' manufacturing process, shortages of raw materials, labor or reagents or failure of any of our key suppliers to deliver necessary components of our platform 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 materially adversely affect our or our third-party vendor's ability to produce our gene therapies on schedule and could therefore harm our results of operations and cause reputational damage.

The raw materials required in our third-party vendors' manufacturing processes are derived from biological sources. We cannot assure that our third-party vendors have or will be able to obtain on commercially reasonable terms, or at all, sufficient rights to these materials derived from biological sources. Such raw materials are difficult to procure and may also 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 clinical and commercial manufacturing of our product candidates, which could materially and adversely affect our operating results and development timelines.

We rely on third-party suppliers for the supply and manufacture of certain components of our technology. Should our ability to procure these material components from our suppliers be compromised, our ability to continuously operate would be impaired until an alternative supplier is sourced, qualified and tested, which could limit our ability to produce a clinical and commercial supply of our product candidates and harm our business.

***We depend on third-party suppliers for materials used in the manufacture of our product candidates, and the loss of these third-party suppliers or their inability to supply us with adequate materials could harm our business.***

We rely on third-party suppliers for certain materials and components required for the production of our product candidates, including the materials used to administer our product candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of materials involve several risks, including limited control over pricing, availability, and quality and delivery schedules. There is substantial demand and limited supply for certain of the raw materials used to manufacture gene therapy products. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors that are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

**Risks Related to Commercialization**

***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 or technologies that are more advanced or effective than ours, which may harm our business and financial condition, and our ability to successfully market or commercialize our product candidates.***

The biotechnology and pharmaceutical industries, including the genetic medicines field, are characterized by rapidly changing technologies, competition and a strong emphasis on intellectual property. We are aware of several companies focused on developing gene therapies in various indications as well as several companies addressing methods for modifying genes and regulating gene expression. We may also face competition from large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

For the treatment of FTD, there are no approved disease-modifying therapies. We consider our most direct competitor with respect to PBFT02 for the treatment of FTD-*GRN* to be AviadoBio Ltd, which began enrolling their Phase 1/2 gene therapy trial in patients with FTD-*GRN* in 2023. AviadoBio Ltd entered into an exclusive option and licensing agreement with Astellas Pharma Inc. in October 2024. Additional companies, including Kyowa Kirin Co., Ltd. and QurAlis Corporation, are conducting preclinical research using genetic medicine approaches to treat patients with FTD-*GRN*. Denali Therapeutics Inc., in partnership with Takeda Pharmaceutical Company Limited, is conducting a Phase 1/2 clinical trial for their recombinant progranulin protein. Vesper Bio ApS completed a Phase 1/2 trial for a small molecule sortilin antagonist in asymptomatic patients with a *GRN* mutation. We are also aware of other therapeutic approaches in preclinical development that may target FTD-*GRN* patients, including the small molecule progranulin enhancer program by Arkuda Therapeutics, who entered into an exclusive option and asset purchase agreement with Johnson & Johnson Innovative Medicine in the first quarter 2024. With respect to PBFT02 for the treatment of FTD-*C9orf72*, Transposon Therapeutics, Inc., conducted a Phase 2 trial with a small molecule autophagy modulator for FTD-*C9orf72*. There are other approaches in preclinical development for the treatment of FTD-*C9orf72*. In addition to the *GRN* and *C9orf72* targeted therapies, there are numerous programs targeting the TDP-43 pathway and other targets for the treatment of FTD.

For the treatment of Huntington's disease, or HD, there are no approved disease-modifying therapies. There are multiple clinical-stage trials evaluating potential disease modifying therapies with mechanisms of action including targeting *HTT* lowering. We consider our most direct competitors to be those directly targeting somatic instability via modulating DNA repair. There are four companies with preclinical gene therapy programs targeting the DNA repair protein MSH3 including Evox Therapeutics Ltd, Latus Bio, Inc., uniQure N.V., and Voyager Therapeutics, Inc. Multiple other companies are exploring different approaches to target MSH3 in preclinical research. Approaches targeting other DNA repair proteins, such as upregulation of FAN1, are also in preclinical development. Numerous companies are exploring other targets for the treatment of HD.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical, and other resources than we do, such as larger research and development, clinical, commercial and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. 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 product candidates that we may develop. Competitors also may obtain FDA or other regulatory approval for their products 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, if ever. Additionally, new or advanced technologies developed by our competitors may render our current or future product candidates uneconomical or obsolete, and we may not be successful in commercializing our product candidates against competitors.

***The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community.***

Ethical, social and legal concerns about gene therapy could result in additional regulations restricting or prohibiting our products. Even with the requisite approvals from the FDA in the United States and other ex-U.S. regulatory authorities, the commercial success of our product candidates will depend, in part, on the acceptance of physicians, patients (which includes caregivers when applicable) and health care payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of gene therapy products and, in particular, our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability 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 ex-U.S. regulatory authorities;
- the willingness of physicians to order genetic testing for potential target patient populations;
- the willingness of potential patients to have genetic testing and counseling;
- the willingness of physicians to prescribe new therapies, including therapies using ICM administration;
- our ability to successfully train neurosurgeons and interventional radiologists in ICM administration of our product candidates;
- the willingness of the target patient population to try new therapies and a therapy with ICM administration;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or ex-U.S. regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products and the perceptions of such competitive products compared to our products;
- publicity concerning our products or competing products and treatments;
- the pricing of our products, particularly as compared to alternative treatments; and
- sufficient third-party payor coverage and adequate reimbursement from government and third-party payors and patients' willingness to pay out-of-pocket in the absence of such coverage and adequate 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.

***If in the future we are unable to establish U.S. or global sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if they are approved and we may not be able to generate any revenue.***

We currently do not have a sales team or marketing team for the sales, marketing, and distribution of any of our product candidates that may receive regulatory approval. In order to commercialize any product candidates after approval, we must build on a territory-by-territory basis sales, reimbursement, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If our product candidates receive regulatory approval, we may decide to establish an internal sales team with technical expertise and supporting distribution capabilities to commercialize our product candidates, which will be expensive and time-consuming and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of any of our product candidates that we obtain approval to market.

With respect to the commercialization of all or certain of our product candidates, we may choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements when needed on acceptable terms, or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval, or any such commercialization may experience delays or limitations. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay the pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. The development of our clinical product candidates and ongoing research programs require significant resources. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

**Risks Related to Intellectual Property**

***If we are unable to obtain and maintain patent protection or other necessary rights for our products and technology, or if the scope of the patent protection obtained is not sufficiently broad or our rights under licensed patents 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 commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other countries for our current product candidates and future products, as well as our core technologies, including our manufacturing know-how. We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business by seeking, maintaining and defending our intellectual property, whether developed internally or licensed from third parties. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of gene therapy. Additionally, for some of our product candidates, we intend to rely on regulatory protection afforded through rare drug designations, data exclusivity and market exclusivity as well as patent term extensions, where available.

Currently, our intellectual property protection includes patents and patent applications that we have in-licensed from Penn under the Penn License Agreement. The in-licensed patent applications are directed to certain new AAV capsids, to recombinant AAV viruses, or rAAV, capable of delivering certain genes into human cells to treat disorders of the CNS, as well as to methods of treating those diseases with rAAV. Our intellectual property also includes patent applications that we solely own that cover processes that we developed for manufacturing our rAAV products, methods of treating adult neurodegenerative diseases such as FTD-*GRN*, FTD-*C9orf72,* and ALS, and an assay for measuring potency of our rAAV product candidate. We also have a patent application co-owned with Penn, directed to rAAV products for treatment of Huntington's disease.

Additionally, we have options under the Gemma Collaboration Agreement to conduct further research into new CNS indications that may create additional intellectual property.

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. The degree of patent protection

we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our own or licensed patent applications will mature into issued patents, and cannot provide any assurances that any such patents, if issued, will include claims with a scope sufficient to protect our current and future product candidates or otherwise provide any competitive advantage. Additionally, patents can be enforced only in those jurisdictions in which the patent has issued. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally twenty years after its first nonprovisional U.S. filing. The natural expiration of a patent outside of the United States varies in accordance with provisions of applicable local law, but is generally 20 years from the earliest local filing date. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. 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.

Moreover, our exclusive license under the Penn License Agreement is subject to field restrictions and retained rights, which may adversely impact our competitive position. Our licensed patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar to our product candidates, including biosimilar versions of such products. In addition, the patent portfolio licensed to us is, or may be, licensed to third parties outside our licensed field, and such third parties may have certain enforcement rights. Thus, patents licensed to us could be put at risk of being invalidated or interpreted narrowly in litigation filed by or against another licensee or in administrative proceedings brought by or against another licensee in response to such litigation or for other reasons.

Other parties have developed technologies that may be related or competitive to our own and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and in other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether the inventors of our own or licensed patents and applications were the first to make the inventions claimed in those patents or pending patent applications, or that they were the first to file for patent protection of such inventions. Further, we cannot assure you that all of the potentially relevant prior art relating to our own or licensed patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application. As a result, the issuance, scope, validity and commercial value of our patent rights cannot be predicted with any certainty. Further, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

In addition, the patent prosecution process is expensive and time-consuming, and we or our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, the scope of the claims initially submitted for examination may be significantly narrowed by the time they issue, if at all. It is also possible that we or our licensors may fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We cannot provide any assurances that we will be able to pursue or obtain additional patent protection based on our research and development efforts, or that any such patents or other intellectual property we generate will provide any competitive advantage. Moreover, we do not have the right to control the preparation, filing and prosecution of patent applications, or to control the maintenance of the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be filed, prosecuted or maintained in a manner consistent with the best interests of our business.

Even if we acquire patent protection that we expect should enable us to maintain competitive advantage, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability. Third parties, including competitors, may challenge the inventorship, scope, validity, or enforceability thereof, which may result in such patents being narrowed, invalidated or held unenforceable. If issued, our own or licensed patents may be challenged in patent offices in the United States and international markets, or in court. For example, we may be subject to a third-party submission of prior art to the USPTO, prior to a patent's issuance, precluding the granting of a patent based on one of our owned or licensed pending patent applications. We may become involved in opposition, reexamination, *inter partes* review, post-grant review, derivation, interference, or similar proceedings in the United States or abroad challenging the claims of

patents that we own or have licensed, once issued. Furthermore, patents that we own or have licensed may be challenged in court, once issued. Competitors may claim that they invented the inventions claimed in such patents or patent applications prior to the inventors of our own or licensed patents, or may have filed patent applications before the inventors of our own or licensed patents did. A competitor may also claim that we are infringing its patents and that we therefore cannot practice our technology as claimed under our own or licensed patent applications and patents, if issued. One or more claims of our own or licensed patents may be narrowed or invalidated. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents.

Even if they are unchallenged, our own or licensed patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our own or licensed patents by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, even if we have a valid and enforceable patent, we may not be able to exclude others from practicing our invention if the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. Moreover, a third party may develop a competitive product that provides benefits similar to one or more of our product candidates but that uses a vector or an expression construct that falls outside the scope of our patent protection or license rights. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business.

Similar risks would apply to any patents or patent applications that we may own or in-license in the future.

In addition to patent protection, if any of our product candidates are approved by the FDA as a biological product under a BLA in the United States, we believe the product would qualify for a 12-year period of exclusivity. Other regulatory exclusivities may be available, such as orphan drug exclusivity, with analogous data, marketing, and orphan exclusivities in various foreign countries. However, the scope of such regulatory exclusivities is subject to change, and may not provide us with adequate and continuing protection sufficient to exclude others from commercializing products similar to our product candidates.

***All of our current product candidates and research programs, including PBFT02, are licensed from or based upon licenses from a third -party and are field limited to certain indications. If the license agreements are terminated or interpreted to narrow our rights, our ability to advance our current product candidates or develop new product candidates based on these technologies will be materially adversely affected.***

We currently rely on licenses and sublicenses from third parties, in particular Penn, and will continue to rely on third parties for the research, development, manufacturing and commercialization of our current product candidates. If any of our licenses or relationships or any in-licenses on which our licenses are based are terminated or breached, we may:

- lose our rights to develop and market our current product candidates;
- lose patent or trade secret protection for our current product candidates;
- experience significant delays in the development or commercialization of our current product candidates;
- not be able to obtain any other licenses on acceptable terms, if at all; or
- incur liability for damages.

Additionally, even if not terminated or breached, our intellectual property licenses or sublicenses may be subject to disagreements over contract interpretation which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations.

If we experience any of the foregoing, it could have a materially adverse effect on our business and could force us to cease operations which could cause you to lose all of your investment.

***If we breach our license agreements it could have a material adverse effect on our commercialization efforts for our product candidates.***

If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates or technology from third parties, we could lose license rights that are important to our business. Our current clinical product candidates, including PBFT02, are licensed from Penn. Under the Penn License Agreement, we are subject to various obligations, including payment obligations, diligence obligations such as development and commercialization obligations, as well as potential royalty payments and other obligations. If we fail to comply with any of these obligations or otherwise breach our license agreements, our licensors may have the right to terminate the applicable license in whole or in part. Generally, the loss of any one of our current licenses, or any other license we may acquire in the future, could harm our business, prospects, financial condition and results of operations.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other intellectual property rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- whether and the extent to which inventors are able to contest the assignment of their rights to our licensors.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms or at all, we may be unable to successfully develop and commercialize the affected product candidates. In addition, if disputes arise as to ownership of licensed intellectual property, our ability to pursue or enforce the licensed patent rights may be jeopardized. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

***Our strategy of obtaining rights to key technologies through in-licenses may not be successful.***

We seek to expand our product candidate pipeline in part by in-licensing the rights to key technologies. The future growth of our business will depend in part on our ability to in-license or otherwise acquire the rights to additional product candidates or technologies. We cannot assure you that we will be able to in-license or acquire the rights to any product candidates or technologies from third parties on acceptable terms or at all.

The in-licensing and acquisition of these technologies is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire product candidates or technologies that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to license rights to us. Furthermore, we may be unable to identify suitable product candidates or technologies within our area of focus. If we are unable to successfully obtain rights to suitable product candidates or technologies, our business, financial condition and prospects could suffer.

***Third parties may initiate legal proceedings alleging claims of intellectual property infringement, the outcome of which would be uncertain and could have a material adverse effect on the success of 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 future products 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 frequent litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates, future products and technology. Our competitors or other third parties may assert infringement or misappropriation claims against us, alleging that our therapeutics, manufacturing methods, formulations or administration methods are covered by their patents. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing product candidates. For example, a third party previously sent us a letter claiming that the use of our AAVhu68 capsid infringes certain patent claims to which the third party has an exclusive license. While this matter has been resolved and we believe that we would have valid defenses to these and any other such claims; however, if any such claims were ultimately successful, we might require a license to continue to use and sell any product candidates using such AAV vector. Such licenses may not be available on commercially reasonable terms, or at all.

Further, we do not know which processes we will use for commercial manufacture of our future products, or which technologies owned or controlled by third parties may prove important or essential to those processes. Given the vast number of patents in our field of technology, we cannot be certain or guarantee that we do not or will not infringe existing patents or that we will not infringe patents that may be granted in the future. Many companies have filed, and continue to file, patent applications related to gene therapy and orphan diseases. Some of these patent applications have already been allowed or issued and others may issue in the future. Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use, sale or importation of our product candidates or future products. If a patent holder believes the manufacture, use, sale, offer for sale or importation of one of our product candidates or future products infringes its patent, the patent holder may sue us even if we have licensed other patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our licensed patent portfolio may therefore have no deterrent effect.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale, importation or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our future products or the manufacture or use of our future products.

Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future. If we were to challenge the validity of an issued U.S. patent in court, such as an issued U.S. patent of potential relevance to some of our product candidates or future products or manufacture or methods of use, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found, or believe there is a risk we may be found, to infringe a third-party's intellectual property rights, we could be required or may choose to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any such 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 access to the same technologies licensed to us. Without such a license, we could be forced, including by

court order, to cease commercializing the infringing technology or product. 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. A finding of infringement could prevent us from commercializing our future products or force us to cease some of our business operations, which could materially harm our business. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. If we lose a foreign patent lawsuit alleging our infringement of a competitor's patents, we could be prevented from marketing our therapeutics in one or more foreign countries and/or be required to pay monetary damages for infringement or royalties in order to continue marketing. Claims that we have misappropriated the confidential information, trade secrets or other intellectual property of third parties could have a similar negative impact on our business. Any of these outcomes would have a materially adverse effect on our business.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our future products or processes. Patent litigation is costly and time-consuming, and some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. We may not have sufficient resources to bring these actions to a successful conclusion. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts, adversely affect our ability to raise additional funds, and could limit our ability to continue our operations.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed.***

In addition to the protection afforded by patents, we rely upon unpatented trade secret protection, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our contractors, collaborators, scientific advisors, employees and consultants and invention assignment agreements with our consultants and employees. We may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the contractors, collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. As a result, we could lose our trade secrets. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time-consuming and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing or unwilling to protect trade secrets.

Our trade secrets could otherwise become known or be independently discovered by our competitors. Competitors could purchase our product candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If our trade secrets are not adequately protected or sufficient to provide an advantage over our competitors, our competitive position could be adversely affected, as could our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in premature abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our product candidates, which would have a material adverse effect on 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, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. 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. Further, licensing partners may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export 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.

Most of our in-licensed patent families are pending in major pharmaceutical markets including the United States, Canada, Europe, Japan, Korea, and China, as well as other jurisdictions; we will not be able to enforce the patent in any jurisdictions in which the application has not been filed. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and we or our licensor may be unable to predict and may fail to seek patent protection in jurisdictions in which protection may ultimately be desired.

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, 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, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, 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.

***We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.***

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may elect to or be required to file infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also 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 material adverse effect on the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

***Changes in patent law in the United States and in ex-U.S. jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.***

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain.

Past or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. For example, in March 2013, under the Leahy-Smith America Invents Act, or America Invents Act, the United States moved from a "first to invent" to a "first-inventor-to-file" patent system. 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 a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO continues to promulgate new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-inventor-to-file" provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the America Invents Act and new regulations on the specific patents discussed in this filing have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Additionally, 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. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in the case, *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.,* the U.S. Supreme Court held that certain claims to DNA molecules are not eligible for patent protection. We cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents. Any similar adverse changes in the patent laws of other jurisdictions could also have a material adverse effect on our business, financial condition, results of operations and prospects.

***We may be subject to claims asserting that our employees, consultants, advisors or collaborators have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of or other rights to what we regard as our own or licensed intellectual property.***

Many of our employees, consultants or advisors, and the employees, consultants or advisors of our licensors, are currently, or were previously, employed at or affiliated with universities, hospitals or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Moreover, some of our licensors, and our or our licensors' employees, consultants or advisors are or have been affiliated or have a contractual relationship with multiple institutions and companies including our competitors and may have or have had an obligation to them. Such institutions and companies could challenge our license rights or our licensors' intellectual property ownership rights. Litigation may be necessary to defend against these claims and we may be obligated to indemnify our employees, consultants, advisors or collaborators in certain instances. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

***Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.***

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 and biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidates might expire before or shortly after we or our partners commercialize those candidates. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to or interchangeable with ours.

***If we do not obtain patent term extension for any product candidates we may develop, our business may be materially harmed.***

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more 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, or the Hatch-Waxman Amendments.

The Hatch-Waxman Amendments permit 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 per product may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, even if we were to seek a patent term extension, it may not be granted because of, for example, the failure to exercise due diligence during the testing phase or regulatory review process, the failure to apply within applicable deadlines, the failure to apply prior to expiration of relevant patents, or any other failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

***Some of the intellectual property rights that we have in-licensed were generated through the use of U.S. government funding and are therefore subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for U.S. based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with ex-U.S. manufacturers.***

Some of the intellectual property rights we have in-licensed were generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act, and implementing regulations. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us or our licensors to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. These time limits have recently been changed by regulation, and may change in the future. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with ex-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

**Risks Related to Government Regulation**

***The pricing, 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.***

Our clinical product candidates currently target indications with small patient populations. In order for products that are designed to treat smaller patient populations to be commercially viable, the reimbursement for such products must be higher, on a relative basis, to account for the lack of volume. Accordingly, we (including our sublicensees) will need to implement a coverage and reimbursement strategy for any approved product candidate that accounts for the smaller potential market size. If we are unable to establish or sustain coverage and adequate reimbursement for any future product candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved.

We expect the cost of a single administration of gene therapy products, such as those we are developing, to be substantial when and if they achieve regulatory approval. Therefore, 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 any of our product candidates will depend substantially, both domestically and internationally, 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. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, since CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. However, no uniform or consistent policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor as well as from state to state. Consequently, the coverage determination process is often a time-consuming and costly process that must be played out across many jurisdictions and different entities. Further, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. It is difficult to predict what CMS will decide with respect to reimbursement for novel products such as ours since there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the EU, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, the prices of products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for 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 product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third-party payors, in the United States and internationally, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. 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 certain third-party payors, such as 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 very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market.

In addition to CMS and private payors, professional organizations such as the American Medical Association can influence decisions about reimbursement for new products by determining standards for care. In addition, many private payors contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our product candidates. Even if favorable coverage and reimbursement status is attained for one or more products for which we or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

***Fast Track Designation by the FDA may not lead to a faster development or regulatory review or approval process.***

We have obtained Fast Track Designation for PBFT02 for the treatment of FTD-*GRN*. We may seek Fast Track Designation for other potential indications for PBFT02, or for one or more of our other product candidates. 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 needs for this condition, the product sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

***If we decide to seek Orphan Drug Designation for some of our product candidates, we may be unsuccessful or may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for supplemental market exclusivity.***

We have obtained Orphan Drug Designation for PBFT02 for the treatment of FTD. We have sought and may continue to seek Orphan Drug Designation for one or more of our other product candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as 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 will be recovered from sales in the United States. In the United States, Orphan Drug Designation entitles a party to financial incentives such as tax advantages and user-fee waivers. Opportunities for grant funding toward clinical trial costs may also be available for clinical trials of drugs for rare diseases, regardless of whether the drugs are designated for the orphan use. In addition, if a product that has Orphan Drug Designation subsequently receives the first FDA approval for the drug to treat the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in limited circumstances. For large molecule drugs, including gene therapies, sameness is determined based on the principal molecular structural features of a product. As applied to gene therapies, the FDA has issued final guidance in which it stated it generally intends to consider certain key features, such as the transgenes expressed by the gene therapy and the vectors used to deliver the transgene, to be principal molecular structural features. With regard to vectors, the FDA generally intends to consider whether two vectors from the same viral class are the same or different on a case-by-case basis. The FDA does not intend to consider minor differences between transgenes and vectors to be different principal molecular structural features. When two gene therapy products express the same transgene and have or use the same vector, determining whether two gene therapies are the same drug may also depend on additional features of the final gene therapy product, such as regulatory elements and the cell type that is transduced (for genetically modified cells). In such cases, the FDA generally intends to determine whether two gene therapy products are different on a case-by-case basis.

Although we have obtained Orphan Drug Designation for our clinical product candidates, and even if we obtain Orphan Drug Designation for additional product candidates or in additional indications, we may not be the first to obtain marketing approval of these product candidates for the orphan-designated disease or condition due to the uncertainties associated with developing pharmaceutical products. If a competitor with a product that is determined by the FDA to be the same as one of our product candidates obtains marketing approval before us for the same disease or condition we are pursuing and obtains orphan drug exclusivity, our product candidate may not be approved until the period of exclusivity ends unless we are able to demonstrate that our product candidate is clinically superior. Even after obtaining approval, we may be limited in our ability to market our product. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated disease or condition or may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different principal molecular structural features can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug with the same

principal molecular structural features for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek Orphan Drug Designation for some of our product candidates, we may never receive such designations. Similarly, the European Commission may also designate a product as an orphan drug under certain circumstances.

***If we decide to pursue accelerated approval for any of our product candidates, it may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval.***

In the future, we may decide to pursue accelerated approval for one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful advantage 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 over available therapy may not be a direct therapeutic advantage but is a clinically important improvement from a patient and public health perspective.

Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive 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, or that, if we decide to pursue any such pathway, our applications will be granted on a timely basis or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further trials prior to considering our application or granting approval of any type. In addition, even if we are able to obtain accelerated approval or any other form of expedited approval for any of our product candidates, we may not obtain such approval in a timely manner or otherwise in accordance with our timelines, and the costs of obtaining such approval and performing any additional trials or analysis may be higher than we currently anticipate. Further, if the results of any such additional trials or analysis do not ultimately support full regulatory approval of the applicable product, it may be withdrawn from the market, which could harm our ability to generate revenue and otherwise negatively impact our business and financial prospects. A failure to obtain, or delay in obtaining, accelerated approval or any other form of expedited development, review, or approval for any of our product candidates would extend the period of time until commercialization, if any, of such product candidate, could increase the cost of development of such product candidate beyond what we anticipate, and could harm our competitive position in the marketplace.

For products granted accelerated approval, sponsors are required to verify and describe the product's anticipated clinical benefit generally in the form of confirmatory trials. These confirmatory trials must be completed with due diligence and the FDA is authorized to require a post-approval trial to be underway prior to approval or within a specified time period following approval. The FDA is also required to specify conditions of any required post-approval trial. Sponsors are required to submit progress reports for required post approval studies and any conditions required by the FDA. The FDA may initiate enforcement action for the failure to conduct with due diligence a required post-approval trial, including a failure to meet any required conditions, which may include enrollment targets, the trial protocol and trial milestones specified by the FDA, or to submit timely reports.

In addition, all promotional materials for products approved under the accelerated approval pathway are subject to prior review by the FDA. If the FDA were to object to promotional pieces regarding products approved via accelerated approval, a company may be required to revise those materials or be subject to untitled or warning letters.

***Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.***

Our product candidates and the activities associated with their development and potential commercialization, including their testing, manufacture, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMPs, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, including periodic inspections by the FDA and other regulatory authorities and requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of any approved product. The FDA closely regulates the post-approval marketing and promotion of drugs and biologics to ensure drugs and biologics are marketed only for the approved indications and in accordance with the provisions of the approved product labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products. If we promote our product candidates beyond their potentially approved indications, we may be subject to enforcement action for off-label promotion. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our product candidates, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such product candidates, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of any approved product from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of product candidates;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our product candidates;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with European requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

***Our product candidates for which we intend to seek approval may face competition from biosimilars approved through an abbreviated regulatory pathway.***

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA created an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated 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 existing reference

product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product is first licensed under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that if any of our product candidates is licensed as a biological product under a BLA, it should qualify for the 12-year period of exclusivity. However, there is a risk that the FDA will not consider any of our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Additionally, this period of regulatory exclusivity does not apply to companies pursuing regulatory approval via their own traditional BLA, rather than via the abbreviated pathway. Moreover, an interchangeable biosimilar, once approved, may be substituted under existing law for any one of our reference products in a way that is similar to traditional generic substitution; any non-interchangeable biosimilar products may also be substituted by a health care provider but, under existing law, will not be automatically substituted at the pharmacy. The FDA is currently evaluating its approach to interchangeability and substitution policies are subject to change. The extent of the impact of such substitution will depend on a number of marketplace and regulatory factors that are still developing. Finally, there has been public discussion of potentially decreasing the period of exclusivity from the current 12 years. If such a change were to be enacted, our product candidates, if approved, could have a shorter period of exclusivity than anticipated.

***Enacted and future legislation may affect pricing and third-party payment for our product candidates, may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set. The full effect of recent United States healthcare reform and other changes in the healthcare industry, laws, and regulations and in healthcare spending is currently unknown, and the reform and other changes may adversely affect our business model.***

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, affect pricing and third-party payment for our product candidates prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and negatively affect our ability to profitably sell any products for which we obtain marketing approval. The commercial potential for our products, if any, could be affected by changes in healthcare spending and policy in the United States and abroad. New laws, regulations, or judicial decisions or new interpretations of existing laws, regulations, or decisions, related to healthcare availability, the method of delivery, or payment for healthcare products and services could adversely affect our business, operations, and financial condition, if and when we are able to obtain marketing approval and commercialize our products.

There have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs in general and the cost of pharmaceuticals in particular.

For example, the Budget Control Act imposed, subject to certain temporary suspension periods, 2% reductions in Medicare payments to providers per fiscal year starting April 1, 2013, and due to subsequent legislative amendments to the statute, will remain in effect through 2032, unless additional Congressional action is taken. In December 2020, CMS issued a final rule implementing significant manufacturer price reporting changes under the Medicaid Drug Rebate Program, including an alternative rebate calculation for a line extension that is tied to the price increases of the original drug, and Best Price reporting related to certain value-based purchasing arrangements. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs is eliminated. Elimination of this cap has, in some cases, required pharmaceutical manufacturers to pay more in rebates than they receive on the sale of products. It is unclear to what extent these regulations or any future legislation or regulations will affect our business, including our ability to generate revenue and achieve profitability.

There has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several presidential executive orders, Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare, and reform government program reimbursement methodologies for drug products.

Several healthcare reform initiatives culminated in the enactment of the Inflation Reduction Act, or IRA, in August 2022, which, among other things, requires the U.S. Department of Health and Human Services, or HHS, to negotiate the selling price of a statutorily specified number of drugs and biologics each year that CMS reimburses under Medicare Part B and Part D. The negotiated price may not exceed a statutory ceiling price. Only high-expenditure single-source biologics that have been approved for at least 11 years (seven years for single-source drugs) can qualify for negotiation, with the negotiated price taking effect two years after the selection year. For 2026, the first year in which negotiated prices become effective, CMS selected 10 high-cost Medicare Part D products in 2023, negotiations began in 2024, and the negotiated maximum fair price for each product has been announced. In addition, CMS has selected and announced the negotiated maximum fair price for 15 additional Medicare Part D drugs, which will become effective for negotiated maximum fair pricing in 2027. For 2028, CMS selected an additional 15 drugs, comprised of drugs covered under Medicare Part D and, for the first time, drugs payable under Medicare Part B. For 2029 and subsequent years, 20 Part B or Part D drugs will be selected. Currently, a drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded from the IRA's price negotiation requirements, but loses that exclusion if it has designations for more than one rare disease or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. However, as a result of a statutory amendment enacted in July 2025, beginning with the 2028 negotiated price applicability year, a drug may be designated for more than one rare disease or condition and still be excluded from price negotiation, as long as the only approved indications are for such rare diseases or conditions. The IRA also imposes rebates on Medicare Part B and Part D drugs whose prices have increased at a rate greater than the rate of inflation. In addition, the law eliminates the "donut hole" under Medicare Part D beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and establishing a new manufacturer discount program, which requires manufacturers that want their drugs to be covered by Medicare Part D to provide statutorily defined discounts to Part D enrollees. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, some significant, including civil monetary penalties. These provisions began taking effect progressively starting in 2023, although they may be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high-expenditure single-source drugs and biologics have been challenged in multiple lawsuits. Thus, it is unclear how the IRA will be implemented but it will likely have a significant impact on the pharmaceutical industry and the pricing of our products and product candidates. The adoption of restrictive price controls in new jurisdictions, more restrictive controls in existing jurisdictions or the failure to obtain or maintain timely or adequate pricing could also adversely impact revenue. We expect pricing pressures will continue globally.

The current administration is pursuing policies to reduce regulations and expenditures across the government including at HHS, which include the FDA and CMS, and related agencies. For example, on May 12, 2025, President Trump issued an Executive Order that, among other things, required HHS, within 30 days, to establish and communicate to drug manufacturers most favored nation, or MFN, price targets designed to bring drug prices for American patients in line with those in comparably developed nations. If significant progress towards MFN pricing is not achieved, the Executive Order requires HHS to propose a rulemaking to implement MFN pricing. Recently, on December 23, 2025, CMS issued proposed regulations to establish, under the Center for Medicare and Medicaid Innovation, two mandatory MFN demonstration models under Medicare Parts B and D, respectively. If these rules or other MFN pricing rules are finalized, they are likely to reduce prices of at least some drugs in the United States, if they are also sold in comparator countries. Even if we do not market drugs in such countries, we will be indirectly affected if our drugs competed with drugs whose prices were reduced as a result of MFN pricing initiatives.

Further, at the U.S. state level, legislatures are increasingly enacting laws and implementing regulations designed to control pharmaceutical and biological product pricing, including price or reimbursement constraints, discount requirements, marketing cost disclosure and price increase transparency reporting, and programs designed to encourage importation from other countries and bulk purchasing. In addition, the FDA issued a final rule in 2020 providing guidance for states to build and submit importation proposals for drugs from Canada, and the FDA authorized the first such plan in Florida in 2024, but implementation of Florida's plan has been extended until May 6, 2026. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted proposals that are pending review by the FDA. Additional state and federal healthcare reform measures may be adopted in the future, any of which could limit the

amounts that federal and state governments will pay for healthcare products and services or otherwise negatively impact our business model.

***Our operations and relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties including criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Healthcare providers and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with providers, third-party payors and customers 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 product candidates for which we obtain marketing approval.

Restrictions under applicable U.S. federal and state healthcare laws and regulations may include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- federal false claims laws, including the federal False Claims Act, imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, knowingly and willfully executing or attempting to execute 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, or HITECH Act, and its implementing regulations, also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, certain types of advanced practice nurses, and teaching hospitals, as well as certain ownership and investment interests held by physicians and their immediate family, which includes annual data collection and reporting obligations; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims 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 drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Other state laws require reporting of certain pricing information, including price increases and prices of newly launched drugs. 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. 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 product candidates from government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, oversight monitoring, contractual damages, reputational harm, diminished profits and future earnings, 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.

**Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business**

***Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.***

We are highly dependent on the research and development, clinical and business development expertise of our management, scientific and clinical team. Although we have entered into employment letter agreements or employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and manufacturing strategy. 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. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Recruiting and retaining qualified scientific, clinical, manufacturing and, if needed, sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs, particularly within the gene therapy space. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

Further, the reductions in our workforce announced in 2022, 2023, and January 2025 may also make retention of our current personnel both more important and more challenging. These workforce reductions resulted in the loss of longer-term employees, the loss of institutional knowledge and expertise and the reallocation and combination of certain roles and responsibilities across the organization, all of which could adversely affect our operations. Given the complexity of our business, we must continue to implement and improve our managerial, operational and financial systems, manage our facilities and continue to recruit and retain qualified personnel.

***We may be required to expand our manufacturing, development and regulatory capabilities in the future, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We may be required to expand our manufacturing, development and regulatory capabilities in the future, which could result in growth to the number of our employees and the scope of our operations, particularly in the areas of manufacturing and clinical strategy, and growing our capability to conduct clinical trials. We may not be able to effectively manage the expansion of our operations in the future or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

***Our internal computer systems, or those of our third-party collaborators or other contractors, may fail or suffer security breaches and cyber-attacks, which could result in a material disruption of our development programs.***

We implement measures designed to safeguard the confidentiality, integrity, availability, and privacy of the information we collect, use, store, and disclose; however, inadvertent or unauthorized access may still occur despite these safeguards. While we believe our controls are effective, our systems could be affected by software vulnerabilities, technical malfunctions, or human error, including employee misconduct. In addition, privacy and data protection laws continue to evolve, and future interpretations or regulatory changes may impose requirements that differ from our current practices. Any such developments could result in fines, litigation, penalties, or the need to modify our third-party relationships, business processes, or product and service offerings. If the measures implemented by us or our third-party partners prove insufficient or are circumvented, we may be subject to breach notification obligations, regulatory inquiries, or other enforcement actions, which could lead to significant financial penalties, operational disruption, loss of patient or partner trust, and reputational harm.

While we have not experienced any material losses as a result of any system failure, accident or security breach to date, we have been the subject of certain phishing attempts in the past. If such an event were to occur and cause interruptions in our operations, 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. Additionally, a party who circumvents our security measures could, among other effects, appropriate patient information or other proprietary data, cause interruptions in our operations, or expose patients to hacks, viruses, and other disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, insurance coverage to compensate for any losses associated with such events may not be adequate to cover all potential losses. 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 increasingly sophisticated.

To the extent that any disruption, security breach, or cyber-attack were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed. Depending on the nature of the information compromised, in the event of a data breach or other unauthorized access to our patient data, we may also have obligations to notify patients and regulators about the incident, and we may need to provide some form of remedy, such as a subscription to credit monitoring services, pay significant fines to one or more regulators, or pay compensation in connection with a class-action settlement (including under the private right of action under the California Consumer Privacy Act of 2018, or the CCPA, which increased the likelihood of security breach litigation). Such breach notification laws continue to evolve and may be inconsistent from one jurisdiction to another. Complying with these obligations could cause us to incur substantial costs and could increase negative publicity surrounding any incident that compromises patient data. Additionally, the financial exposure from the events referenced above could either not be insured against or not be fully covered through any insurance that we may maintain, and there can be no assurance that the limitations of liability in any of our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages as a result of the events referenced above. Any of the foregoing could have an adverse effect on our business, reputation, operating results, and financial condition.

***Our ability to utilize our net operating loss carryforwards may be subject to limitation.***

As of December 31, 2025, we had federal and state net operating loss, or NOL, carryforwards of $398.0 million, and local NOL carryforwards of $277.8 million. $0.3 million of the federal NOLs will begin to expire in 2037, and the remainder will carry forward indefinitely. Our state NOL carryforwards will begin to expire in 2037, and expire through 2045, and our local NOL will begin to expire in 2042 and expire through 2045.

To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any. U.S. federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the ability to utilize such federal net operating losses to offset taxable income is limited to 80% of our taxable income (without regard to certain deductions).

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset its post-change income and post-change tax liability may be limited. We have not undertaken a Section 382 study, and it is possible that we have previously undergone one or more ownership changes so that our use of net operating losses is currently limited. We may experience ownership changes in the future as a result of equity offerings or other shifts in our stock ownership, some of which are outside of our control. As a result, even if we earn net taxable income, our ability to use our pre-change NOLs and other tax attributes to offset taxable income and tax liability may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. Any such limitations may result in greater tax liabilities than we would incur in the absence of such limitations and any increased liabilities could adversely affect our business, results of operations, financial position and cash flows.

***U.S. federal income tax reform and changes in other tax laws could adversely affect us.***

Tax laws are being re-examined and evaluated globally, and tax authorities are increasingly scrutinizing the tax positions of companies. Changes in tax laws and regulations in federal, state, local, and foreign jurisdictions could have material adverse impacts on our business, cash flows, operating results, or financial condition, and could materially affect our tax obligations and effective tax rate. For example, the Tax Cuts and Jobs Act significantly reformed the Code. This legislation, among other things, included changes to U.S. federal tax rates, imposed significant additional limitations on the deductibility of interest and the use of net operating losses generated in tax years beginning after December 31, 2017. For our 2022 through 2024 tax years, the Tax Cuts and Jobs Act eliminated the option to immediately deduct research and development expenditures and required taxpayers to amortize domestic expenditures over five years and foreign expenditures over fifteen years. Beginning with our 2025 tax year, the One Big Beautiful Bill Act, or OBBBA, restored immediate deductibility of domestic expenditures, while foreign expenditures will continue to be capitalized and amortized over fifteen years. Changes in corporate tax rates, the realization of net deferred tax assets, the deductibility of expenses under the Tax Cuts and Jobs Act, the OBBBA, or future changes in tax laws could have a material impact on the value of our deferred tax assets, could result in significant one-time charges in the current or future taxable years, and could increase our future U.S. tax expense. In addition, it is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act, the OBBBA, or any newly enacted federal tax legislation. Changes in tax laws or regulations in the various tax jurisdictions we are subject to that are applied adversely to us or our clients could increase the costs of our products and harm our business.

Additionally, we use our best judgment in attempting to quantify and reserve for our tax obligations. However, a challenge by a taxing authority, a limitation on our ability to utilize tax benefits such as carryforwards or tax credits, or a deviation from other tax-related assumptions could have a material adverse effect on our business, results of operations, or financial condition.

***Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.***

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and ex-U.S. regulators, provide accurate information to the FDA and ex-U.S. regulators, 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, pricing, discounting, 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 may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical studies, 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 governmental 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, including the imposition of significant fines or other sanctions.

***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 will face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and will face an even greater risk if we commercialize any of our product candidates. 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;
- injury to our reputation and significant negative media attention;
- initiation of investigations by regulators;
- withdrawal of clinical trial participants;
- significant time and expenses to defend the related litigation;
- diversion of management and scientific resources from our business operations;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any product candidates that we may develop.

We currently hold limited product liability insurance coverage. We will need to purchase additional product liability insurance coverage as we expand our clinical trials, and if we commence commercialization of our product candidates. 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. A successful product liability claim or series of claims brought against us, could decrease our cash and adversely affect our business and financial condition.

***We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations that can harm our business.***

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

**Risks Related to Our Common Stock**

***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for holders of our common stock.***

Our stock price has been and is likely to continue to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- results of preclinical studies or clinical trials of our product candidates or those of our competitors;
- unanticipated or serious safety concerns related to the use of any of our product candidates;
- adverse regulatory decisions, including failure to receive regulatory approval for any of our product candidates;
- the success of competitive drugs or technologies;
- regulatory or legal developments in the United States and other countries applicable to our product candidates;
- the size and growth of our prospective patient populations;
- developments concerning our collaborators, our external manufacturers or in-house manufacturing capabilities;
- inability to obtain adequate product supply for any product candidate for preclinical studies, clinical trials or future commercial sale or inability to do so at acceptable prices;
- 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 drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts or publications of research reports about us or our industry;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the biotechnology sector;
- our cash position or the announcement or expectation of additional financing efforts;
- health pandemics could adversely impact our business, including our clinical trials and clinical trial operations;
- general economic, industry and market conditions, including fluctuating interest rates, tariffs, market volatility, a potential federal government shutdown and inflation;
- general economic uncertainty and capital markets disruptions, which has been substantially impacted by geopolitical instability due to the ongoing military conflicts around the world; and
- other factors, including those described in this “Risk Factors” section, many of which are beyond our control.

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

We have never declared or paid any cash dividends on our common stock and do not currently intend to do so for the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will be limited to the appreciation of stock. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in value of the stock. We cannot guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased their shares.

***If we fail to establish and maintain proper and effective internal control over financial reporting in the future, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.***

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting within our Form 10-K. However, while we remain a smaller reporting company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be frequently evaluated. Our failure to maintain the effectiveness of our internal controls in accordance with the requirements of the Sarbanes-Oxley Act could have a material adverse effect on our business. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

We may hire additional personnel and may utilize external temporary resources to implement, document and modify policies and procedures to maintain effective internal controls. However, it is possible that we may identify deficiencies and weaknesses in our internal controls. If material weaknesses or deficiencies in our internal controls exist and go undetected or unremediated, our financial statements could contain material misstatements that, when discovered in the future, could cause us to fail to meet our future reporting obligations and cause the price of our common stock to decline.

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

As a public company we will continue to incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. We are a "smaller reporting company," and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We are a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We will continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million. We may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and have reduced disclosure obligations regarding executive compensation.

***The exclusive forum provisions in our restated certificate of incorporation and amended and restated bylaws may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims.***

Our restated certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware will be the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, or the DGCL, our restated certificate of incorporation, or our restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, or the Exchange Act. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum

provision and asserts claims under the Securities Act, inasmuch as Section 22 of the Securities Act, creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. There is uncertainty as to whether a court would enforce such provision with respect to claims under the Securities Act, and our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

Our amended and restated bylaws also provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or a Federal Forum Provision. Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While there can be no assurance that federal or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court.

These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our restated certificate of incorporation or amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations and financial condition.

In addition, Section 203 of the DGCL may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on mergers, business combinations and other transactions between us and holders of 15% or more of our common stock.

***Provisions in our corporate charter documents and under 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 restated certificate of incorporation and our restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also 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 so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our restated certificate of incorporation and restated bylaws;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan, also known as a "poison pill";
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

Moreover, we are governed by the provisions of Section 203 of the DGCL, 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.

Any of these provisions of our charter documents or Delaware law could, under certain circumstances, depress the market price of our common stock.

**General Risk Factors**

***We may be subject to securities litigation, which could result in substantial expenses and could divert management attention.***

The market price of our common stock has been and may continue to be volatile. The stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

***If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.***

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. We do not have any control over the analysts, or the content and opinions included in their reports. If one or more of the analysts covering our business downgrades their evaluations of our stock, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***We are subject to a variety of privacy and data security laws, and our failure to comply with them could harm our business.***

We maintain a large quantity of sensitive information, including confidential business and personal information in connection with the operation of our business, and are subject to laws and regulations governing the privacy and security of such information. We also process personal information in connection with clinical trials and research activities, including data subject to heightened contractual, ethical, and regulatory expectations.

In the United States, there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including federal and state health information privacy laws, federal and state security breach notification laws, and federal and state consumer protection laws. Each of these constantly evolving laws can be subject to varying interpretations. Additionally, the SEC and many jurisdictions have enacted or may enact laws and regulations requiring companies to disclose or otherwise provide notifications regarding data security breaches. For example, the SEC adopted cybersecurity risk management and disclosure rules, which require the disclosure of information pertaining to cybersecurity incidents and cybersecurity risk management, strategy, and governance. In addition, states are constantly adopting new laws or amending existing laws, requiring attention to frequently changing regulatory requirements with inconsistent or conflicting standards.

For example, California has enacted the CCPA, which became operative on January 1, 2020 and became enforceable by the California Attorney General on July 1, 2020. Additionally, the California Privacy Rights Act, or CPRA, which expands upon the CCPA, became effective on January 1, 2023. The CCPA and CPRA require covered companies to, among other things, provide new disclosures to California residents, and affords such residents new privacy rights such

as the ability to opt-out of certain sales of personal information and expanded rights to access and require deletion of their personal information, opt-out of certain personal information sharing, and receive detailed information about how their personal information is collected, used, and shared. The CCPA and CPRA provide for civil penalties for violations, as well as a private right of action for security breaches that may increase security breach litigation. Potential uncertainty surrounding the CCPA and CPRA may increase our compliance costs and potential liability, particularly in the event of a data breach, and could have a material adverse effect on our business, including how we use personal information, our financial condition, the results of our operations or prospects. Virginia's Consumer Data Protection Act, which took effect on January 1, 2023, requires opt-in consent from consumers to acquire and process their sensitive personal information, which includes information revealing a consumer's physical and mental health diagnosis and genetic and biometric information that can identify a consumer.

Other states have passed similar laws, and a number of other states are actively considering bills with similar laws. To the extent multiple state-level laws are later introduced, it may require costly and difficult efforts to achieve compliance with such laws that could expose us to fines and penalties for non-compliance.

In the European Economic Area, or the EEA, the General Data Protection Regulation, or the GDPR, governs the collection, use, disclosure, transfer or other processing of personal data of European persons. Among other things, the GDPR imposes requirements regarding the security of personal data and notification of data processing obligations to the competent national data processing authorities, changes the lawful bases on which personal data can be processed, expands the definition of personal data and requires changes to informed consent practices, as well as more detailed notices for clinical trial subjects and investigators. In addition, the GDPR increases the scrutiny of transfers of personal data from clinical trial sites located in the EEA to the United States and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws (sometimes referred to as "third countries"), and imposes strict rules subject to substantial fines for breaches and violations (up to the greater of €20 million or 4% of our annual worldwide gross revenue). These obligations may be interpreted and applied in a manner that is inconsistent from one jurisdiction to another and may conflict with other requirements or our practices.

Additionally, in the United Kingdom, or U.K., the Data Protection Act contains provisions, including its own derogations, for how GDPR is applied in the U.K. We have to continue to comply with the GDPR and also the U.K.'s Data Protection Act, with each regime having the ability to fine up to the greater of €20 million (£17.5 million) or 4% of global turnover.

As of January 1, 2024, although effective July 10, 2023, the new EU-U.S. Data Privacy Framework, or DPF, has been recognized as adequate under EU law to allow transfers of personal data from the EU (as well as the U.K. and Switzerland) to certified companies in the U.S. However, the DPF is likely to face legal challenge at the Court of Justice of the European Union which could cause the legal requirements for personal data transfers from Europe to the U.S. to become uncertain once again. We will monitor these legal developments and continue to use best practices to follow established European legal standards to conduct cross-border transfer of personal data.

In addition, while the Court of Justice of the European Union upheld the adequacy of the standard contractual clauses (a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism, and potential alternative to the Privacy Shield), it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Use of the standard contractual clauses must now be assessed on a case-by-case basis, taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals. The use of standard contractual clauses for the transfer of personal data specifically to the United States remains under review by a number of European data protection supervisory authorities, along with those of some other EU member states. Certain European Data Protection Authorities, including German and Irish supervisory authorities, have questioned whether standard contractual clauses, without supplementary measures, provide sufficient protection for certain cross-border transfers, including to the United States. Further, on June 4, 2021, the European Commission finalized new versions of the Standard Contractual Clauses, with the Implementing Decision now in effect as of June 27, 2021. To comply with the Implementing Decision and the new Standard Contractual Clauses, we may need to implement additional safeguards to further enhance the security of data transferred out of the EEA, conduct data transfer impact assessments, and review existing agreements which could increase our compliance costs, expose us to further regulatory scrutiny and liability, and adversely affect our business. The new standard contractual clauses apply only to the transfer

of data outside of the EEA and/or Switzerland and not the United Kingdom, though the U.K.'s Information Commissioner's Office launched a public consultation on its draft international data transfer agreement in August 2021, and subsequently issued a new international data transfer agreement and addendum which we are required to use under Article 46 of the U.K. GDPR when making restricted data transfers outside of the U.K.

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 these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations. Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly.

We generally seek to comply with industry standards and are subject to the terms of our privacy policies and privacy-related obligations to third parties. We seek to comply with applicable laws and contractual obligations, relating to privacy and data protection. However, it is possible that these obligations may be interpreted and applied in a manner that is inconsistent from one jurisdiction to another and may conflict with other rules or our practices. Any failure or perceived failure by us, even if unfounded, to comply with applicable privacy and data security laws and regulations, our privacy policies, or our privacy-related obligations to users or other third parties, or any compromise of security that results in the unauthorized release or transfer of personal information or other sensitive data, may result in governmental enforcement actions, litigation, or public statements against us by consumer advocacy groups or others and could cause our users to lose trust in us, which would have an adverse effect on our reputation and business.

Any significant change to applicable laws, regulations or industry practices regarding the use or disclosure of our users' data, or regarding the manner in which the express or implied consent of users for the use and disclosure of such data is obtained – or in how these applicable laws, regulations or industry practices are interpreted and enforced by state, federal and international privacy regulators – could require us to modify our practices, possibly in a material manner, may subject us to regulatory enforcement actions and fines, and may limit our ability to operate using the data that was voluntarily shared with us.

***Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.***

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets, and, in recent months, the global economy has been impacted by fluctuating interest rates, tariffs, and inflation. Likewise, the capital and credit markets may be adversely affected by ongoing military conflicts around the world, global sanctions imposed in response thereto, and potential recessions. Moreover, we may also be impacted by turmoil in the global banking system. We regularly maintain cash balances at third-party financial institutions in excess of the FDIC insurance limit and there is no guarantee that the federal government would guarantee all depositors if such financial institutions were to fail, in the event of bank closures and continued instability in the global banking system. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

***We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that damaged critical infrastructure, such as our manufacturing facilities, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. In addition, the long-term effects of climate change on general economic conditions and the pharmaceutical industry in particular are unclear, and may heighten or intensify existing risk of natural disasters. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

**Item 1B.** ***Unresolved Staff Comments***

None

**Item 1C.** ***Cybersecurity***

We maintain a cybersecurity risk management program designed to identify, assess, and manage material risks arising from cybersecurity threats. Our program incorporates elements of widely adopted industry cybersecurity frameworks standards and includes processes for threat monitoring, vulnerability and patch management, incident detection and response, security awareness training, and business continuity planning.

Our information systems support clinical trial operations, research and development activities, manufacturing collaborations, and corporate functions and include sensitive clinical data, research data, and intellectual property.

We conduct periodic risk assessments to evaluate emerging threats and potential impacts to our research, clinical, manufacturing, and corporate systems. These assessments inform our technical and administrative safeguards, which include identity and access controls, network segmentation, encryption, logging, and continuous monitoring. We also maintain an incident response plan and conduct tabletop exercises to evaluate readiness.

*Risk Management and Strategy*

As one of the critical elements of the Company's overall risk management and compliance approach, the Company's cybersecurity program is focused on the following key areas:

**Governance**: The board of directors' oversight of cybersecurity risk management is led by the Audit Committee of the board of directors, which regularly interacts with our Chief Compliance Officer, our Chief Financial Officer, and other members of management.

**Collaborative Approach**: We have implemented a comprehensive, cross-functional approach for monitoring, identifying, preventing, detecting, and mitigating cybersecurity threats and incidents, while also implementing controls and procedures that provide for the prompt escalation of cybersecurity incidents so that decisions regarding the public disclosure and reporting of such incidents can be made by management in a timely manner.

**Administrative Safeguards**: We maintain a comprehensive set of administrative safeguards designed to govern the oversight, implementation, and continuous improvement of our cybersecurity program. These safeguards include detailed policies and procedures and ongoing employee training to ensure security is embedded in daily activities. We engage in periodic assessment of our policies, standards, processes and practices that are designed to address cybersecurity threats and incidents. These efforts include a wide range of activities, including audits, assessments, vulnerability testing and other exercises focused on evaluating the effectiveness of our cybersecurity program and corresponding controls. The results of such assessments, audits and reviews are reported to the Audit Committee and the board of directors, and we adjust our cybersecurity policies, standards, processes and practices as necessary based on the insights gained from the assessments, audits and reviews.

**Technical Safeguards**: We maintain a layered set of technical safeguards to protect the confidentiality, integrity, availability, and privacy of our systems and data. Key controls include firewalls, network segmentation, intrusion detection and prevention, multi-factor authentication, encryption, anti-malware, endpoint protection, real-time threat intelligence and mitigation, and 24/7 logging, monitoring, and response.

**Incident Response and Recovery Planning**: We have established and maintain comprehensive incident response and recovery plans to address our response to a cybersecurity incident, and such plans are tested and evaluated on a regular basis.

**Third-Party Risk Management**: We maintain a risk-based approach to identifying and overseeing cybersecurity risks presented by third parties, including vendors, contract research organizations, contract development

and manufacturing organizations, technology service providers and other third parties that could adversely impact our business in the event of a cybersecurity incident affecting those third-party systems.

**Education and Awareness**: We provide regular, mandatory training for personnel regarding cybersecurity threats as a means of providing our employees with effective tools to address cybersecurity threats, and to communicate our evolving information security policies, standards, processes and practices. We also perform periodic email phishing tests to keep cybersecurity awareness top of mind.

*Governance*

The board of directors, with leadership from the Audit Committee, oversees our cybersecurity risk management process. The Audit Committee receives regular presentations and reports on cybersecurity risks, which address a wide range of topics including recent developments, evolving standards, vulnerability assessments, the threat environment, technological trends and information security considerations arising with respect to our peers and third parties. The board of directors and the Audit Committee also receive prompt and timely information regarding any cybersecurity incident that meets established escalation and materiality thresholds consistent with applicable SEC reporting requirements, as well as ongoing updates regarding any such incident until it has been addressed. On a periodic basis, the board of directors, through the Audit Committee, discuss our approach to cybersecurity risk management with management.

Our management team has implemented a program designed to protect our information systems from cybersecurity threats and to promptly respond to any cybersecurity incidents in accordance with our incident response and recovery plans. Through ongoing communications with our entire employee base and appropriate third-party contractors, the management team oversees the prevention, detection, mitigation and remediation of cybersecurity threats and incidents through risk-based monitoring and periodic reporting to the Audit Committee when appropriate.

Our enterprise risk management team consists of the Executive team and cross-functional professionals who collaborate with subject matter specialists, as necessary, including an independent third-party expert we have retained to identify and assess material risks from cybersecurity threats, their severity, and potential mitigation steps. Technical experts at our Managed Security Services Provider, or MSSP, also provide technical support and monitoring services under the oversight of management of our Company cybersecurity program, leveraging real-time threat intelligence and mitigation tools.

As of the date of this filing, we have not experienced a cybersecurity incident that we have determined to be material to our business, operations, or financial condition. However, we continue to monitor and enhance our cybersecurity capabilities in response to evolving threats.

**Item 2.** ***Properties***

Our principal executive office is located in Philadelphia, Pennsylvania, where we lease a total of approximately 37,000 square feet of office space, or the 2005 Market Street Lease Agreement, which commenced in February 2021 and will expire in December 2031, subject to our option to extend the term of the lease by up to two additional five-year terms. In August 2023 and September 2023, we entered into two sublease agreements, for certain periods of time, which subleased substantially all of our office space under the 2005 Market Street Lease Agreement.

Our Philadelphia employee base has transitioned to remote working arrangements.

We also lease approximately 62,000 square feet of laboratory space at the Princeton West Innovation Campus in Hopewell, New Jersey, or the Laboratory Lease Agreement. This lease has a 15-year term from the lease commencement date of March 2021. In September 2024, we entered into a sublease agreement through December 2029, which subleased approximately 3,200 square feet, or 5%, of our laboratory space under the Laboratory Lease Agreement. The subtenant has the option to extend the term of the lease by three additional years. In January 2025, we implemented a restructuring plan which included ceasing lab operations. As a result, we are no longer using any of the space covered by the Laboratory Lease Agreement and are actively pursuing opportunities to sublease all remaining space in the Laboratory Lease Agreement as well as discussing with the landlord potential alternatives.

We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

**Item 3.** ***Legal Proceedings***

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business.

We are the defendant in litigation with a former employee, who filed a lawsuit in the Court of Common Pleas of Philadelphia County asserting claims for breach of contract and violation of the Pennsylvania Wage Payment and Collection Law. The plaintiff, who was terminated from their employment in 2019, contended that we entered into a binding settlement agreement in February 2020 under which he was to receive shares of company stock and additional compensation. Specifically, he contended that before the announcement of our initial public offering in February 2020, he was promised 150,000 shares of stock as part of the settlement, and that those shares were not subject to the reverse stock split that was implemented for all shareholders. We responded that the shares offered in settlement negotiations in 2020 were to be subject to the reverse split, and that had the settlement been finalized, the plaintiff would have been entitled to 33,836 shares (1,692 shares adjusted for the Reverse Stock Split effected in 2025). A trial in this case was held in October 2024. The jury found that an agreement was reached, but it agreed with us that any shares to be awarded to the plaintiff were subject to the reverse split. The jury awarded damages in an amount that was roughly equal to what we contended had been offered to the plaintiff before the initial public offering. Both sides then challenged the verdict, and on December 12, 2024, the judge who presided over the trial delivered a judgment in our favor, finding that no binding agreement was reached and that the plaintiff was not entitled to recover any damages. On December 23, 2024, the plaintiff filed an appeal with the Superior Court of Pennsylvania. On September 25, 2025, the appellate court affirmed the entry of judgment in favor of the Company and on October 7, 2025, the plaintiff filed an Application for Reargument to the Superior Court of Pennsylvania. In December 2025, the Superior Court of Pennsylvania denied the Application for Reargument. In December 2025, the plaintiff petitioned for review of their appeal to the Pennsylvania Supreme Court which is currently pending. We intend to continue to defend against this claim.

Other than the above, we are not presently a party to any legal proceedings that, in the opinion of management, would, if decided against us, have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm, and other factors.

**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*

**Market Information for Common Stock**

Our common stock has been listed on The Nasdaq Capital Market under the symbol "PASG" since January 30, 2025. From February 28, 2020 to January 29, 2025 our common stock was listed on The Nasdaq Global Select Market under the symbol "PASG."

**Holders of Record**

As of February 26, 2026, there were approximately 26 stockholders 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.

**Dividend Policy**

We currently intend to retain future earnings, if any, for use in operation of our business and to fund future growth. We have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. Payment of cash dividends, if any, in the future will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

**Unregistered Sales of Equity Securities**

None.

**Use of Proceeds from Registered Securities**

None.

**Purchases of Equity Securities by the Issuer and Affiliated Purchasers**

None.

### Item 6. *[Reserved]*

Not Applicable.

## 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 in conjunction with our financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. In addition to historical financial information, this discussion and analysis contains forward-looking statements based upon current expectations that involve risks and uncertainties, such as statements of our plans, objectives, expectations, intentions and beliefs. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth in the section titled "Risk Factors" under Item 1A above.*

### Overview

We are a clinical stage genetic medicines company focused on improving the lives of patients with neurodegenerative diseases. Our primary focus is the development and advancement of cutting-edge, one-time therapies designed to target critical underlying pathology in these conditions.

We were incorporated in July 2017 under the laws of the State of Delaware. Since inception, our operations have consisted primarily of conducting preclinical studies, developing licensed technology, conducting clinical trials, and manufacturing clinical supply to support clinical trials. We have incurred recurring losses, the majority of which are attributable to research and development activities, and negative cash flows from operations. Historically, we have funded our operations through the sale of convertible preferred stock and public offerings of common stock. Our net losses were $45.5 million and $64.8 million for the years ended December 31, 2025 and 2024, respectively. As of December 31, 2025, we had an accumulated deficit of $704.8 million. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures and general and administrative expenditures. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance our product candidates through all stages of development and clinical trials and, ultimately, seek regulatory approval. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

We will need to raise substantial additional capital to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we plan to finance our operations through the sale of equity, debt financings or other capital sources, which may include collaborations with other companies or other strategic transactions. There are no assurances that we will be successful in obtaining an adequate level of financing as and when needed to finance our operations on terms acceptable to us or at all. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to secure adequate additional funding, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more product candidates or delay our pursuit of potential in-licenses or acquisitions.

As of December 31, 2025, we had cash and cash equivalents of $46.3 million. We expect our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements through the end of the first quarter of 2027.

**Financial Operations Overview**

***License Agreements***

*University of Pennsylvania*

As a result of the Outlicense Transaction Agreements, as discussed below, we restructured our research, collaboration and licensing agreement with the Trustees of the University of Pennsylvania, or Penn, as amended, previously the Penn Agreement and now referred to as the Penn License Agreement. Pursuant to the Penn License Agreement, as of July 31, 2024, we (i) terminated the funding of discovery research programs; (ii) terminated the research and exploratory research programs; (iii) terminated the remaining eight options we had for future central nervous system, or CNS, indications; (iv) terminated the transaction fee payable to Penn in the event of certain corporate transactions; and (v) retained our current exclusive and non-exclusive licenses to our programs in FTD, GM1, Krabbe, and MLD, and certain platform technologies resulting from the discovery programs that we funded.

For our licensed programs in FTD, GM1, Krabbe and MLD, the Penn License Agreement requires that we make payments of up to $16.5 million per product candidate. Each payment will be due upon the achievement of specific development milestone events by such licensed product for a first indication, reduced development milestone payments for the second and third indications and no development milestone payments for subsequent indications. In addition, on a product-by-product basis, we are obligated to make up to $55.0 million in sales milestone payments on each licensed product based on annual worldwide net sales of the licensed product in excess of defined thresholds. Pursuant to the Amended Gemma Sublicenses, as discussed below, Gemma Biotherapeutics, Inc., or Gemma, is responsible for the payments to Penn related to GM1, Krabbe and MLD, collectively the Outlicensed Programs.

Upon successful commercialization of a product using the licensed technology, we are obligated to pay to Penn, on a licensed product-by-licensed product and country-by-country basis, tiered royalties (subject to customary reductions) in the mid-single digits percentage on annual worldwide net sales of such licensed product. In addition, other than the Amended Gemma Sublicenses, we are obligated to pay to Penn a percentage of sublicensing income, ranging from the mid-single digits to low double digits, for sublicenses under the Penn License Agreement. The agreement will expire on a licensed product-by-licensed product and country-by-country basis upon the later of (i) the expiration of the last valid claim of the licensed patent rights that covers the exploitation of such licensed product in such country, and (ii) the expiration of the royalty period. Pursuant to the Amended Gemma Sublicenses, Gemma is responsible for the payments to Penn related to the Outlicensed Programs.

*Gemma - Research, Collaboration and License Agreement*

In connection with the transfer of the Outlicensed Programs, on July 31, 2024, we entered into a research, collaboration and license agreement with Gemma, or the Gemma Collaboration Agreement. Pursuant to the Gemma Collaboration Agreement, (i) Gemma will conduct certain preclinical and IND application enabling work for our active research program in Huntington's disease and a currently paused research program in Temporal Lobe Epilepsy, or TLE, which were previously being conducted by Penn under the Penn Agreement and (ii) Gemma will grant us options to conduct mutually agreed research programs in four new CNS indications.

The Gemma Collaboration Agreement requires that we make payments of up to (i) $16.5 million per product candidate in the aggregate for Huntington's disease and any future CNS indications available to us under our four options and (ii) $39.0 million per product candidate in the aggregate arising from the research program for TLE. Each payment will be due upon the achievement of specific development milestone events by such licensed product for a first indication, reduced development milestone payments for the second and third indications and no development milestone payments for subsequent indications. In addition, on a product-by-product basis, we are obligated to make up to $55.0 million in sales milestone payments on each licensed product based on annual worldwide net sales of the licensed product in excess of defined thresholds.

Upon successful commercialization of a product using the licensed technology, we are obligated to pay to Gemma, on a licensed product-by-licensed product and country-by-country basis, tiered royalties (subject to customary reductions) in

the mid-single digits percentage on annual worldwide net sales of such licensed product. In addition, we are obligated to pay to Gemma a percentage of sublicensing income, ranging from the mid-single digits to low double digits, for sublicenses under the Gemma Collaboration Agreement. The agreement will expire on a licensed product-by-licensed product and country-by-country basis upon the later of (i) the expiration of the last valid claim of the licensed patent rights that covers the exploitation of such licensed product in such country, and (ii) the expiration of the royalty period.

If we were to exercise any of the four options, we would owe Gemma a non-refundable aggregate fee of $1.0 million per product indication, with $0.5 million due upfront and another $0.5 million fee owed upon a further developmental milestone.

*Gemma - Sublicense Agreements and Transition Services Agreement*

In connection with the transfer of the Outlicensed Programs to Gemma, in July 2024, we entered into the Gemma Sublicenses. On May 7, 2025, we agreed to amend each of the Gemma Sublicenses to revise certain financial terms related to the Outlicensed Programs, or the Amended Gemma Sublicenses. Pursuant to the Amended Gemma Sublicenses, we are entitled to receive (i) an aggregate total of $15.0 million in initial payments for licenses and clinical product supply, of which $7.5 million was previously received, $2.5 million of which was due in May 2025, and $5.0 million of which is due in March 2026; (ii) an additional $5.0 million contingent on Gemma completing certain business milestones; (iii) up to an additional $114.0 million in development and commercial milestone payments; and (iv) single digit royalties as a percentage of annual worldwide net sales in exchange for sublicenses to relevant intellectual property, transfer of regulatory dossiers and transfer of clinical trial materials and product supply related to the Outlicensed Programs. In addition, Gemma is responsible for all payments to Penn related to the Outlicensed Programs under the Penn License Agreement.

In addition, we entered into the Transition Services Agreement, as amended by the First Amendment to the Transition Services Agreement, dated January 31, 2025, pursuant to which, we provided transitional services at cost to Gemma through May 31, 2025, and are entitled to reimbursement for transitional services performed retroactively from March 1, 2024, related to the transfer of the Outlicensed Programs. As of December 31, 2025, we have collected $7.5 million in initial payments and $4.8 million in transition services payments under these agreements. In addition, we have applied $1.5 million in amounts owed to Gemma for the Huntington's disease program against amounts due to us for transition services.

We refer to the Amended Gemma Sublicenses, the Transition Services Agreement, and the Gemma Collaboration Agreement, collectively, as the Outlicense Transaction Agreements.

***Collaboration and Manufacturing and Supply Agreements***

*Catalent*

We have entered into a collaboration agreement, and a development services and clinical supply agreement, or the Amended Catalent Agreements, with Catalent Maryland, a unit of Catalent, Inc. acquired by Novo Holdings A/S, or Catalent, to secure clinical scale manufacturing capacity for batches of active pharmaceutical ingredients for our gene therapy product candidates. Under the terms of the Amended Catalent Agreements, Catalent agreed to manufacture batches of drug product for our gene therapy product candidates.

The Amended Catalent Agreements remain in effect until November 6, 2030, and establish a limited exclusive relationship between us and Catalent for the manufacture of bulk drug substance and drug product for our adeno-associated virus delivery therapeutic product candidates for the treatment of FTD and GM1. The limited exclusive relationship under the Amended Catalent Agreements converts to a non-exclusive relationship (i) in the event Catalent fails to meet certain performance standards and (ii) following certain conditional events related to the divestiture by us of either FTD or GM1, in which case, if such events occur, we would pay Catalent certain fees. In the event of certain transactions, we may terminate the Amended Catalent Agreements for convenience with respect to such products, in which case, we would pay Catalent a certain termination fee.

The outlicense and completed transition of GM1 to Gemma under the Outlicense Transaction Agreements is deemed by Catalent to be a divestiture under the Amended Catalent Agreements. As such, we are required to make payment of $0.9 million to Catalent which has been accrued as of and during the year ended December 31, 2025.

**Components of Results of Operations**

*Research and Development*

Research and development expenses consist primarily of costs incurred in connection with the development of our product candidates. These expenses include:

- personnel expenses, including salaries, benefits and share-based compensation expense for employees engaged in research and development functions;
- expenses incurred at and for our lab facilities, including rent, utilities, depreciation, amortization, and maintenance;
- expenses incurred to conduct the necessary preclinical studies and clinical trials required to obtain regulatory approval, including payments to clinical research organizations, or CROs, and payments to Gemma and Penn for preclinical research and development;
- expenses and fees paid to consultants who assist with research and development activities; and
- expenses incurred under agreements with contract development and manufacturing organizations, or CDMOs, including the cost of acquiring and manufacturing preclinical trial and clinical trial materials.

We track outsourced development expenses and other external research and development expenses to specific product candidates on a program-by-program basis, such as fees paid to CROs, CDMOs and research laboratories in connection with our preclinical development, process development, manufacturing and clinical development activities, expenses incurred under our prior collaboration with Penn, and expenses incurred under the Gemma Collaboration Agreement. However, we do not track our internal research and development expenses on a program-by-program basis as they primarily relate to compensation, lab operations and lab facility costs, and other expenses which are deployed across multiple projects under development.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development expenses than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

We expect the reduction of expenses related to the Outlicensed Programs pursuant to the Outlicense Transaction Agreements will offset the increased expenses of advancing our remaining product candidates. As such, we expect our research and development expenses to remain consistent in the near future. If our product candidate portfolio progresses into later-stage clinical trials, we expect that our research and development expenses will increase in the future to support continued research and development activities and production of clinical supply.

*General and Administrative Expenses*

General and administrative expenses consist primarily of personnel expenses, including salaries, benefits and share-based compensation expense, for employees and consultants in executive, finance, accounting, legal, information technology, product strategy, quality, regulatory, operations and human resource functions. General and administrative expenses also include professional and consulting services, headquarters facility costs, including rent, utilities, depreciation, amortization and maintenance, legal expenses related to intellectual property, litigation and corporate matters, insurance expense, expenses related to contract modifications or terminations, software expenses, expenses incurred to engage with patient advocacy organizations, and recruitment related expenses. We expect our general and administrative expenses to remain consistent in the near future.

If our product candidate portfolio progresses into later-stage clinical trials, we expect that our general and administrative expenses will increase in the future to support our continued research and development activities and potential commercialization efforts. These increases will likely include increased expenses related to the hiring of additional

personnel in general and administrative functions, and expenses related to pre-commercialization efforts. If any of our current or future product candidates obtain regulatory approval, we expect that we would incur significantly increased expenses associated with building a commercial sales and marketing team.

*Impairment of Long-Lived Assets*

Impairment of long-lived assets consists of non-cash impairment charges recorded to our assets. We review long-lived assets, such as the right of use assets, or ROU assets, or property and equipment, for impairments when events or changes in circumstances indicate the carrying amount of the assets may not be recoverable. During the year ended December 31, 2025, we recognized impairment expenses related to the ROU assets, property and equipment, net, and certain other assets.

As a result of the announcement in January 2025 to reduce our workforce by 55% and cease our lab operations in Hopewell, New Jersey, we reassessed asset groups and evaluated such asset groups for impairment. We determined the laboratory equipment was a separate asset group based on management's implemented plans to sell the laboratory equipment and estimated the fair value of the laboratory equipment based on the estimated future cash flows from the sale of such equipment.

In December 2025, we determined an impairment indicator was present for the asset groups related to the Laboratory Lease Agreement at Hopewell, New Jersey. We compared the estimated total future undiscounted cash flows to the carrying values, which includes ROU assets and leasehold improvements allocable to the laboratory space for those asset groups. We concluded the carrying value was not recoverable for one asset group as it exceeded the estimated undiscounted cash flows.

*Other Income (Expense), Net*

Other income (expense), net consists of interest earned on our cash equivalents and marketable securities, amortization of premium and discount on our marketable securities, income from subleases, and the sale of certain tax credits.

***Results of Operations***

*Comparison of the Years Ended December 31, 2025 and 2024*

The following table sets forth our results of operations for the years ended December 31, 2025 and 2024.

| | Year ended December 31, | | |
|---|---|---|---|
| **(in thousands)** | **2025** | **2024** | **Change** |
| Operating expenses: | | | |
| Research and development | $ 23,276 | $ 40,179 | $ (16,903) |
| General and administrative | 19,875 | 24,988 | (5,113) |
| Impairment of long-lived assets | 6,145 | 5,233 | 912 |
| Loss from operations | (49,296) | (70,400) | 21,104 |
| Other income (expense), net | 3,774 | 5,633 | (1,859) |
| Net loss | $ (45,522) | $ (64,767) | $ 19,245 |

*Research and Development Expenses*

Research and development expenses decreased by $16.9 million to $23.3 million for the year ended December 31, 2025 from $40.2 million for the year ended December 31, 2024. The decrease was primarily due to the following:

- a decrease of $4.8 million in wages and benefits due to a lower headcount from our restructuring in January 2025;

- a decrease of $3.7 million in preclinical research expenses primarily related to the termination of our discovery research obligation under the Penn Agreement and reduced Huntington's disease program expenses;
- a decrease of $2.6 million in facility and other expenses related primarily to decreased depreciation expenses in connection with the disposal of our laboratory equipment;
- a decrease of $1.9 million in chemistry, manufacturing and control expenses primarily related to reduced costs in connection with the restructuring and ceased operations of the lab in Hopewell, New Jersey;
- a decrease of $1.7 million in share-based compensation expense related to reductions in headcount;
- a decrease of $1.3 million in professional fees and consulting expenses; and
- a decrease of $0.9 million in clinical operations expenses due to decreased activity in the GM1 program partially offset by increased activity supporting the FTD program.

*General and Administrative Expenses*

General and administrative expenses decreased by $5.1 million to $19.9 million for the year ended December 31, 2025 from $25.0 million for the year ended December 31, 2024. The decrease was primarily due to the following:

- a decrease of $2.6 million in professional fees and consulting expenses;
- a decrease of $1.5 million and $1.1 million in wages and benefits and share-based compensation expense, respectively, related to reductions in headcount; and
- a decrease of $0.8 million in facility and other expenses.

The decrease was partially offset by:

- an increase of $0.9 million in accruals for the GM1 divestiture fee due to Catalent.

*Impairment of Long-Lived Assets*

During the year ended December 31, 2025, we recorded $6.1 million of impairment expenses related to the Hopewell laboratory space. The impairment charges consisted of $2.6 million of impairment expenses related to laboratory equipment and certain other assets which were revalued and subsequently sold in March 2025; and $2.6 million and $0.9 million related to ROU assets and leasehold improvements, respectively, in connection with impairment testing in December 2025.

During the year ended December 31, 2024, we recorded $5.2 million of impairment expenses related to the Hopewell laboratory space. The impairment charges consisted of $2.5 million and $2.3 million recorded to the ROU assets and property and equipment, net, respectively. In addition, we recorded $0.4 million of impairment expenses related to property and equipment for certain other assets we no longer planned to deploy.

*Other Income (Expense), net*

Other income (expense), net decreased by $1.8 million to $3.8 million for the year ended December 31, 2025 from $5.6 million for the year ended December 31, 2024. The decrease was primarily due to the following:

- a decrease of $2.0 million attributable to interest income and the amortization of premium and discount on our marketable securities; and
- a decrease of $0.3 million related to the sale of certain tax credits in 2024.

These decreases were partially offset by:

- an increase of $0.5 million attributable to income from subleases.

***Liquidity and Capital Resources***

*Overview*

As of December 31, 2025, we had $46.3 million in cash and cash equivalents and had an accumulated deficit of $704.8 million. We expect our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements through the end of the first quarter of 2027.

*Funding Requirements*

Our primary use of cash is to fund operating expenses, most significantly research and development expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable, accrued expenses and prepaid expenses.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, timing, progress and results of discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the expenses of manufacturing our product candidates for clinical trials and in preparation for marketing approval and commercialization;
- the extent to which we enter into collaborations or other arrangements with additional third parties in order to further develop our product candidates;
- the expenses of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the expenses and fees associated with the discovery, acquisition or in-license of additional product candidates or technologies;
- the expenses related to general and administrative functions to support our product candidates;
- our ability to establish additional collaborations on favorable terms, if at all;
- the expenses required to scale up our clinical, regulatory and manufacturing capabilities;
- the expenses of future commercialization activities, if any, including establishing sales, marketing, manufacturing and distribution capabilities, for any of our product candidates for which we receive marketing approval; and
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval.

We will need additional funds to meet operational needs and capital requirements for clinical trials, other research and development expenditures, and business development activities. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical studies.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, existing stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect existing stockholders' rights as common stockholders. 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, making acquisitions or capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing,

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

On March 5, 2021, we entered into a Sales Agreement, or the Sales Agreement, with Cowen and Company, LLC, or Cowen, relating to the applicable terms of at-the-market equity offerings, or the ATM Facility, pursuant to which we may, but are not obligated to, offer and sell, from time to time, shares of our common stock with an aggregate offering price up to $125.0 million through Cowen, as sales agent in the ATM Facility. We issued 300,000 shares of common stock under the ATM Facility, resulting in net proceeds of $8.7 million, after deducting offering costs of $0.3 million in March 2024. As a result of our public float, we are currently limited in our capacity to offer and sell shares of our common stock under the Sales Agreement pursuant to the prospectus supplement to our shelf registration statement on Form S-3, filed on March 5, 2025.

*Cash Flows*

The following table shows a summary of our cash flows for the periods indicated:

| | Year ended December 31, | |
|---|---|---|
| **(in thousands)** | **2025** | **2024** |
| Cash provided by (used in) operating activities | $ (31,509) | $ (47,956) |
| Cash provided by (used in) investing activities | 40,216 | 54,946 |
| Cash provided by (used in) financing activities | 23 | 8,874 |
| Net increase (decrease) in cash and cash equivalents | $ 8,730 | $ 15,864 |

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

During the year ended December 31, 2025, we used $31.5 million of net cash in operating activities, primarily to fund our operations related to the development of our product candidates and related general and administrative support activities. Cash used in operating activities reflected our net loss of $45.5 million, which was partially offset by a net decrease in our operating assets of $4.0 million and net non-cash charges of $10.0 million primarily related to depreciation, amortization, share-based compensation, amortization of premium and discount, net, impairment of long-lived assets, and other non-cash items.

During the year ended December 31, 2024, we used $48.0 million of net cash in operating activities, primarily to fund our operations related to the development of our product candidates and related general and administrative support activities. Cash used in operating activities reflected our net loss of $64.8 million, which was partially offset by a net decrease in our operating assets of $4.2 million and net non-cash charges of $12.6 million primarily related to depreciation, amortization, share-based compensation, amortization of premium and discount, net, and impairment of long-lived assets.

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

During the year ended December 31, 2025, we had sales and maturities of $39.0 million in marketable securities and received $1.2 million related to the sale of property and equipment in connection with ceased operations of the lab in Hopewell, New Jersey.

During the year ended December 31, 2024, we purchased $88.2 million in marketable securities and had sales and maturities of $143.2 million in marketable securities.

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

During the year ended December 31, 2025, we received de minimis proceeds from the issuance of common stock under our Employee Stock Purchase Plan, or the ESPP.

During the year ended December 31, 2024, we received $8.7 million in net proceeds from the issuance of common stock under the ATM Facility. We received gross proceeds of $9.0 million, net of offering costs of $0.3 million. We received $0.2 million in proceeds from the issuance of common stock under the ESPP and exercises of employee stock options.

***Contractual Obligations and Other Commitments***

We lease approximately 37,000 square feet of office space in Philadelphia, Pennsylvania, or the 2005 Market Street Lease Agreement. The lease will expire in December 2031. We have an option to extend the term of the lease by up to two additional five-year terms. Our sublease agreements do not relieve us from our primary obligations under the 2005 Market Street Lease Agreement, however, we do expect cash inflows from the agreements to partially offset our future obligations for the duration of the sublease agreements.

We lease approximately 62,000 square feet of laboratory space in Hopewell, New Jersey, or the Laboratory Lease Agreement. The lease will expire in March 2036. Our sublease agreement does not relieve us from our primary obligations under the Laboratory Lease Agreement, however, we do expect cash inflows from the agreement to partially offset our future obligations for the duration of the sublease agreement.

The aggregate estimated rent payments due over the remaining terms of our leases are $37.3 million.

Under the exclusive relationship under the Amended Catalent Agreements, following certain conditional events related to the divestiture by us of either FTD or GM1, we would pay Catalent certain fees. In the event of certain transactions, we may terminate the Amended Catalent Agreements for convenience with respect to such products, in which case, we would pay Catalent a certain termination fee.

The outlicense and completed transition of GM1 to Gemma under the Outlicense Transaction Agreements, is deemed by Catalent to be a divestiture under the Amended Catalent Agreements. As such, we are required to make payment of $0.9 million to Catalent which has been accrued as of and during the year ended December 31, 2025.

These contractual obligations and commitments are associated with contracts that are enforceable and legally binding and that specify all significant terms, including fixed or minimum services to be used, fixed, minimum or variable price provisions, and the approximate timing of the actions under the contracts. Payments due upon cancellation consisting only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation are not included as the amount and timing of such payments are not known.

The contractual obligations and commitments above do not include any potential milestone or royalty payments that we may be required to make under the Penn License Agreement. Under the Amended Gemma Sublicenses, Gemma will be responsible for all potential milestone and royalty payments to Penn for the Outlicensed Programs.

The contractual obligations and commitments above do not include any potential milestone or royalty payments that we may be required to make under the Gemma Collaboration Agreement.

***Critical Accounting Policies and Estimates***

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to long-lived assets and accrued expenses. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be

reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 3 to our annual financial statements included elsewhere in this Form 10-K, we believe the following accounting policies are the most critical to the judgments and estimates used in the preparation of our financial statements.

*Long-Lived Assets*

We assess long-lived assets for impairment when events or changes in circumstances indicate that the carrying value of the assets or the asset group may not be recoverable. We measure the recoverability of assets that we will continue to use in our operations by comparing the carrying value of the asset groups to our estimate of the related total future undiscounted net cash flows. If an asset group's carrying value is not recoverable through the related undiscounted cash flows, the asset group is considered to be impaired.

In the event the carrying value exceeds the future undiscounted net cash flows, we estimate the fair values using either the income approach, market approach, or a combination of the two. The income approach is based on the present value of future cash flows of each asset group, while the market approach is based on industry and economic conditions, including estimates on prevailing prices and rates for similar assets. The approaches are asset group specific and may incorporate a number of market participant assumptions in assessing fair value including future growth rates, discount rates, and market activity. We measure the impairment by comparing the difference between the asset group's carrying value and its fair value. Long-lived assets are considered a non-financial asset and are recorded at fair value only if an impairment charge is recognized. Impairments are determined for groups of assets related to the lowest level of identifiable independent cash flows.

During the year ended December 31, 2025, we recorded impairments of long-lived assets (ROU asset, property and equipment, net, and certain other assets) of $6.1 million. The impairment charges consisted of $2.6 million of impairment expenses to property and equipment, net, and certain other assets in connection with the January 2025 restructuring and ceasing our lab operations in Hopewell, New Jersey and $2.6 million and $0.9 million recorded to the ROU assets and property and equipment, net, respectively in connection with the December 2025 impairment testing related to the Hopewell laboratory space. As of December 31, 2025, we had property and equipment, net of $4.1 million and ROU assets of $10.2 million recorded on our balance sheet.

During the year ended December 31, 2024, we recorded impairments of long-lived assets (ROU assets, property and equipment, net, and certain other assets) of $5.2 million primarily due to impairment testing in connection with the Hopewell laboratory space.

Actual future net cash flows are uncertain, subject to risks, and may change depending upon several factors, including industry or economic trends. If our estimates of future net cash flows differ from actual future net cash flows, our estimates of fair value could materially change. Additionally, future events or changes in circumstances could indicate the carrying value of our long-lived assets may not be recoverable and lead to future impairments.

*Research and Development Expenses*

Research and development costs are expensed as incurred and consist primarily of employee-related expenses, including salaries, benefits, and share-based compensation, as well as expenses incurred with contract research organizations, contract manufacturing organizations, internal analytical and testing activities, and preclinical and discovery expenses through our collaboration arrangements with Penn and Gemma.

We make estimates of our external accrued research and development expenses, which primarily relates to activities performed by our contract research organizations and contract manufacturing organizations, as of each balance sheet date in our financial statements based on an estimate of progress to completion of specific tasks using facts and circumstances known to us at that time. We determine the estimates by reviewing contracts, vendor agreements and change orders, invoicing to date, reviewing vendor provided supporting documentation and through discussions with our internal personnel and external service providers as to the progress to completion of services and the agreed-upon fee to be paid for such services.

Actual costs and estimates of progress to completion of our contract research organizations and contract manufacturing organizations are uncertain, subject to risks and may change depending upon a number of factors, including our enrollment levels and status of our clinical trials, and timing of our manufacturing activities. Such estimates are uncertain given the level of visibility we have towards the activities of our contract research organizations and contract manufacturing organizations. If the actual timing of the performance of services or the level of effort varies from the estimate, we will adjust the accrual and related expenses accordingly.

*License and Other Revenue*

We may enter into license agreements and transition services agreements under which we may license rights to research, develop, manufacture, and commercialize our product candidates to third parties, and provide transition services for such licenses. Payments under these arrangements may include non-refundable, upfront fees, reimbursement of certain costs, payments upon the achievement of certain milestones, and royalties on product sales.

We apply the Financial Accounting Standards Board's Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers*, or ASC 606, when all of the following criteria are met, to determine a valid contract exists: (i) the parties have approved the contract and are committed to perform their respective obligations; (ii) we can identify each party's rights regarding the goods or services to be transferred; (iii) we can identify the payment terms for the goods or services to be transferred; (iv) the contract has commercial substance; and (v) we will collect substantially all of the consideration to which we will be entitled in exchange for the goods or services that will be transferred to the customer. Once it is determined that a valid contract exists, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including consideration of the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations on a relative stand-alone selling price basis; and (v) recognition of revenue when (or as) we satisfy each performance obligation. As part of the accounting for these arrangements, we must use our judgment to determine the number of performance obligations, the transaction price, the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price, the contract term and pattern of satisfaction of the performance obligations. We use judgment to determine whether milestones or other variable consideration, except for certain sales-based milestone payments and royalties, should be included in the transaction price as described further below.

At the inception of each arrangement that includes milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method set forth in ASC 606. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee, such as those subject to regulatory approvals, are not considered probable of being achieved until those approvals are received. We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, we reevaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the statements of operations in the period of adjustment.

For customer contracts in the scope of ASC 606, amounts due to us are recorded as accounts receivable on our balance sheet when our right to consideration is unconditional. Amounts received prior to satisfying the related performance

obligations are classified on our balance sheet as current deferred revenue if expected to be recognized as revenue within 12 months following the balance sheet date and as deferred revenue, net of current portion, if amounts are not expected to be recognized as revenue within the 12 months following the balance sheet date. We do not evaluate a contract for a significant financing component if payment is expected within one year or less from the transfer of promised items to the customer.

***Recent Accounting Pronouncements***

See Note 3 to our financial statements found elsewhere in this Form 10-K for a description of recent accounting pronouncements applicable to our financial statements.

**Item 7A.** ***Quantitative and Qualitative Disclosures about Market Risk***

We are exposed to market risks in the ordinary course of our business. 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 are in marketable securities. Our marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. However, we believe that our exposure to interest rate risk is not significant as the majority of our investments are short-term in duration and due to the low risk profile of our investments, a 10% change in interest rates would not have a material effect on the total market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

As of December 31, 2025, we held $46.3 million in cash and cash equivalents, all of which was denominated in U.S. dollar assets, and consisting primarily of cash accounts in banking institutions and investments in money market funds.

We are exposed to market risk related to changes in foreign currency exchange rates, as a result of entering into transactions denominated in currencies other than U.S. dollars. Due to the uncertain timing of expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. For the year ended December 31, 2025, a majority of our expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our financial statements.

Inflation may affect us by increasing our cost of labor, cost of external services, and cost of external goods and raw materials. We do not believe that inflation has had a material effect on our business, financial condition or results of operations for any period presented herein.

**Item 8.** ***Financial Statements and Supplementary Data***

**PASSAGE BIO, INC.**

**INDEX TO AUDITED FINANCIAL STATEMENTS**

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors
Passage Bio, Inc.:

*Opinion on the Financial Statements*

We have audited the accompanying balance sheets of Passage Bio, Inc. (the Company) as of December 31, 2025 and 2024, the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2025 and 2024, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

*Basis for Opinion*

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

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

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

*Critical Audit Matter*

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

*Evaluation of long-lived assets for impairment*

As discussed in Notes 3 and 10 to the financial statements, the Company assesses long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of the assets or the asset group may not be recoverable. The Company's property and equipment, net, and right of use assets – operating leases as of December 31, 2025 were $4.1 million and $10.2 million, respectively. The Company measures the recoverability of assets by comparing the carrying value of the asset groups to an estimate of the related total future undiscounted net cash flows. If an asset group's carrying value is not recoverable through the related undiscounted net cash flows, the asset group is considered impaired. The Company measures the impairment by comparing the difference between the asset group's carrying value and its fair value which is

estimated using either an income approach based on the present value of estimated future cash flows or a market approach based on industry and economic conditions including estimates on prevailing prices and rates for similar assets. The approaches are asset group specific and may incorporate a number of market participant assumptions in assessing fair value including future growth rates, discount rates, and market activity. The Company recognized impairment charges for long-lived assets of $6.1 million during the year ended December 31, 2025.

We identified the evaluation of the impairment of an asset group related to the Company's laboratory space as a critical audit matter. Challenging auditor judgment, and specialized skills and knowledge, were required to evaluate certain assumptions used in the determination of the fair value of the asset group, including sublease market activity and the discount rate.

The following are the primary procedures we performed to address this critical audit matter. We involved valuation professionals with specialized skills and knowledge, who assisted in 1) evaluating sublease market activity used in determining the fair value of the asset group by comparing it to publicly available market data and 2) evaluating the discount rate used by management by comparing it to a range of independently developed discount rates.

/s/ KPMG LLP

We have served as the Company's auditor since 2019.

Philadelphia, Pennsylvania
March 3, 2026

**Passage Bio, Inc.**
**Balance Sheets**

| (in thousands, except share and per share data) | December 31, 2025 | December 31, 2024 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 46,303 | $ 37,573 |
| Marketable securities | — | 39,183 |
| Prepaid expenses and other current assets | 629 | 838 |
| Prepaid research and development | 830 | 1,221 |
| Total current assets | 47,762 | 78,815 |
| Property and equipment, net | 4,107 | 9,331 |
| Right of use assets - operating leases | 10,168 | 13,803 |
| Other assets | 244 | 463 |
| Total assets | $ 62,281 | $ 102,412 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 1,113 | $ 742 |
| Accrued expenses and other current liabilities | 4,653 | 6,707 |
| Non-refundable sublicense and transition services payments | 13,750 | 8,226 |
| Operating lease liabilities | 3,567 | 3,688 |
| Total current liabilities | 23,083 | 19,363 |
| Operating lease liabilities - noncurrent | 20,443 | 21,788 |
| Total liabilities | 43,526 | 41,151 |
| Commitments and contingencies (note 11) | | |
| Stockholders' equity: | | |
| Preferred stock, $0.0001 par value: 10,000,000 shares authorized; no shares issued and outstanding at both December 31, 2025 and December 31, 2024 | — | — |
| Common stock, $0.0001 par value: 300,000,000 shares authorized; 3,182,810 shares issued and outstanding at December 31, 2025 and 3,161,503 shares issued and outstanding at December 31, 2024 | — | — |
| Additional paid-in capital | 723,512 | 720,488 |
| Accumulated other comprehensive income (loss) | — | 8 |
| Accumulated deficit | (704,757) | (659,235) |
| Total stockholders' equity | 18,755 | 61,261 |
| Total liabilities and stockholders' equity | $ 62,281 | $ 102,412 |

*See accompanying notes to financial statements.*

**Passage Bio, Inc.**
**Statements of Operations and Comprehensive Loss**

| (in thousands, except share and per share data) | Year Ended December 31, 2025 | 2024 |
|---|---|---|
| Operating expenses: | | |
| Research and development | $ 23,276 | $ 40,179 |
| General and administrative | 19,875 | 24,988 |
| Impairment of long-lived assets | 6,145 | 5,233 |
| Loss from operations | (49,296) | (70,400) |
| Other income (expense), net | 3,774 | 5,633 |
| Net loss | $ (45,522) | $ (64,767) |
| Per share information: | | |
| Net loss per share of common stock, basic and diluted | $ (14.35) | $ (21.04) |
| Weighted average common shares outstanding, basic and diluted | 3,172,870 | 3,078,665 |
| Comprehensive loss: | | |
| Net loss | $ (45,522) | $ (64,767) |
| Unrealized gain (loss) on marketable securities | (8) | 51 |
| Comprehensive loss | $ (45,530) | $ (64,716) |

*See accompanying notes to financial statements.*

**Passage Bio, Inc.**
**Statements of Stockholders' Equity**

| (in thousands, except share data) | Common stock Shares | Common stock Amount | Additional paid-in capital | Accumulated other comprehensive income (loss) | Accumulated deficit | Total |
|---|---|---|---|---|---|---|
| **Balance at January 1, 2024** | 2,805,618 | $ — | $ 705,794 | $ (43) | $ (594,468) | $ 111,283 |
| Issuance of common stock under the ATM Facility, net of offering costs | 300,000 | — | 8,742 | — | — | 8,742 |
| Exercise of stock options and vesting of restricted stock units | 45,649 | — | 35 | — | — | 35 |
| Issuance of shares in connection with employee stock purchase plan | 10,236 | — | 97 | — | — | 97 |
| Unrealized gain (loss) on marketable securities | — | — | — | 51 | — | 51 |
| Share-based compensation expense | — | — | 5,820 | — | — | 5,820 |
| Net loss | — | — | — | — | (64,767) | (64,767) |
| **Balance at December 31, 2024** | 3,161,503 | $ — | $ 720,488 | $ 8 | $ (659,235) | $ 61,261 |

| (in thousands, except share data) | Common stock Shares | Common stock Amount | Additional paid-in capital | Accumulated other comprehensive income (loss) | Accumulated deficit | Total |
|---|---|---|---|---|---|---|
| **Balance at January 1, 2025** | 3,161,503 | $ — | $ 720,488 | $ 8 | $ (659,235) | $ 61,261 |
| Exercise of stock options and vesting of restricted stock units | 16,825 | — | — | — | — | — |
| Issuance of shares in connection with employee stock purchase plan | 4,482 | — | 23 | — | — | 23 |
| Unrealized gain (loss) on marketable securities | — | — | — | (8) | — | (8) |
| Share-based compensation expense | — | — | 3,001 | — | — | 3,001 |
| Net loss | — | — | — | — | (45,522) | (45,522) |
| **Balance at December 31, 2025** | 3,182,810 | $ — | $ 723,512 | $ — | $ (704,757) | $ 18,755 |

*See accompanying notes to financial statements.*

**Passage Bio, Inc.**
**Statements of Cash Flows**

| (in thousands) | Year Ended December 31, 2025 | 2024 |
|---|---|---|
| Cash flows used in operating activities: | | |
| Net loss | $ (45,522) | $ (64,767) |
| Adjustments to reconcile net loss to net cash provided by (used in) operating activities: | | |
| Depreciation and amortization | 728 | 3,081 |
| Share-based compensation | 3,001 | 5,820 |
| Amortization of premium and discount on marketable securities, net | 129 | (1,527) |
| Impairment of long-lived assets | 6,145 | 5,233 |
| Other non-cash items | 14 | — |
| Changes in operating assets and liabilities: | | |
| Prepaid expenses and other current assets, and other assets | 228 | 255 |
| Prepaid research and development | 391 | 1,521 |
| Non-refundable sublicense and transition services payments received | 4,015 | 8,226 |
| Right of use assets and operating lease liabilities | (464) | (279) |
| Accounts payable | 1,880 | (556) |
| Accrued expenses and other current liabilities | (2,054) | (4,963) |
| Net cash provided by (used in) operating activities | (31,509) | (47,956) |
| Cash flows provided by (used in) investing activities: | | |
| Purchases of marketable securities | — | (88,170) |
| Sales or maturities of marketable securities | 39,046 | 143,150 |
| Purchases of property and equipment and other assets | — | (34) |
| Sales of property and equipment and other assets | 1,170 | — |
| Net cash provided by (used in) investing activities | 40,216 | 54,946 |
| Cash flows provided by (used in) financing activities: | | |
| Proceeds from issuance of common stock under the ATM Facility, net of offering costs | — | 8,742 |
| Proceeds from the exercise of stock options | — | 35 |
| Proceeds from the issuance of common stock under employee stock purchase plan | 23 | 97 |
| Net cash provided by (used in) financing activities | 23 | 8,874 |
| Net increase (decrease) in cash and cash equivalents | 8,730 | 15,864 |
| Cash and cash equivalents at beginning of year | 37,573 | 21,709 |
| Cash and cash equivalents at end of year | $ 46,303 | $ 37,573 |
| Supplemental disclosure of non-cash activities: | | |
| Unrealized gain (loss) on marketable securities | $ (8) | $ 51 |
| Right of use assets recognized upon the commencement of sublease | $ — | $ (422) |
| Operating lease liabilities recognized upon the commencement of sublease | $ — | $ 422 |

*See accompanying notes to financial statements.*

**Passage Bio, Inc.**
**Notes to Financial Statements**

## 1. Nature of Operations

Passage Bio, Inc., or the Company, a Delaware corporation incorporated in July 2017, is a clinical stage genetic medicines company focused on improving the lives of patients with neurodegenerative diseases. The Company's primary focus is the development and advancement of cutting-edge, one-time therapies designed to target critical underlying pathology in these conditions. The Company's lead clinical product candidate is PBFT02 for the treatment of frontotemporal dementia, or FTD, caused by progranulin deficiency, or FTD-*GRN*, which seeks to elevate progranulin levels to restore lysosomal function and slow disease progression.

## 2. Risks and Liquidity

The Company has incurred recurring losses and negative cash flows from operations since inception and had an accumulated deficit of $704.8 million as of December 31, 2025. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant sales of its product candidates currently in development. Substantial additional capital will be needed by the Company to fund its operations and to develop its product candidates.

The Company's operations have consisted primarily of conducting preclinical studies, developing licensed technology, conducting clinical trials, and the development and manufacturing of clinical supply to support clinical trials. The Company faces risks associated with early-stage biotechnology companies whose product candidates are in development. Product candidates currently under development will require significant additional research and development efforts and establishing manufacturing capacity and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital for the Company to complete its research and development, achieve its regulatory objectives, defend its intellectual property rights, and recruit and retain skilled personnel, and key members of management. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

On March 5, 2021, the Company entered into a Sales Agreement, or the Sales Agreement, with Cowen and Company, LLC, or Cowen, relating to the applicable terms of at-the-market equity offerings, or the ATM Facility, pursuant to which the Company may, but is not obligated to, offer and sell, from time to time, shares of its common stock with an aggregate offering price up to $125.0 million through Cowen, as sales agent in the ATM Facility. The Company issued 300,000 shares of its common stock under the ATM Facility, resulting in net proceeds of $8.7 million, after deducting offering costs of $0.3 million in March 2024. The Company is currently limited in its capacity to offer and sell shares of its common stock under the Sales Agreement pursuant to the prospectus supplement to its shelf registration statement on Form S-3, filed on March 5, 2025.

The Company plans to seek additional funding through public or private equity offerings, debt financings, other collaborations, strategic alliances and licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into strategic alliances or other arrangements on favorable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. If the Company is unable to obtain funding or prospects of funding are unfavorable, the Company could be required to further delay, reduce or eliminate research and development programs, product portfolio expansion or future commercialization efforts, which could adversely affect its business prospects.

In accordance with the Financial Accounting Standards Board's, or FASB, Accounting Standards Codification, or ASC, Topic 205-40, *Presentation of Financial Statements – Going Concern*, the Company has evaluated whether there are certain conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued. As of the issuance date of these financial statements, the Company expects that its cash and cash equivalents will be sufficient to fund its forecasted operating expenses and capital expenditure requirements for at least the next 12 months from the issuance date of these financial statements.

## 3. Summary of Significant Accounting Policies

### *Basis of Presentation*

The accompanying financial statements have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the ASC and Accounting Standard Updates, or ASUs, promulgated by the FASB.

On July 14, 2025, the Company effected a 1-for-20 reverse stock split of its common stock, or the Reverse Stock Split. No fractional shares were issued in connection with the Reverse Stock Split. Stockholders who were otherwise entitled to receive fractional shares received the number of shares of Common Stock as rounded up to the nearest whole share. All share and per share amounts in these financial statements and notes thereto, including the stock options, restricted stock units, and employee stock purchase plan activity, have been adjusted retroactively to reflect the Reverse Stock Split for all periods presented.

### *Use of Estimates*

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and contingent liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Estimates and assumptions are periodically reviewed, and the effects of the revisions are reflected in the accompanying financial statements in the period they are determined to be necessary.

### *Fair Value of Financial Instruments*

Management believes that the carrying amounts of the Company's financial instruments, including cash equivalents, prepaid expenses, and accounts payable, approximate fair value due to the short-term nature of those instruments.

### *Concentration of Credit Risk*

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains a deposit account in a federally insured financial institution in excess of federally insured limits. The Company also maintains a portfolio of money market funds, which is diversified to limit exposure related to counterparty and industry risks. The Company maintains an investment policy which dictates the allocation of funds within its portfolio of money market funds. The Company has not experienced any losses in such accounts and believes it is not exposed to significant risk on its cash and cash equivalents beyond the normal credit risk associated with commercial banking relationships and money market funds.

### *Cash and Cash Equivalents*

The Company considers all highly-liquid investments that have maturities of three months or less when acquired to be cash equivalents. Cash equivalents as of December 31, 2025 consisted of money market funds. Cash consists of cash deposits at banking institutions.

### *Marketable Securities*

The Company classifies its marketable securities with original maturities of greater than three months as available-for-sale. The Company held no marketable securities as of December 31, 2025. Marketable securities as of December 31, 2024 consisted of various securities as described in Note 4. Marketable securities are carried at fair market

value, with unrealized gains and losses reported in comprehensive loss and accumulated other comprehensive income (loss) within stockholders' equity. Any premium or discount arising at purchase of debt securities is amortized and/or accreted over the term of the security to other income (expense), net. Gains or losses on marketable securities sold are recognized as a component of other income (expense), net in the statement of operations and comprehensive loss on the specific identification method. All marketable securities are available for use, as needed, to fund operations and therefore, the Company classifies all marketable securities as current assets within the balance sheet.

***Property and Equipment, Net***

Property and equipment, net consists of laboratory equipment, office equipment, computer hardware and software, furniture and fixtures, and leasehold improvements and is initially recorded at cost. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed as incurred. Property and equipment are depreciated on a straight-line basis over their estimated useful lives. The Company estimates useful life on an asset-by-asset basis, which generally consists of three years for computer hardware and software, five years for office equipment, five years for laboratory equipment, and seven years for furniture and fixtures. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset.

When property and equipment are retired or otherwise disposed of, the costs and accumulated depreciation and amortization are removed from the respective accounts, with any resulting gain or loss recognized concurrently. The Company recognized de minimis losses on disposals of property and equipment for the year ended December 31, 2025. The Company did not recognize any losses on disposals of property and equipment for the year ended December 31, 2024.

The Company reviews long-lived assets, such as property and equipment, for impairment when events or changes in circumstances indicate the carrying amount of the assets may not be recoverable. The Company recognized impairment expenses for property and equipment of $3.5 million for the year ended December 31, 2025, $2.5 million of which was for lab equipment, $0.9 of which was for leasehold improvements, and $0.1 million of which was for certain other assets.

As a result of the Company's January 2025 announcement to reduce its overall workforce and cease its lab operations, the Company reassessed asset groups at its lab in Hopewell, New Jersey, and evaluated such asset groups for impairment under FASB ASC Topic 360, *Long-lived assets: Impairment or disposal of long-lived assets*. The Company determined the laboratory equipment was a separate asset group based on management's implemented plans to sell the laboratory equipment and estimated the fair value of the laboratory equipment based on the estimated future cash flows from the sale of such equipment, resulting in impairment of laboratory equipment and certain other assets of $2.6 million. Subsequent to recording the impairment, the Company sold substantially all the laboratory equipment and certain other assets for $1.2 million.

In December 2025, the Company determined triggering events were present based on rental market activity. The Company determined whether an impairment indicator was present for each of the asset groups. Where an impairment indicator was present, the Company compared the estimated undiscounted cash flows to the carrying values, which includes ROU assets and leasehold improvements allocable to the laboratory space for those asset groups. The Company concluded the carrying value of one asset group was not recoverable as it exceeded the estimated undiscounted cash flows. With support from a valuation specialist, the Company estimated the fair value of that asset group by creating a discounted cash flow model which incorporated the net identifiable estimated cash flows for the remaining term of the Laboratory Lease Agreement and an estimated market participant subtenant borrowing rate and compared that to the carrying value of the asset group, resulting in impairment to leasehold improvements of $0.9 million. The impairment expense for the leasehold improvements relate to the proportional allocation of total impairment recognized for the asset group subject to impairment testing.

The Company recognized impairment expenses for property and equipment and certain other assets of $2.7 million for the year ended December 31, 2024, which primarily relates to the proportional allocation of total impairments recognized for asset groups subject to impairment testing as further described in Note 10.

***Leasing***

The Company evaluates leases at their inception to determine if they are an operating lease or a finance lease. As of December 31, 2025, the Company has classified all leases with terms greater than one year, as operating leases.

The Company recognizes assets and liabilities for operating leases at their inception, based on the present value of all payments due under the lease agreement. The Company uses its incremental borrowing rate to determine the present value of operating leases, which is determined by referencing collateralized borrowing rates for debt instruments with terms similar to the respective lease. The Company utilizes the accounting policy election to not separate lease and non-lease components and the accounting policy election to not apply the recognition requirement to leases with a term of 12 months or less.

The Company reviews long-lived assets, such as right of use assets, or ROU assets, for impairment when events or changes indicate the carrying amount of the ROU assets may not be recoverable. The Company recognized impairment expenses for ROU assets of $2.6 million and $2.5 million in the years ended December 31, 2025 and 2024, respectively. These impairment expenses include the proportional allocation of total impairments recognized for the asset groups subject to impairment testing as further described in Note 10.

***Research and Development***

Research and development costs are expensed as incurred and consist primarily of expenses incurred with the University of Pennsylvania's Gene Therapy Program, or GTP, and Gemma Biotherapeutics, Inc., or Gemma, contract research organizations, contract manufacturing organizations, internal analytical and testing activities, and employee-related expenses, including salaries, benefits, and share-based compensation. Management makes estimates of the Company's external accrued research and development expenses, which primarily relates to contract research organizations and contract manufacturing organizations, as of each balance sheet date in the Company's financial statements based on an estimate of progress to completion of specific tasks using facts and circumstances known to the Company at that time. The Company determines the estimates by reviewing contracts, vendor agreements, change orders, and through discussions with the Company's internal clinical personnel and external service providers as to the progress to completion of services and the agreed-upon fee to be paid for such services. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual and related expenses accordingly.

***Other Income (Expense), Net***

Other income (expense), net consists of interest earned on cash equivalents and marketable securities, amortization of premium and discount on marketable securities, income from subleases, and the sale of certain tax credits.

The Company recorded $3.8 million to other income (expense), net for the year ended December 31, 2025, which consisted of $2.3 million attributable to interest income and the amortization of premium and discount on the Company's marketable securities and $1.5 million from sublease income.

The Company recorded $5.6 million to other income (expense), net for the year ended December 31, 2024, which consisted of $4.3 million attributable to interest income and the amortization of premium and discount on the Company's marketable securities, $1.0 million from sublease income, and $0.3 million related to the sale of certain tax credits.

***Share-Based Compensation***

The Company measures share-based awards at grant-date fair value and records compensation expense on a straight-line basis over the vesting period of the awards. The Company's share-based compensation consists of restricted stock units, or RSUs, and options to purchase common stock, or stock option awards.

The Company uses the Black-Scholes option pricing model to value its stock option awards.

Estimating the fair value of stock option awards requires the input of assumptions, including the expected term of stock options and stock price volatility. The assumptions used in estimating the fair value of share-based awards represent management's estimate and involve inherent uncertainties and the application of management's judgment. As a result, if factors change and management uses different assumptions, share-based compensation expense could be materially different for future awards.

The expected term of the stock options is estimated using the "simplified method," as the Company has limited historical information from which to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants. The simplified method is the midpoint between the vesting period and the contractual term of the option.

For stock price volatility, the Company uses a composite of comparable public company data as a basis for its expected volatility and considers the historic volatility of its common stock from its initial public offering to date to calculate the fair value of option grants. The selection of comparable public company data requires the application of management's judgement.

The Company accounts for forfeitures of RSUs and stock option awards as they occur.

***License and Other Revenue***

The Company may enter into license agreements and transition services agreements (see Note 8) under which it may license rights to research, develop, manufacture, and commercialize its product candidates to third parties, and provide transition services for such licenses. Payments under these arrangements may include non-refundable, upfront fees, reimbursement of certain costs, payments upon the achievement of certain milestones, and royalties on product sales.

The Company applies FASB ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606, when all of the following criteria are met, to determine a valid contract exists: (i) the parties have approved the contract and are committed to perform their respective obligations; (ii) the Company can identify each party's rights regarding the goods or services to be transferred; (iii) the Company can identify the payment terms for the goods or services to be transferred; (iv) the contract has commercial substance; and (v) the Company will collect substantially all of the consideration to which it will be entitled in exchange for the goods or services that will be transferred to the customer. Once it is determined that a valid contract exists, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including consideration of the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations on a relative stand-alone selling price basis; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use its judgment to determine the number of performance obligations, the transaction price, the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price, the contract term and pattern of satisfaction of the performance obligations. The Company uses judgment to determine whether milestones or other variable consideration, except for certain sales-based milestone payments and royalties, should be included in the transaction price as described further below.

At the inception of each arrangement that includes milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method set forth in ASC 606. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as those subject to regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the statements of operations and comprehensive loss in the period of adjustment.

For customer contracts in the scope of ASC 606, amounts due to the Company are recorded as accounts receivable on the Company's balance sheet when the Company's right to consideration is unconditional. Amounts received prior to satisfying the related performance obligations are classified on the Company's balance sheet as current deferred revenue if expected to be recognized as revenue within 12 months following the balance sheet date and as deferred revenue, net of current portion, if amounts are not expected to be recognized as revenue within the 12 months following the balance sheet date. The Company does not evaluate a contract for a significant financing component if payment is expected within one year or less from the transfer of promised items to the customer.

***Income Taxes***

Income taxes are accounted for under the asset-and-liability method as required by FASB ASC Topic 740, *Income Taxes*, or ASC 740. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period corresponding to the enactment date. Under ASC 740, a valuation allowance is required when it is more likely than not all or some portion of the deferred tax assets will not be realized through generating sufficient future taxable income.

FASB ASC Subtopic 740-10, *Accounting for Uncertainty of Income Taxes*, or ASC 740-10, defines the criterion an individual tax position must meet for any part of the benefit of the tax position to be recognized in financial statements prepared in conformity with GAAP. The Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not such tax position will be sustained on examination by the taxing authorities, based solely on the technical merits of the respective tax position. The tax benefits recognized in the financial statements from such a tax position should be measured based on the largest benefit having a greater than 50% likelihood of being realized upon ultimate settlement with the tax authority. In accordance with the disclosure requirements of ASC 740-10, the Company's policy on statement of operations classification of interest and penalties related to income tax obligations is to include such items as part of total interest income, net, within other income (expense), net.

***Net Loss Per Share***

Basic net loss per share of common stock is computed by dividing net loss by the weighted average number of shares of common stock outstanding during each period. Diluted loss per share of common stock includes the effect, if any, from the potential exercise or conversion of securities, such as stock options, which would result in the issuance of incremental shares of common stock. For diluted net loss per share, the weighted-average number of shares of common stock is the same for basic net loss per share due to the fact that when a net loss exists, dilutive securities are not included in the calculation as the impact is anti-dilutive.

The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares of common stock outstanding, as they would be anti-dilutive:

| | Year Ended December 31, | |
|---|---|---|
| | 2025 | 2024 |
| Stock options | 658,973 | 577,581 |
| Unvested restricted stock units | 50,000 | 7,093 |
| Employee stock purchase plan | 696 | 2,636 |
| | 709,669 | 587,310 |

***Recently Issued Accounting Pronouncements Not Yet Adopted***

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement – Reporting Comprehensive Income – Expense Disaggregation Disclosures (Subtopic 220-40) Disaggregation of Income Statement Expenses*, or ASU 2024-03, which requires entities to provide disclosures to disaggregate operating expenses into specific categories, such as salaries and wages, depreciation, and amortization, to provide enhanced transparency into the nature and function of expenses. ASU 2024-03 is effective for the Company's first fiscal year beginning after December 15, 2026, and for interim periods within the Company's first fiscal year beginning after December 15, 2027, with early adoption permitted. ASU 2024-03 may be applied retrospectively or prospectively. The Company is currently evaluating the impact of this guidance on its disclosures.

In September 2025, the FASB issued ASU No. 2025-06, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Targeted Improvements to the Accounting for Internal-Use Software*, or ASU 2025-06. ASU 2025-06 is intended to increase the operability of the accounting for internal-use software costs by removing all references to software development project stages. ASU 2025-06 requires capitalization of software costs to start when management has authorized and committed to funding the software project, it is probable that the project will be completed, and the software will be used to perform the function intended. ASU 2025-06 is effective for the Company's first fiscal year beginning after December 15, 2027, and for interim periods within that year with early adoption permitted. The Company is currently evaluating the impact of this guidance on its financial statements.

In December 2025, the FASB issued ASU No. 2025-11, *Interim Reporting (Topic 270): Narrow-Scope Improvements*, or ASU 2025-11. The amendments reorganize and clarify the interim disclosure requirements in U.S. GAAP and establish a single, principles based framework for determining the information that should be disclosed in interim periods. ASU 2025-11 is effective for the Company for interim periods within annual periods beginning after December 15, 2027, with early adoption permitted. The guidance can be applied prospectively or retrospectively. The Company is currently evaluating the impact of ASU 2025-11 on its interim financial statement disclosures.

***Recently Adopted Accounting Pronouncements***

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*, or ASU 2023-09, which requires that an entity, on an annual basis, disclose additional income tax information, primarily related to the rate reconciliation and income taxes paid. The amendments in ASU 2023-09 are intended to enhance the transparency and decision usefulness of income tax disclosures. The amendments in this ASU are effective for annual periods beginning after December 15, 2024 with early adoption permitted. The Company adopted this new accounting pronouncement retrospectively during the year ended December 31, 2025. Refer to Note 14 for additional disclosures.

## 4. Cash, Cash Equivalents, and Marketable Securities

The following table provides details regarding the Company's portfolio of cash and cash equivalents:

| (in thousands) | Cost or Amortized cost | Unrealized gains | Unrealized losses | Fair value |
|---|---|---|---|---|
| **December 31, 2025:** | | | | |
| Cash accounts in banking institutions | $ 2,500 | $ — | $ — | $ 2,500 |
| Money market funds | 43,803 | — | — | 43,803 |
| Total | $ 46,303 | $ — | $ — | $ 46,303 |
| **December 31, 2024:** | | | | |
| Cash accounts in banking institutions | $ 3,527 | $ — | $ — | $ 3,527 |
| Money market funds | 29,058 | — | — | 29,058 |
| Commercial paper | 4,988 | — | — | 4,988 |
| Total | $ 37,573 | $ — | $ — | $ 37,573 |

The following table provides details regarding the Company's portfolio of marketable securities:

| (in thousands) | Amortized cost | Unrealized gains | Unrealized losses | Fair value |
|---|---|---|---|---|
| **December 31, 2025:** | | | | |
| Certificates of deposit | $ — | $ — | $ — | $ — |
| Commercial paper | — | — | — | — |
| Corporate debt securities | — | — | — | — |
| U.S. government securities | — | — | — | — |
| Total | $ — | $ — | $ — | $ — |
| **December 31, 2024:** | | | | |
| Certificates of deposit | $ 5,970 | $ 1 | $ — | $ 5,971 |
| Commercial paper | 25,433 | 6 | — | 25,439 |
| Corporate debt securities | 1,864 | 1 | — | 1,865 |
| U.S. government securities | 5,908 | 1 | (1) | 5,908 |
| Total | $ 39,175 | $ 9 | $ (1) | $ 39,183 |

As of December 31, 2025, all of the Company's marketable securities matured and the proceeds were invested into money market funds, which are included in cash and cash equivalents on the Company's balance sheet.

## 5. Fair Value of Financial Instruments and Non-Financial Instruments

### *Financial Instruments*

Fair value is the price that could be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. Fair value determination in accordance with applicable accounting guidance requires that a number of significant judgments be made. Additionally, fair value is used on a nonrecurring basis to evaluate assets for impairment or as required for disclosure purposes by applicable accounting guidance on disclosures about fair value of financial instruments. Depending on the nature of the assets and liabilities, various valuation techniques and assumptions are used when estimating fair value. The carrying amounts of certain of the Company's financial instruments, including prepaid expense and accounts payable are shown at cost, which approximates fair value due to the short-term nature of

these instruments. The Company follows the provisions of FASB ASC Topic 820, *Fair Value Measurement*, for financial assets and liabilities measured on a recurring basis. The guidance requires fair value measurements be classified and disclosed in one of the following three categories:

- *Level 1:* Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities.
- *Level 2:* Quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liabilities.
- *Level 3:* Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

The following fair value hierarchy table presents information about the Company's assets measured at fair value on a recurring basis. Included within cash and cash equivalents on the balance sheet, but excluded from the fair value hierarchy table, are cash deposits held at financial institutions:

| | Fair value measurement at reporting date using | | |
|---|---|---|---|
| (in thousands) | Quoted prices in active markets for identical assets (Level 1) | Significant other observable inputs (Level 2) | Significant unobservable inputs (Level 3) |
| **December 31, 2025:** | | | |
| **Assets** | | | |
| Cash equivalents: | | | |
| Money market funds | $ 43,803 | $ — | $ — |
| Total cash equivalents | 43,803 | — | — |
| Total financial assets | $ 43,803 | $ — | $ — |
| **December 31, 2024:** | | | |
| **Assets** | | | |
| Cash equivalents: | | | |
| Money market funds | $ 29,058 | $ — | $ — |
| Commercial paper | — | 4,988 | — |
| Total cash equivalents | 29,058 | 4,988 | — |
| Marketable securities: | | | |
| Certificates of deposit | — | 5,971 | — |
| Commercial paper | — | 25,439 | — |
| Corporate debt securities | — | 1,865 | — |
| U.S. government securities | — | 5,908 | — |
| Total marketable securities | — | 39,183 | — |
| Total financial assets | $ 29,058 | $ 44,171 | $ — |

***Non-Financial Instruments***

Long-lived non-financial assets are measured at fair value on a nonrecurring basis for purposes of calculating impairment using Level 3 inputs as defined in the fair value hierarchy. The fair value of long-lived assets using Level 3 inputs is determined by estimating the amount and timing of net future cash flows (which are unobservable inputs) and

discounting them using a risk-adjusted rate of interest. Significant increases or decreases in actual cash flows may result in valuation changes.

The following long-lived assets were measured at fair value, on a nonrecurring basis, during the years ended December 31, 2025 and 2024. Assets remeasured in 2024 or sold in 2025 are not included in the fair value presented as of December 31, 2025. The significant assumptions utilized are further described in Notes 3 and 10:

| | Fair Value Measurements as of December 31, 2025 of assets remeasured during 2025 | | | Year ended December 31, 2025 |
|---|---|---|---|---|
| (in thousands) | Level 1 | Level 2 | Level 3 | Impairment Losses |
| Property and equipment, net | $ — | $ — | $ 3,155 | $ 3,373 |
| Right of use assets | — | — | 9,489 | 2,633 |
| Other assets | — | — | — | 139 |
| Total | $ — | $ — | $ 12,644 | $ 6,145 |

| | Fair Value Measurements as of December 31, 2024 of assets remeasured during 2024 | | | Year ended December 31, 2024 |
|---|---|---|---|---|
| (in thousands) | Level 1 | Level 2 | Level 3 | Impairment Losses |
| Property and equipment, net | $ — | $ — | $ 1,668 | $ 2,279 |
| Right of use assets | — | — | 1,642 | 2,516 |
| Other assets | — | — | 200 | 438 |
| Total | $ — | $ — | $ 3,510 | $ 5,233 |

## 6. Property and Equipment, Net

Property and equipment, net, consists of the following:

| (in thousands) | December 31, 2025 | December 31, 2024 |
|---|---|---|
| Laboratory equipment | $ — | $ 10,020 |
| Office equipment | 107 | 119 |
| Computer hardware and software | 988 | 1,111 |
| Furniture and fixtures | 419 | 419 |
| Leasehold improvements | 6,510 | 7,386 |
| Total property and equipment | 8,024 | 19,055 |
| Accumulated depreciation and amortization | (3,917) | (9,724) |
| | $ 4,107 | $ 9,331 |

In connection with the Company's January 2025 announcement to reduce its overall workforce by 55% and cease its lab operations in Hopewell, New Jersey, management implemented plans to sell substantially all the laboratory equipment and certain other assets and estimated the fair value of the assets based on the estimated future cash flows from the sale of such assets. Subsequent to recording the impairment of $2.6 million, the Company sold substantially all the laboratory equipment and certain other assets for $1.2 million. As a result, the Company did not record any depreciation on the impaired and disposed laboratory equipment during the year ended December 31, 2025 as the equipment was considered held-for-sale in January 2025. Neither laboratory equipment nor accumulated depreciation related to such equipment are recorded on the balance sheet as of December 31, 2025.

Depreciation and amortization expense was $0.7 million and $3.1 million for the years ended December 31, 2025 and 2024, respectively.

## 7. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

| (in thousands) | December 31, 2025 | December 31, 2024 |
|---|---|---|
| Professional fees | $ 347 | $ 406 |
| Compensation and related benefits | 2,740 | 4,405 |
| Research and development | 642 | 1,896 |
| Divestiture fee due to Catalent | 924 | — |
| | $ 4,653 | $ 6,707 |

## 8. Gemma License Agreement

On July 31, 2024, the Company entered into a series of sublicense agreements with Gemma in connection with the outlicense of PBGM01 for the treatment of GM1 gangliosidosis, or GM1, PBKR03 for the treatment of Krabbe disease, or Krabbe, and PBML04 for the treatment of metachromatic leukodystrophy, or MLD, collectively the Outlicensed Programs, and such agreements, the Gemma Sublicenses. On May 7, 2025, the Company agreed to amend each of the Gemma Sublicenses to revise certain financial terms related to the Outlicensed Programs, or the Amended Gemma Sublicenses. Pursuant to the Amended Gemma Sublicenses, the Company is entitled to receive (i) an aggregate total of $15.0 million in initial payments for licenses and clinical product supply, of which $7.5 million was previously received, $2.5 million of which was due in May 2025, and $5.0 million of which is due in March 2026; (ii) an additional $5.0 million contingent on Gemma completing certain business milestones; (iii) up to an additional $114.0 million in development and commercial milestone payments; and (iv) single digit royalties as a percentage of annual worldwide net sales, in exchange for sublicenses to relevant intellectual property, transfer of regulatory dossiers and transfer of clinical trial materials and product supply related to the Outlicensed Programs. Gemma will be responsible for all payments due to the Trustees of the University of Pennsylvania's, or Penn, under the Company's research, collaboration and licensing agreement with Penn, or the Penn License Agreement, related to the Outlicensed Programs. On July 31, 2024, the Company also entered into a transition services agreement with Gemma, or the Transition Services Agreement, as amended by the First Amendment to the Transition Services Agreement, dated January 31, 2025, pursuant to which, the Company provided transitional services at cost to Gemma through May 31, 2025, and is entitled to reimbursement for transitional services performed retroactively from March 1, 2024, related to the transfer of the Outlicensed Programs. As of December 31, 2025, the Company has collected $7.5 million in initial payments, $4.8 million in transition services payments, and applied $1.5 million in amounts owed to Gemma for the Huntington's disease program against amounts due to the Company for transition services under these agreements.

As Gemma has a limited history of operations, the Company will not recognize revenue under ASC 606 until the Company either (i) has received payment and there are no remaining obligations to transfer goods and services under the Amended Gemma Sublicenses and Transition Services Agreement (as payments received by Gemma are nonrefundable), or (ii) concludes that substantially all of the transaction price is collectible. As of December 31, 2025, the Company has received initial payments of $7.5 million associated with the aggregate $15.0 million of initial payments to be made under the Amended Gemma Sublicenses for licenses and clinical product supply and $4.8 million associated with the Transition Services Agreement and applied $1.5 million in amounts owed to Gemma for the Huntington's disease program against amounts due to the Company for transition services under these agreements. The Company recorded these amounts ($13.8 million) as non-refundable sublicense and transition services payments on the balance sheet as of December 31, 2025, as the criteria set forth above have not yet been met.

## 9. Severance

In January 2025, the Company announced a workforce reduction to reduce operating expenses and to extend its cash runway. In connection with the announcement, the Company reduced headcount by approximately 55%.

In accordance with ASC 420, *Exit and Disposal Activities*, the Company recorded severance and termination-related costs of $0.4 million in general and administrative expenses and $1.3 million in research and development expenses for the year ended December 31, 2025. During the year ended December 31, 2024, the Company recorded no severance and termination-related costs. As of December 31, 2025, there were no unpaid severance and termination-related costs.

## 10. Leases

### *2005 Market Street Lease Agreement*

The Company is party to a lease agreement for office space, or the 2005 Market Street Lease Agreement, in Philadelphia, Pennsylvania. Under the 2005 Market Street Lease Agreement, the Company leased approximately 37,000 square feet. The 2005 Market Street Lease Agreement commenced in February 2021 and is expected to expire in December 2031. The Company has an option to extend the term of the 2005 Market Street Lease Agreement by two additional terms of five years each. The Company has an option to early terminate the 2005 Market Street Lease Agreement as of April 2029, given notice is provided to the landlord no less than fifteen months prior to April 2029. The optional extension and termination terms were not recognized as part of the Company's measurement of the ROU asset and operating lease liability as of December 31, 2025. During 2023 the Company subleased all of the space at 2005 Market Street as further described in Sublease Agreement A and Sublease Agreement B below.

### *Sublease Agreement A*

On August 7, 2023, the Company entered into a sublease agreement with a counterparty, or Sublessee A, to sublease approximately 8,000 square feet of the 2005 Market Street Lease Agreement, or Sublease Agreement A. This sublease term began on November 1, 2023, and continues through March 31, 2029. In the event the Company does not elect its early termination option under the 2005 Market Street Lease Agreement, Sublessee A has an option to extend the sublease agreement through November 30, 2031. The base sublease rent is $0.1 million per year and increases by 2.75% annually through the expiration of the agreement. Additionally, Sublessee A is required to pay the portion of the common area maintenance expenses, operating expenses, and use and occupancy taxes which the Company is required to pay under the 2005 Market Street Lease Agreement.

Pursuant to ASC Topic 842, *Leases*, or ASC 842, the Company concluded the sublease is a separate lease, as the Company was not relieved of the primary obligation under the 2005 Market Street Lease Agreement. The Company continues to account for the 2005 Market Street Lease Agreement as a lessee and in the same manner as prior to the execution of Sublease Agreement A. The Company accounted for Sublease Agreement A as the lessor, and concluded the lease qualified as an operating lease, as it did not meet the criteria of a sales-type or direct financing lease.

### *Sublease Agreement B*

On September 29, 2023, the Company entered into a sublease agreement with a counterparty, or Sublessee B, to sublease approximately 29,000 square feet of the 2005 Market Street Lease Agreement, or Sublease Agreement B. This sublease term began on March 1, 2024, and continues through August 2026. Sublessee B has an option to extend the term of the sublease agreement through March 31, 2029. The base sublease rent is $0.9 million per year for the entire term of the sublease. Additionally, Sublessee B is required to pay applicable use and occupancy taxes but is not obligated to make payments for operating expenses and common area maintenance expenses which the Company is required to pay under the 2005 Market Street Lease Agreement.

Pursuant to ASC 842, the Company concluded the sublease is a separate lease, as the Company was not relieved of the primary obligation under the 2005 Market Street Lease Agreement. The Company continues to account for the 2005 Market Street Lease Agreement as a lessee and in the same manner as prior to the execution of the Sublease Agreement B. The Company accounted for Sublease Agreement B as the lessor, and concluded the lease qualified as an operating lease, as it did not meet the criteria of a sales-type or direct financing lease.

***1835 Market Street Sublease Agreement***

On February 20, 2024, the Company entered into a sublease agreement with a counterparty, or the 1835 Market Street Sublease Agreement. Under the 1835 Market Street Sublease Agreement, the Company subleased approximately 16,000 square feet of office space in Philadelphia, Pennsylvania. The sublease term began on March 26, 2024 and expired on September 30, 2025. The Company had the option but did not elect to extend the term of the sublease agreement through February 28, 2029. The base sublease rent was $0.3 million per year for the original 18-month term of the sublease. Additionally, the Company was required to pay utility costs associated with the subleased premises.

***Laboratory Lease Agreement***

The Company is also party to a lease agreement for laboratory space, or the Laboratory Lease Agreement, in Hopewell, New Jersey. The Laboratory Lease Agreement commenced in March 2021 and is expected to expire in March 2036. The Company has an option to early terminate the Laboratory Lease Agreement as of March 2032 given notice is provided to the landlord no less than twelve months prior to March 2032. The Company has an option to extend the term of the Laboratory Lease Agreement by up to two five-year terms. These options were not recognized as part of the Company's measurement of the ROU asset and operating lease liability as of December 31, 2025.

In January 2025, the Company implemented a restructuring plan which included ceasing lab operations. As a result, the Company is no longer using any of the space covered by the Laboratory Lease Agreement and is actively pursuing opportunities to sublease all remaining space in the Laboratory Lease Agreement as well as discussing with the landlord potential alternatives.

***Hopewell Sublease Agreement***

On September 4, 2024, the Company entered into a sublease agreement with a counterparty, or Sublessee C, to sublease approximately 3,200 square feet, or 5% of its approximately 62,000 square feet of leased laboratory space under the Laboratory Lease Agreement, or Hopewell Sublease Agreement. This sublease term began on September 11, 2024 and expires on December 31, 2029. Sublessee C has the option to extend the term of the sublease through December 2032. The base sublease rent is $0.1 million per year and increases by 2.5% annually through the expiration of the Hopewell Sublease Agreement. Additionally, Sublessee C is required to pay the portion of the common area maintenance expenses, operating expenses, and use and occupancy taxes that the Company is required to pay under the Laboratory Lease Agreement.

Pursuant to ASC 842, the Company concluded the sublease is a separate lease, as the Company was not relieved of the primary obligation under the Laboratory Lease Agreement. The Company continues to account for the Laboratory Lease Agreement as a lessee and in the same manner as prior to the execution of the Hopewell Sublease Agreement. The Company accounted for the Hopewell Sublease Agreement as the lessor, and concluded the lease qualified as an operating lease, as it did not meet the criteria of a sales-type or direct financing lease.

In 2024, the Company determined triggering events were present and reassessed the asset groups related to its laboratory space under the Laboratory Lease Agreement, which resulted in changes to the Company's identified asset groups. The Company determined whether an impairment indicator was present for each of the new asset groups. Where an impairment indicator was present, the Company compared the estimated undiscounted cash flows to the carrying values, which includes ROU assets, leasehold improvements, and other property and equipment allocable to the laboratory space

for those asset groups. The Company concluded the carrying values of certain asset groups were not recoverable as they exceeded the estimated undiscounted cash flows. The Company calculated the amount of impairment on those asset groups using a discounted cash flow model to calculate the fair value of the asset group which incorporated the net identifiable cash flows for the term of the Hopewell Sublease Agreement, including an estimate for cash flows in the residual period, and an estimated borrowing rate of a market participant subtenant. As a result, certain asset groups were impaired and the Company recognized impairment expense of $5.2 million, including $2.5 million for the ROU assets, $2.3 million for the property and equipment, net, and $0.4 million for certain other assets during the year ended December 31, 2024.

In connection with the January 2025 announcement to reduce its overall workforce by 55% and cease its lab operations in Hopewell, New Jersey, the Company determined triggering events were present and reassessed its asset groups related to its laboratory space under the Laboratory Lease Agreement. Laboratory equipment was separated from the ROU assets and leasehold improvements allocable to the laboratory space as the equipment was no longer being used in operations and the Company had implemented a plan to sell those assets. For the ROU assets and allocable leasehold improvements, the Company compared the estimated undiscounted cash flows from subleasing to the carrying value and determined there was no impairment.

In December 2025, the Company determined triggering events were present based on rental market activity. The Company determined whether an impairment indicator was present for each of the asset groups. Where an impairment indicator was present, the Company compared the estimated undiscounted cash flows to the carrying values, which includes ROU assets and leasehold improvements allocable to the laboratory space for those asset groups. The Company concluded the carrying value of one asset group was not recoverable as it exceeded the estimated undiscounted cash flows. With support from a valuation specialist, the Company estimated the fair value of that asset group by creating a discounted cash flow model which incorporated the net identifiable estimated cash flows for the remaining term of the Laboratory Lease Agreement based upon sublease market activity and an estimated market participant subtenant borrowing rate and compared that to the carrying value of the asset group. As a result, the Company recognized impairment expense of $3.5 million, including $2.6 million for the ROU assets and $0.9 million for the leasehold improvements during the year ended December 31, 2025.

The following table summarizes future minimum lease payments for the Company's lessee operating leases, which comprises of the 2005 Market Street Lease Agreement and the Laboratory Lease Agreement. The below table does not include expected cash inflows related to Sublease Agreement A, Sublease Agreement B, and the Hopewell Sublease Agreement as the Company was not relieved of its primary obligation under the 2005 Market Street Lease Agreement and Laboratory Lease Agreement:

| **(in thousands)** | | |
|---|---|---|
| 2026 | $ | 3,757 |
| 2027 | | 3,863 |
| 2028 | | 3,973 |
| 2029 | | 4,085 |
| 2030 | | 4,200 |
| Thereafter | | 17,421 |
| Total undiscounted lease payments | | 37,299 |
| Less: imputed interest | | (13,289) |
| Total lease liabilities | $ | 24,010 |

The following table summarizes lease expense by lease type that was recognized during the years ended December 31, 2025 and 2024:

| | Year Ended | |
|---|---|---|
| **(in thousands)** | **December 31, 2025** | **December 31, 2024** |
| Operating lease cost | $ 3,419 | $ 3,505 |
| Variable lease cost | 2,103 | 2,127 |
| | $ 5,522 | $ 5,632 |

The following table shows the weighted average discount rate and weighted average remaining lease term of the operating leases:

| | Year Ended | |
|---|---|---|
| | **December 31, 2025** | **December 31, 2024** |
| Weighted-average discount rate | 9.7% | 9.7% |
| Weighted-average remaining lease term (years) | 9.3 | 10.2 |

The cash paid for amounts included in the measurement of the Company's operating lease liabilities for the years ended December 31, 2025 and 2024 were $3.9 million and $3.8 million, respectively, recorded in operating cash flows.

The following table summarizes sublease income that was recognized in other income (expense), net during the years ended December 31, 2025 and 2024:

| | Year Ended | |
|---|---|---|
| **(in thousands)** | **December 31, 2025** | **December 31, 2024** |
| Sublease rental income | $ 1,467 | $ 987 |

## 11. Commitments and Contingencies

***Amended and Restated Research, Collaboration and License Arrangement with Penn***

In connection with the transfer of the Outlicensed Programs (GM1, Krabbe, and MLD), the Company restructured its research, collaboration and license agreement with Penn, as amended, previously the Penn Agreement and now referred to as the Penn License Agreement. Pursuant to the Penn License Agreement, as of July 31, 2024, the Company (i) terminated the funding of discovery research programs; (ii) terminated the research and exploratory research programs; (iii) terminated the remaining eight options it had for future central nervous system, or CNS, indications; (iv) terminated the transaction fee payable to Penn in the event of certain corporate transactions; and (v) retained its current exclusive and non-exclusive licenses to its programs in FTD, GM1, Krabbe, and MLD and certain platform technologies resulting from the discovery programs that it funded.

For the Company's licensed programs in FTD, GM1, Krabbe, and MLD, the Penn License Agreement requires that it make payments of up to $16.5 million per product candidate. Each payment will be due upon the achievement of specific development milestone events by such licensed product for a first indication, reduced development milestone payments for the second and third indications, and no development milestone payments for subsequent indications. In addition, on a product-by-product basis, the Company is obligated to make up to $55.0 million in sales milestone payments on each licensed product based on annual worldwide net sales of the licensed product in excess of defined thresholds. Pursuant to the Amended Gemma Sublicenses, Gemma is responsible for the payments to Penn related to the Outlicensed Programs.

Upon successful commercialization of a product using the licensed technology, the Company is obligated to pay to Penn, on a licensed product-by-licensed product and country-by-country basis, tiered royalties (subject to customary

reductions) in the mid-single digits percentage on annual worldwide net sales of such licensed product. In addition, other than the Amended Gemma Sublicenses, the Company is obligated to pay to Penn a percentage of sublicensing income, ranging from the mid-single digits to low double digits, for sublicenses under the Penn License Agreement. The agreement will expire on a licensed product-by-licensed product and country-by-country basis upon the later of (i) the expiration of the last valid claim of the licensed patent rights that covers the exploitation of such licensed product in such country, and (ii) the expiration of the royalty period. Pursuant to the Amended Gemma Sublicenses, Gemma is responsible for the payments to Penn related to the Outlicensed Programs.

***Gemma - Research, Collaboration and License Agreement***

In connection with the transfer of the Outlicensed Programs, on July 31, 2024, the Company entered into a research, collaboration and license agreement with Gemma, or the Gemma Collaboration Agreement. Pursuant to the Gemma Collaboration Agreement, (i) Gemma will conduct certain preclinical and Investigational New Drug-enabling work for the Company's active research program in Huntington's disease and a currently paused research program in Temporal Lobe Epilepsy, or TLE, which were previously being conducted by Penn under the Penn Agreement and (ii) Gemma will grant the Company options to conduct mutually-agreed research programs in four new CNS indications.

The Gemma Collaboration Agreement requires the Company to make payments of up to (i) $16.5 million per product candidate in the aggregate for Huntington's disease and any future CNS indications available to the Company under its four options and (ii) $39.0 million per product candidate in the aggregate arising from the research program for TLE. Each payment will be due upon the achievement of specific development milestone events by such licensed product for a first indication, reduced development milestone payments for the second and third indications and no development milestone payments for subsequent indications. In addition, on a product-by-product basis, the Company is obligated to make up to $55.0 million in sales milestone payments on each licensed product based on annual worldwide net sales of the licensed product in excess of defined thresholds.

Upon successful commercialization of a product using the licensed technology, the Company is obligated to pay to Gemma, on a licensed product-by-licensed product and country-by-country basis, tiered royalties (subject to customary reductions) in the mid-single digits percentage on annual worldwide net sales of such licensed product. In addition, the Company is obligated to pay to Gemma a percentage of sublicensing income, ranging from the mid-single digits to low double digits, for sublicenses under the Gemma Collaboration Agreement. The agreement will expire on a licensed product-by-licensed product and country-by-country basis upon the later of (i) the expiration of the last valid claim of the licensed patent rights that covers the exploitation of such licensed product in such country, and (ii) the expiration of the royalty period.

If the Company was to exercise any of the four options under the Gemma Collaboration Agreement, it would owe Gemma a non-refundable aggregate fee of $1.0 million per product indication, with $0.5 million due upfront and another $0.5 million fee owed upon a further developmental milestone.

The Company has also entered into the Amended Gemma Sublicenses and Transition Services Agreement as described in Note 8.

The Amended Gemma Sublicenses, the Transition Services Agreement, and the Gemma Collaboration Agreement are collectively referred to as the Outlicense Transaction Agreements.

***Catalent Agreements***

The Company has entered into a collaboration agreement, and a development services and clinical supply agreement, or the Amended Catalent Agreements, with Catalent Maryland, a unit of Catalent, Inc. acquired by Novo Holdings A/S, or Catalent, to secure clinical scale manufacturing capacity for batches of active pharmaceutical ingredients for the

Company's gene therapy product candidates. Under the terms of the Amended Catalent Agreements, Catalent agreed to manufacture batches of drug product for the Company's gene therapy product candidates.

The Amended Catalent Agreements remain in effect until November 6, 2030, and establish a limited exclusive relationship between the Company and Catalent for the manufacture of bulk drug substance and drug product for the Company's adeno-associated virus delivery therapeutic product candidates for the treatment of FTD and GM1. The limited exclusive relationship under the Amended Catalent Agreements converts to a non-exclusive relationship (i) in the event Catalent fails to meet certain performance standards and (ii) following certain conditional events related to the divestiture by the Company of either FTD or GM1, in which case, if such events occur, the Company would pay Catalent certain fees. In the event of certain transactions, the Company may terminate the Amended Catalent Agreements for convenience with respect to such products, in which case, the Company would pay Catalent a certain termination fee.

The outlicense and completed transition of GM1 to Gemma under the Outlicense Transaction Agreements, is deemed by Catalent to be a divestiture under the Amended Catalent Agreements. As such, the Company is required to make payment of $0.9 million to Catalent which has been accrued as of and during the year ended December 31, 2025.

***Litigation***

In the normal course of business, the Company from time to time is named as a party to legal claims and actions. The Company records a loss contingency reserve for a legal proceeding when the potential loss is considered probable and can be reasonably estimated. The Company has not recorded any amounts for loss contingencies as of December 31, 2025.

The Company is the defendant in litigation with a former employee, who filed a lawsuit in the Court of Common Pleas of Philadelphia County asserting claims for breach of contract and violation of the Pennsylvania Wage Payment and Collection Law. The plaintiff, who was terminated from their employment in 2019, contended that the Company entered into a binding settlement agreement in February 2020 under which he was to receive shares of company stock and additional compensation. Specifically, he contended that before the announcement of the Company's initial public offering in February 2020, he was promised 150,000 shares of stock as part of the settlement, and that those shares were not subject to the reverse stock split that was implemented for all shareholders. The Company responded that the shares offered in settlement negotiations in 2020 were to be subject to the reverse split, and that had the settlement been finalized, the plaintiff would have been entitled to 33,836 shares (1,692 shares adjusted for the Reverse Stock Split effected in 2025). A trial in this case was held in October 2024. The jury found that an agreement was reached, but it agreed with the Company that any shares to be awarded to the plaintiff were subject to the reverse split. The jury awarded damages in an amount that was roughly equal to what the Company contended had been offered to the plaintiff before the initial public offering. Both sides then challenged the verdict, and on December 12, 2024, the judge who presided over the trial delivered a judgment in the Company's favor, finding that no binding agreement was reached and that the plaintiff was not entitled to recover any damages. On December 23, 2024, the plaintiff filed an appeal with the Superior Court of Pennsylvania. On September 25, 2025, the appellate court affirmed the entry of judgment in favor of the Company and on October 7, 2025, the plaintiff filed an Application for Reargument to the Superior Court of Pennsylvania. In December 2025, the Superior Court of Pennsylvania denied the Application for Reargument. In December 2025, the plaintiff petitioned for review of their appeal to the Pennsylvania Supreme Court which is currently pending. The Company intends to continue to defend against this claim.

Other than the above, we are not presently a party to any legal proceedings that, in the opinion of management, would, if decided against us, have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm, and other factors.

***Employment Agreements***

The Company has employment agreements with certain key personnel providing for up to 18 months of salary continuation, up to 150% of target annual bonus amounts, and acceleration of vesting in stock-based compensation awards in certain circumstances.

**12. Common Stock**

On March 5, 2021, the Company entered into a Sales Agreement, or the Sales Agreement, with Cowen and Company, LLC, or Cowen, relating to the applicable terms of at-the-market equity offerings, or the ATM Facility, pursuant to which the Company may, but is not obligated to, offer and sell, from time to time, shares of its common stock with an aggregate offering price up to $125.0 million through Cowen, as sales agent in the ATM Facility. The Company issued 300,000 shares of common stock under the ATM Facility, resulting in net proceeds of $8.7 million, after deducting offering costs of $0.3 million in March 2024. The Company is currently limited in its capacity to offer and sell shares of its common stock under the Sales Agreement pursuant to the prospectus supplement to its shelf registration statement on Form S-3, filed on March 5, 2025.

On July 14, 2025, the Company effected the Reverse Stock Split. The Reverse Stock Split did not reduce the number of authorized shares of the common stock and did not change the par value of the common stock. In addition, proportionate adjustments were made to the number of shares of common stock available for issuance under the Company's equity inducement and incentive plans; the number of shares underlying, and the exercise prices of outstanding equity awards under such plans. All share information in these financial statements has been adjusted for this Reverse Stock Split.

**13. Share-Based Compensation**

***Equity Incentive Plan***

The Company has three equity incentive plans: the 2018 Equity Incentive Plan, as amended, or the 2018 Plan, the 2020 Equity Incentive Plan, or the Incentive Plan, and the 2021 Equity Inducement Plan, or the Inducement Plan. New awards can only be granted under the Incentive Plan and the Inducement Plan.

The total number of shares authorized under the Incentive Plan as of December 31, 2025 was 947,598. Additionally, 204,732 shares previously issued under the 2018 Plan which were forfeited are available for issuance under the Incentive Plan. As of December 31, 2025, 433,624 shares were available for future grants under the Incentive Plan. The number of shares of the Company's common stock that may be issued pursuant to rights granted under the Incentive Plan shall automatically increase on January 1st of each year, commencing on January 1, 2021 and continuing for ten years, in an amount equal to five percent of the total number of shares of the Company's common stock outstanding on December 31st of the preceding calendar year, subject to the discretion of the board of directors to determine a lesser number of shares shall be added for such year. As a result, the number of shares reserved for issuance under the Incentive Plan increased by 159,141 and 155,155 shares in January 2026 and 2025, respectively.

The Incentive Plan provides for the granting of common stock, incentive stock options, nonqualified stock options, restricted stock awards, and/or stock appreciation rights to employees, directors, and other persons, as determined by the Company's board of directors. The Company's stock options awarded to date under the Incentive Plan vest based on a requisite service period, generally over four-year periods, and have a term of ten years.

The Inducement Plan was approved by the Company's board of directors in July 2021. The total number of shares authorized under the Inducement Plan as of December 31, 2025 was 125,000. Of this amount, 87,166 shares were available for future grants as of December 31, 2025. The Inducement Plan provides for the granting of nonqualified stock options and restricted stock awards to employees hired by the Company, as determined by the Company's board of directors. The Company's stock options awarded to date under the Inducement Plan vest based on requisite service

period and have a term of ten years. The Company's restricted stock units awarded to date under the Inducement Plan vest based on requisite service period and have a term based on each award agreement.

The Company measures share-based awards at their grant-date fair value and records compensation expense on a straight-line basis over the vesting period of the awards. The Company recorded share-based compensation expense in the following expense categories in its accompanying statements of operations and comprehensive loss for the period presented:

| | Year Ended December 31, | |
|---|---|---|
| **(in thousands)** | **2025** | **2024** |
| Research and development | $ 842 | $ 2,529 |
| General and administrative | 2,159 | 3,291 |
| | $ 3,001 | $ 5,820 |

The following table summarizes stock option activity for the year ended December 31, 2025:

| | Number of shares | Weighted average exercise price per share | Weighted average remaining contractual term (years) |
|---|---|---|---|
| Outstanding at January 1, 2025 | 577,581 | $ 77.56 | 7.5 |
| Granted | 248,208 | 7.78 | |
| Exercised | — | — | |
| Forfeited | (125,526) | 82.56 | |
| Expired | (41,290) | 175.24 | |
| Outstanding at December 31, 2025 | 658,973 | $ 44.20 | 7.1 |
| Vested and exercisable at December 31, 2025 | 357,766 | $ 78.82 | 5.6 |
| Vested or expected to vest at December 31, 2025 | 658,973 | $ 44.20 | 7.1 |

The weighted-average grant date fair value of options granted was $6.07 and $20.20 for the years ended December 31, 2025 and 2024, respectively.

The aggregate intrinsic value of options outstanding was $0.9 million at December 31, 2025 and was de minimis at December 31, 2024. The aggregate intrinsic value of options exercisable was $0.2 million at December 31, 2025 and was de minimis at December 31, 2024. There were no options exercised during the year ended December 31, 2025 and the aggregate intrinsic value of options exercised during the year ended December 31, 2024 was de minimis.

As of December 31, 2025, the total unrecognized compensation expense related to unvested stock option awards was $3.0 million, which the Company expects to recognize over a weighted-average period of 2.2 years.

The fair value of each option was estimated on the date of grant using the weighted average assumptions in the table below:

| | Year Ended December 31, | |
|---|---|---|
| | 2025 | 2024 |
| Expected volatility | 93.7 % | 88.4 % |
| Risk-free interest rate | 4.1 % | 4.2 % |
| Expected term | 5.9 years | 6.0 years |
| Expected dividend yield | — | — |

***Restricted Stock Units***

The Company issues restricted stock units, or RSUs, to employees that vest over periods of time as determined by the board of directors. Any unvested shares are forfeited upon termination of services. The fair value of the RSUs is equal to the fair market value of the Company's common stock on the date of grant. Compensation expense is recognized on a straight-line basis over the vesting period of the RSUs.

The following table summarizes activity related to RSU awards during the year ended December 31, 2025:

| | Number of shares | Weighted average grant date fair value |
|---|---|---|
| Unvested balance at January 1, 2025 | 7,093 | $ 44.80 |
| Granted | 60,000 | 11.70 |
| Vested | (16,825) | 27.92 |
| Forfeited | (268) | 90.40 |
| Unvested balance at December 31, 2025 | 50,000 | $ 10.52 |

As of December 31, 2025, the total unrecognized expense related to all RSUs was $0.3 million, which the Company expects to recognize over a weighted-average period of 1.0 years.

***Employee Stock Purchase Plan***

The Company's 2020 Employee Stock Purchase Plan, or the ESPP, became effective on February 28, 2020. The ESPP authorizes the issuance of up to 99,088 shares of the Company's common stock. Of this amount, 59,103 were available for future grants as of December 31, 2025. The number of shares of the Company's common stock that may be issued pursuant to rights granted under the ESPP shall automatically increase on January 1st of each year and continuing for ten years, in an amount equal to one percent of the total number of shares of the Company's common stock outstanding on December 31st of the preceding calendar year, subject to the discretion of the board of directors to determine a lesser number of shares shall be added for such year. As a result, on January 1, 2026 and 2025, subject to the discretion of the board of directors, the shares authorized for issuance under the ESPP was not increased.

Under the ESPP, eligible employees can purchase the Company's common stock through accumulated payroll deductions at such times as are established by the board of director's Compensation Committee. Eligible employees may purchase the Company's common stock at 85% of the lower of the fair market value of the Company's common stock on the first day of the offering period or on the last day of the offering period. The offering periods under the ESPP have a duration of six months, with periods ending in May and November of each calendar year. Eligible employees may contribute up to 15% of their eligible compensation. Under the ESPP, a participant may not accrue rights to purchase more than $25,000 worth of the Company's common stock for each calendar year in which such right is outstanding or purchase more than 200 shares of the Company's common stock in any single offering period. Beginning in May 2026,

the limit will increase from 200 shares to 2,000 shares in any single offering period, not to exceed $25,000 in any calendar year.

In accordance with the guidance in ASC Topic 718-50, *Compensation – Stock Compensation*, the ability to purchase shares of the Company's common stock at 85% of the lower of the price on the first day of the offering period or the last day of the offering period (i.e. the purchase date) represents an option and**,** therefore, the ESPP is a compensatory plan under this guidance. Accordingly, share-based compensation expense is determined based on the option's grant-date fair value as estimated by applying the Black Scholes option-pricing model and is recognized over the withholding period. No share-based compensation expense related to the ESPP was recorded during the years ended December 31, 2025 and 2024.

## 14. Income Taxes

The tax effects of temporary differences that gave rise to significant portions of the deferred tax assets and liabilities were as follows:

| | December 31, | |
|---|---|---|
| **(in thousands)** | **2025** | **2024** |
| Deferred tax assets: | | |
| Net operating loss carryforwards | $ 105,425 | $ 94,923 |
| Research and development credits | 55,020 | 50,842 |
| Collaboration and license agreement | 2,832 | 3,422 |
| Capitalized research and development | 46,041 | 59,803 |
| Share-based compensation | 4,329 | 5,863 |
| Accrued expenses and other | 4,581 | 1,404 |
| Operating lease liabilities | 6,520 | 7,560 |
| Depreciation and amortization | 1,048 | 461 |
| Total gross deferred tax assets before valuation allowance | 225,796 | 224,278 |
| Valuation allowance | (222,752) | (219,833) |
| Net deferred tax assets | 3,044 | 4,445 |
| Deferred tax liabilities: | | |
| Right of use assets - operating leases | (3,044) | (4,445) |
| Total deferred tax liabilities | (3,044) | (4,445) |
| Net deferred taxes | $ — | $ — |

In assessing the need for a valuation allowance, management must determine that there will be sufficient taxable income to allow for the realization of deferred tax assets. Based upon the historical and anticipated future losses, management has determined the deferred tax assets do not meet the more-likely-than-not threshold for realizability. Accordingly, a full valuation allowance has been recorded against the Company's net deferred tax assets as of December 31, 2025 and 2024. The valuation allowance increased by $2.9 million and $19.1 million during the years ended December 31, 2025 and 2024, respectively.

During the year ended December 31, 2025, the Company adopted ASU No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* retrospectively. A reconciliation of the federal income tax rate to the Company's effective tax rate is as follows:

| | Year ended December 31, | | | |
|---|---|---|---|---|
| | 2025 | | 2024 | |
| (in thousands) | Amount | Percent | Amount | Percent |
| US federal statutory tax rate | $ (9,560) | 21.0 % | $ (13,601) | 21.0 % |
| Federal: | | | | |
| Tax credits: | | | | |
| Research and development tax credits | (175) | 0.4 | (626) | 1.0 |
| Orphan drug tax credits | (4,003) | 8.8 | (4,896) | 7.6 |
| Changes in valuation allowances | 12,334 | (27.2) | 17,422 | (27.0) |
| Nontaxable or nondeductible items: | | | | |
| Share-based payment awards | 241 | (0.5) | 459 | (0.7) |
| Expiration of share-based payment awards | 1,159 | (2.5) | 1,233 | (1.9) |
| Other | 4 | 0.0 | 9 | 0.0 |
| State and local income taxes, net of federal income tax effect [1] | — | — | — | — |
| Effective tax rate | $ — | — % | $ — | — % |

[1] *In 2025 and 2024, state and local income taxes in Pennsylvania and Philadelphia comprise the majority of the state and local income taxes, net of federal income tax effect category.*

During the years ended December 31, 2025 and 2024, the Company made no income tax payments. Additionally, the Company generated no foreign pre-tax income or losses during these periods, as all operations were conducted within the United States.

The following table summarizes carryforwards of federal, state and local net operating losses, or NOL, and research and development and orphan drug tax credits:

| | December 31, | |
|---|---|---|
| (in thousands) | 2025 | 2024 |
| Federal | $ 398,039 | $ 339,055 |
| State | 398,035 | 339,051 |
| Local | 277,828 | 218,844 |
| Research tax credits | 55,020 | 50,842 |

For federal income tax purposes, $0.3 million of NOL carryforwards expire in 2037. The remaining federal NOL carryforwards were generated subsequent to January 1, 2018, and therefore, are able to be carried forward indefinitely.

For state income tax purposes, NOL carryforwards begin expiring in 2037, and expire through 2045.

For local income tax purposes related to the city of Philadelphia, NOL carryforwards begin expiring in 2042, and expire through 2045.

As of December 31, 2025, the Company also had $11.6 million of federal research and development and $43.4 million orphan drug tax credit carryforwards that will begin to expire in 2038 and 2040, respectively, unless previously utilized.

The NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50 percent, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state

provisions. This could limit the amount of tax attributes 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 the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not done an analysis to determine whether or not ownership changes have occurred since inception. Certain state NOL carryforwards may also be limited, including Pennsylvania, which limits NOL utilization as a percentage of apportioned taxable income.

The Company will recognize interest and penalties related to uncertain tax positions as a component of interest income, net. As of December 31, 2025, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statement of operations. Tax years from 2022 and after remain subject to examination by the taxing jurisdictions. The NOL and tax credit carryforwards remain subject to review until utilized.

**15. Segment Reporting**

Operating segments are defined as components of an enterprise which engages in business activities from which it may recognize revenues and incur expenses about which separate discrete information is available for evaluation by the chief operating decision maker, or CODM, in deciding how to allocate resources and in assessing performance. The Company operates in a single reportable segment, developing and advancing genetic medicines designed to target critical underlying pathology of neurodegenerative diseases.

The accounting policies of the single segment are the same as those described in the summary of significant accounting policies. The Company's CODM is its chief executive officer.

The measure of segment assets is reported on the balance sheet as total assets. All assets are located within the United States.

The CODM uses net loss as reported on the Company's statement of operations to assess the Company's performance. The CODM also uses cash forecasts in deciding where to invest or expand operations within the business. In these cash forecasts, research and development expenses and general and administrative expenses exclude certain non-cash items such as share-based compensation and depreciation and amortization expenses.

The following table summarizes significant segment expenses:

| (in thousands) | Year Ended December 31, 2025 | 2024 |
|---|---|---|
| Research and development | | |
| Wages, benefits, and other payroll | $ 7,462 | $ 12,265 |
| Third-party costs | 14,532 | 22,691 |
| Share-based compensation | 842 | 2,529 |
| Depreciation and amortization | 440 | 2,694 |
| Total research and development expenses | 23,276 | 40,179 |
| General and administrative | | |
| Wages, benefits, and other payroll | 7,784 | 9,255 |
| Third-party costs | 9,644 | 12,055 |
| Share-based compensation | 2,159 | 3,291 |
| Depreciation and amortization | 288 | 387 |
| Total general and administrative expenses | 19,875 | 24,988 |
| Impairment of long-lived assets | 6,145 | 5,233 |
| Loss from operations | 49,296 | 70,400 |
| Other (income) expense, net | (3,774) | (5,633) |
| Net loss | $ 45,522 | $ 64,767 |

The components of Other (income) expense, net are further described in note 3 to the financial statements.

**16. Subsequent Events**

None.

**Item 9.** ***Changes in and Disagreements with Accountants on Accounting and Financial Disclosure***

None.

**Item 9A.** ***Controls and Procedures***

**Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures**

Under the supervision of and with the participation of our management, including our chief executive officer, who is our principal executive officer, and our chief financial officer, who is our principal financial officer, we conducted an evaluation of the effectiveness of our disclosure controls and procedures as of December 31, 2025, the end of the period covered by this Annual Report. The term "disclosure controls and procedures," as set forth in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to provide reasonable assurance 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 rules and forms promulgated by the SEC. Disclosure controls and procedures include, without limitation, controls and procedures 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 accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. 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. Based on the evaluation of our disclosure controls and procedures as of December 31, 2025, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

**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) promulgated under the Exchange Act as a process designed by, or under the supervision of, our chief executive officer and chief financial officer and effected by our 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 U.S. GAAP. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of our assets;

- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, and that our 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 our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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. Additionally, in designing disclosure controls and procedures, our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible disclosure controls and procedures. The design of any disclosure controls and procedures also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions.

Our management, with the participation of our chief executive officer and chief financial officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2025. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in its *Internal Control – Integrated Framework (2013)*. Based on our assessment, our management has concluded that, as of December 31, 2025, our internal control over financial reporting is effective based on those criteria.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. For as long as we remain a "smaller reporting company" as defined in Item 10(f)(1) of Regulation S-K, and a non-accelerated filer as defined in the Exchange Act, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

**Changes in Internal Control over Financial Reporting**

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the three months ended December 31, 2025, that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

**Item 9B.** ***Other Information***

During the three months ended December 31, 2025, none of our directors or officers, as defined in Rule 16a-1(f), informed us of the adoption, modification or termination of a "Rule 10b5-1 trading agreement" or "non-Rule 10b-51 trading agreement," as those terms are defined in Regulation S-K, Item 408.

**Item 9C.** ***Disclosure Regarding Foreign Jurisdictions that Prevent Inspections***

Not applicable.

## PART III

**Item 10.** ***Directors, Executive Officers and Corporate Governance***

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2026 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

**Item 11.** ***Executive Compensation***

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2026 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

**Item 12.** ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2026 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

**Item 13.** ***Certain Relationships and Related Transactions and Director Independence***

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2026 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

**Item 14.** ***Principal Accountant Fees and Services***

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2026 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

## PART IV

**Item 15.** ***Exhibits and Financial Statement Schedules***

**(1) Financial Statements**

The financial statements required by Item 15(a) are filed as part of this Annual Report on Form 10-K under Item 8 "Financial Statements and Supplementary Data."

**(2) Financial Statement Schedules**

The financial statement schedules required by Item 15(a) are omitted because they are not applicable, not required or the required information is included in the financial statements or notes thereto as filed in Item 8 of this Annual Report on Form 10-K.

**(3) Exhibits**

| Exhibit Number | Description | Form | File No. | Exhibit Filing Date | Filed/ Furnished Herewith |
|---|---|---|---|---|---|
| 3.1 | Restated Certificate of Incorporation, dated May 30, 2023, as amended. | 10-Q | 001-39231 | November 10, 2025 | |
| 3.2 | Amended and Restated Bylaws, dated December 1, 2022. | 8-K | 001-39231 | December 2, 2022 | |
| 4.1 | Form of Common Stock Certificate. | S-1/A | 333-236214 | February 18, 2020 | |
| 4.2 | Description of Registrant's Securities. | | | | X |
| 10.1 | Lease, dated April 10, 2020, by and between the Registrant and Commerce Square Partners - Philadelphia Plaza, L.P. | 10-Q | 001-39231 | May 11, 2020 | |
| 10.2 | First Amendment to Lease, dated April 10, 2020, by and between the Registrant and Philadelphia Plaza, L.P. – Phase II | 10-Q | 001-39231 | May 11, 2020 | |
| 10.3 | Form of Indemnification Agreement between the Registrant and its directors and officers. | S-1 | 333-236214 | February 3, 2020 | |
| 10.4 | Amended and Restated 2018 Equity Incentive Plan, as amended, and forms of award agreements. | S-1 | 333-236214 | February 3, 2020 | |
| 10.5 | 2020 Equity Incentive Plan of the Registrant, and forms of award agreements. | | | | X |
| 10.6 | 2020 Employee Stock Purchase Plan of the Registrant. | | | | X |

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| 10.7^ | Lease, dated December 15, 2020 by and between the Registrant and Hopewell Campus Owner, LLC. | 8-K | 001-39231 | December 18, 2020 |
| 10.8 | 2021 Equity Inducement Plan. | S-8 | 333-258000 | July 19, 2021 |
| 10.9+† | Employment Agreement, dated October 10, 2022 by and between the Registrant and William Chou. | 10-Q | 001-39231 | November 10, 2022 |
| 10.10+† | Employment Agreement dated September 10, 2019, as amended on February 26, 2020, by and between the Registrant and Edgar B. (Chip) Cale. | 10-K | 001-39231 | March 6, 2023 |
| 10.11†^ | Amended and Restated Development Services and Clinical Supply Agreement, dated November 9, 2023, by and between the Registrant and Catalent Maryland, Inc. | 10-K | 001-39231 | March 4, 2024 |
| 10.12+† | Employment Agreement, dated March 1, 2024, by and between the Registrant and Kathleen Borthwick. | 10-K | 001-39231 | March 4, 2024 |
| 10.13+ | Non-Employee Director Compensation Policy effective as of April 4, 2024. | 10-Q | 001-39231 | May 14, 2024 |
| 10.14†^ | Exclusive License Agreement (PBGM01), dated July 31, 2024, by and between the Registrant and Gemma Biotherapeutics, Inc. | 10-Q | 001-39231 | November 13, 2024 |
| 10.15†^ | Exclusive License Agreement (PBKR03), dated July 31, 2024, by and between the Registrant and Gemma Biotherapeutics, Inc. | 10-Q | 001-39231 | November 13, 2024 |
| 10.16†^ | Exclusive License Agreement (PBML04), dated July 31, 2024, by and between the Registrant and Gemma Biotherapeutics, Inc. | 10-Q | 001-39231 | November 13, 2024 |
| 10.17†^ | Transition Services Agreement, dated July 31, 2024, by and between the Registrant and Gemma Biotherapeutics, Inc. | 10-Q | 001-39231 | November 13, 2024 |
| 10.18†^ | Research, Collaboration & License Agreement, dated July 31, 2024, by and between the Registrant and Gemma Biotherapeutics, Inc. | 10-Q | 001-39231 | November 13, 2024 |
| 10.19†^ | Second Amended and Restated Research, Collaboration & License Agreement, dated July 31, 2024, by and between the | 10-Q | 001-39231 | November 13, 2024 |

| | | | | | |
|---|---|---|---|---|---|
| | Registrant and the Trustees of the University of Pennsylvania. | | | | |
| 10.20†^ | Amendment to the Exclusive License Agreement (PBGM01), dated May 7, 2025, by and between the Registrant and Gemma Biotherapeutics, Inc. | 10-Q | 001-39231 | August 12, 2025 | |
| 10.21^ | Amendment to the Exclusive License Agreement (PBKR03), dated May 7, 2025, by and between the Registrant and Gemma Biotherapeutics, Inc. | 10-Q | 001-39231 | August 12, 2025 | |
| 10.22^ | Amendment to the Exclusive License Agreement (PBML04), dated May 7, 2025, by and between the Registrant and Gemma Biotherapeutics, Inc. | 10-Q | 001-39231 | August 12, 2025 | |
| 19.1^ | Insider Trading Policy. | 10-K | 001-39231 | March 3, 2025 | |
| 23.1 | Consent of KPMG LLP, an independent registered public accounting firm. | | | | X |
| 24.1 | Power of Attorney. Reference is made to the signature page hereto. | | | | X |
| 31.1 | Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | | | | X |
| 31.2 | Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | | | | X |
| 32.1* | Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. | | | | X |
| 32.2* | Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. | | | | X |
| 97 | Policy Relating to Recovery of Erroneously Awarded Compensation. | 10-K | 001-39231 | March 4, 2024 | |
| 101.INS | Inline XBRL Instance Document. | | | | X |

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|---|---|---|
| 101.SCH | XBRL Taxonomy Extension Schema Document. | X |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase Document. | X |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase Document. | X |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document. | X |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase Document. | X |
| 104 | Cover Page Interactive Data File (formatted as Inline XBRL). | X |

+ Indicates management contract or compensatory plan, contract or agreement.

† Registrant has omitted portions of the exhibit as permitted under Item 601(b)(10) of Regulation S-K.

^ Registrant has omitted schedules and exhibits pursuant to Item 601(a)(5) of Regulation S-K. The Registrant agrees to furnish supplementally a copy of the omitted schedules and exhibits to the SEC upon request.

* This certification is deemed not filed for purposes of section 18 of the Exchange Act or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.

**Item 16. Form 10-K Summary.**

Registrants may voluntarily include a summary of information required by Form 10-K under Item 16. We have elected not to include such summary.

## SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

PASSAGE BIO, INC.

Date: March 3, 2026

By: /s/ William Chou, M.D.
Name: William Chou, M.D.
Title: Chief Executive Officer and Director

Date: March 3, 2026

By: /s/ Kathleen Borthwick
Name: Kathleen Borthwick
Title: Chief Financial Officer

## POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints William Chou, M.D. and Kathleen Borthwick, and each of them, with full power of substitution and resubstitution, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agents full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorney-in-fact and agents or his substitute or substitutes may lawfully do or cause to be done by virtue thereof. Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

| Signature | Title | Date |
|---|---|---|
| /s/ William Chou, M.D. | President, Chief Executive Officer and Director | March 3, 2026 |
| William Chou, M.D. | *(Principal Executive Officer)* | |
| /s/ Kathleen Borthwick | Chief Financial Officer | March 3, 2026 |
| Kathleen Borthwick | *(Principal Financial and Accounting Officer)* | |
| /s/ Maxine Gowen, Ph.D. | Director | March 3, 2026 |
| Maxine Gowen, Ph.D. | | |
| /s/ Athena Countouriotis, M.D. | Director | March 3, 2026 |
| Athena Countouriotis, M.D. | | |
| /s/ Sandip Kapadia | Director | March 3, 2026 |
| Sandip Kapadia | | |
| /s/ Thomas Kassberg | Director | March 3, 2026 |
| Thomas Kassberg | | |
| /s/ Derrell Porter, M.D. | Director | March 3, 2026 |
| Derrell Porter, M.D. | | |
| /s/ Dolan Sondhi, Ph.D. | Director | March 3, 2026 |
| Dolan Sondhi, Ph.D. | | |

## About Passage Bio

Passage Bio (Nasdaq: PASG) is a clinical-stage genetic medicines company on a mission to improve the lives of patients with neurodegenerative diseases. Our primary focus is the development and advancement of cutting-edge, one-time therapies designed to target the underlying pathology of these conditions. Passage Bio's lead product candidate, PBFT02, seeks to treat neurodegenerative conditions, including frontotemporal dementia, by elevating progranulin levels to restore lysosomal function and slow disease progression.

## Leadership Team

**William Chou, M.D.**, President and Chief Executive Officer

**Kathleen Borthwick**, Chief Financial Officer

**Sue Browne, Ph.D.**, Chief Scientific Officer

**Eden Fucci**, Senior Vice President, Technical Operations

**Stuart Henderson**, Chief Business Officer

**Karl Whitney, Ph.D.**, Senior Vice President, Global Regulatory Affairs

## Board of Directors

**William Chou, M.D.**

**Athena Countouriotis, M.D.**

**Maxine Gowen, Ph.D.**, Chairwoman

**Sandip Kapadia**

**Tom Kassberg**

**Derrell D. Porter, M.D.**

**Dolan Sondhi, Ph.D.**

## Corporate Counsel

**Fenwick & West LLP**
401 Union Street
Seattle, WA 98101

## Independent Auditors

**KPMG LLP**
1735 Market Street
Philadelphia, PA 19103-2499

## Transfer Agent & Registrar

**Computershare Trust Company, N.A.**
Shareholder Services
(800) 736-3001 or (781) 575-3100
P.O. Box 43078
Providence, RI 02940-3078

## Common Stock

Passage Bio, Inc. common stock is traded on the Nasdaq Capital Market under the ticker PASG.

## Annual Meeting (Virtual)

Tuesday, May 19, 2026, 9:00 am ET

## Forward-Looking Statements

This annual report contains "forward-looking statements" within the meaning of, and made pursuant to the safe harbor provisions of, the Private Securities Litigation Reform Act of 1995, including, but not limited to: our expectations about timing and execution of anticipated milestones, including the progress of clinical trials, the availability of clinical data from such trials, and the timing of engagement with, and feedback from, regulatory authorities; our expectations about our collaborators' and partners' ability to execute key initiatives; our expectations about cash runway; and the ability of our product candidates to treat their respective target CNS disorders; and the potential development of other product candidates. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "continue," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "might," "plan," "potential," "possible," "should," "target," "will," "would," and other words and terms of similar meaning. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including: our ability to develop and obtain regulatory approval for our product candidates; the timing and results of preclinical studies and clinical trials; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; the occurrence of adverse safety events; the risk that positive results in a preclinical study or clinical trial may not be replicated in subsequent trials or success in early stage clinical trials may not be predictive of results in later stage clinical trials; failure to protect and enforce our intellectual property, and other proprietary rights; our dependence on collaborators and other third parties for the development and manufacture of product candidates and other aspects of our business, which are outside of our full control; risks associated with current and potential delays, work stoppages, or supply chain disruptions; and the other risks and uncertainties that are described in the Risk Factors section in documents the company files from time to time with the Securities and Exchange Commission (SEC), and other reports as filed with the SEC. Passage Bio undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments, or otherwise.

PassageBio

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2005 Market Street, 39th Floor
Philadelphia, PA 19103

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