Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549
FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 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 (State or other jurisdiction of incorporation or organization)	**82-2729751** (I.R.S. Employer Identification No.)
One Commerce Square **2005 Market Street, 39th Floor** **Philadelphia, PA** (Address of principal executive offices)	**19103** (Zip Code)

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

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)

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

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

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

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

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

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

As of November 6, 2025, the registrant had 3,178,710 shares of common stock, $0.0001 par value per share, outstanding.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements. All statements other than statements of historical facts contained in this Quarterly 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 Quarterly 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, tariffs, the ongoing federal government shutdown and 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 Quarterly 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 Quarterly Report and are subject to a number of known and unknown risks, uncertainties and assumptions, including those described under the sections in this Quarterly Report entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Quarterly 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 Quarterly 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.

Table of Contents

PART I-FINANCIAL INFORMATION

Item 1. Interim Financial Statements.

Passage Bio, Inc.
Balance Sheets

(in thousands, except share and per share data)	(Unaudited) September 30, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 52,773	$ 37,573
Marketable securities	—	39,183
Prepaid expenses and other current assets	1,637	838
Prepaid research and development	1,320	1,221
Total current assets	55,730	78,815
Property and equipment, net	5,159	9,331
Right of use assets - operating leases	13,001	13,803
Other assets	270	463
Total assets	$ 74,160	$ 102,412
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 952	$ 742
Accrued expenses and other current liabilities	4,001	6,707
Non-refundable sublicense and transition services payments	13,750	8,226
Operating lease liabilities	3,542	3,688
Total current liabilities	22,245	19,363
Operating lease liabilities - noncurrent	20,795	21,788
Total liabilities	43,040	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 September 30, 2025 and December 31, 2024	—	—
Common stock, $0.0001 par value: 300,000,000 shares authorized; 3,178,710 shares issued and outstanding at September 30, 2025 and 3,161,503 shares issued and outstanding at December 31, 2024	—	—
Additional paid-in capital	722,894	720,488
Accumulated other comprehensive income (loss)	—	8
Accumulated deficit	(691,774)	(659,235)
Total stockholders' equity	31,120	61,261
Total liabilities and stockholders' equity	$ 74,160	$ 102,412

See accompanying notes to unaudited interim financial statements.

Passage Bio, Inc.
Statements of Operations and Comprehensive Loss
(Unaudited)

(in thousands, except share and per share data)	Three Months Ended September 30, 2025	Three Months Ended September 30, 2024	Nine Months Ended September 30, 2025	Nine Months Ended September 30, 2024
Operating expenses:				
Research and development	$ 4,307	$ 8,656	$ 17,858	$ 30,621
General and administrative	4,348	7,251	14,953	20,276
Impairment of long-lived assets	—	4,795	2,637	5,233
Loss from operations	(8,655)	(20,702)	(35,448)	(56,130)
Other income (expense), net	906	1,362	2,909	4,088
Net loss	$ (7,749)	$ (19,340)	$ (32,539)	$ (52,042)
Per share information:				
Net loss per share of common stock, basic and diluted	$ (2.44)	$ (6.15)	$ (10.26)	$ (17.04)
Weighted average common shares outstanding, basic and diluted	3,178,710	3,146,582	3,170,573	3,054,440
Comprehensive loss:				
Net loss	$ (7,749)	$ (19,340)	$ (32,539)	$ (52,042)
Unrealized gain (loss) on marketable securities	—	99	(8)	75
Comprehensive loss	$ (7,749)	$ (19,241)	$ (32,547)	$ (51,967)

See accompanying notes to unaudited interim financial statements.

Passage Bio, Inc.
Statements of Stockholders' Equity
(Unaudited)

(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 July 1, 2025	3,178,710	$ —	$ 722,283	$ —	$ (684,025)	$ 38,258
Share-based compensation expense	—	—	611	—	—	611
Net loss	—	—	—	—	(7,749)	(7,749)
Balance at September 30, 2025	3,178,710	$ —	$ 722,894	$ —	$ (691,774)	$ 31,120

(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	14,325	—	—	—	—	—
Issuance of shares in connection with employee stock purchase plan	2,882	—	14	—	—	14
Unrealized gain (loss) on marketable securities	—	—	—	(8)	—	(8)
Share-based compensation expense	—	—	2,392	—	—	2,392
Net loss	—	—	—	—	(32,539)	(32,539)
Balance at September 30, 2025	3,178,710	$ —	$ 722,894	$ —	$ (691,774)	$ 31,120

See accompanying notes to unaudited interim financial statements.

Passage Bio, Inc.
Statements of Stockholders' Equity
(Unaudited)

(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 July 1, 2024	3,146,154	$ —	$ 717,794	$ (67)	$ (627,170)	$ 90,557
Exercise of stock options and vesting of restricted stock units	625	—	—	—	—	—
Unrealized gain (loss) on marketable securities	—	—	—	99	—	99
Share-based compensation expense	—	—	1,400	—	—	1,400
Net loss	—	—	—	—	(19,340)	(19,340)
Balance at September 30, 2024	3,146,779	$ —	$ 719,194	$ 32	$ (646,510)	$ 72,716

(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	36,232	—	35	—	—	35
Issuance of shares in connection with employee stock purchase plan	4,929	—	50	—	—	50
Unrealized gain (loss) on marketable securities	—	—	—	75	—	75
Share-based compensation expense	—	—	4,573	—	—	4,573
Net loss	—	—	—	—	(52,042)	(52,042)
Balance at September 30, 2024	3,146,779	$ —	$ 719,194	$ 32	$ (646,510)	$ 72,716

See accompanying notes to unaudited interim financial statements.

Passage Bio, Inc.
Statements of Cash Flows
(Unaudited)

(in thousands)	Nine Months Ended September 30, 2025	2024
Cash flows used in operating activities:		
Net loss	$ (32,539)	$ (52,042)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Depreciation and amortization	551	2,362
Share-based compensation	2,392	4,573
Amortization of premium and discount on marketable securities, net	129	(1,162)
Impairment of long-lived assets	2,637	5,233
Other non-cash items	14	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets, and other assets	(806)	(117)
Prepaid research and development	(99)	1,562
Non-refundable sublicense and transition services payments received	4,015	5,000
Right of use assets and operating lease liabilities	(337)	(171)
Accounts payable	1,719	191
Accrued expenses and other current liabilities	(2,706)	(4,941)
Net cash provided by (used in) operating activities	(25,030)	(39,512)
Cash flows provided by (used in) investing activities:		
Purchases of marketable securities	—	(72,594)
Sales or maturities of marketable securities	39,046	113,882
Sale of property and equipment and other assets	1,170	(20)
Net cash provided by (used in) investing activities	40,216	41,268
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	14	50
Net cash provided by (used in) financing activities	14	8,827
Net increase (decrease) in cash and cash equivalents	15,200	10,583
Cash and cash equivalents at beginning of period	37,573	21,709
Cash and cash equivalents at end of period	$ 52,773	$ 32,292
Supplemental disclosure of non-cash activities:		
Unrealized gain (loss) on marketable securities	$ (8)	$ 75
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 unaudited interim financial statements.

Passage Bio, Inc.
Notes to Unaudited Interim 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 $691.8 million as of September 30, 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, the establishment of 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 6,000,000 shares of common stock (300,000 shares adjusted for the 1-for-20 reverse stock split of its common stock effected in 2025) 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 limited in its capacity to offer and sell shares of its common stock under this sales agreement pursuant to the prospectus supplement to its shelf registration statement on Form S-3, filed on March 5, 2025. As of September 30, 2025, $15.8 million of capacity remains available to be sold under the ATM Facility.

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 Accounting Standards Update, or ASU, No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a 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

The Company's complete summary of significant accounting policies can be found in "Note 3. Summary of Significant Accounting Policies" in the audited financial statements included in the Company's Annual Report filed on Form 10-K for the year ended December 31, 2024.

Basis of Presentation

The accompanying unaudited 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 Accounting Standards Codification, or ASC, and Accounting Standards Updates promulgated by the Financial Accounting Standards Board, or FASB.

On May 28, 2025, the Company's stockholders provided authorization for the Company's Board of Directors to effect a reverse stock split to regain compliance with Nasdaq's listing requirements. 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.

Interim Financial Statements

The accompanying unaudited interim financial statements have been prepared from the books and records of the Company in accordance with GAAP for interim financial information and Rule 10-01 of Regulation S-X promulgated by the SEC, which permits reduced disclosures for interim periods. All adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the accompanying balance sheets, statements of operations and comprehensive loss, stockholders' equity, and cash flows have been made. Although these interim financial statements do not include all of the information and notes required for complete annual financial statements, management believes the disclosures are adequate to make the information presented not misleading. Unaudited interim results of operations and cash flows are not necessarily indicative of the results that may be expected for the full year. Unaudited interim financial statements and notes should be read in conjunction with the audited financial statements and notes included in the Company's 2024 Annual Report filed on Form 10-K.

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 risk, industry risk, and security type risk. 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 September 30, 2025 consisted of money market funds as described in Note 4. 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. These 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. As of September 30, 2025, the Company had no marketable securities.

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 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 nine months ended September 30, 2025. The Company did not recognize any losses on disposals of property and equipment for the three months ended September 30, 2025 or the three and nine months ended September 30, 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 laboratory equipment and certain other assets of $2.6 million for the nine months ended September 30, 2025. The Company did not recognize any impairment expenses for long-lived assets for the three months ended September 30, 2025. The Company recognized impairment expenses for property and equipment of $2.3 million and $2.7 million for the three and nine months ended September 30, 2024, respectively.

The impairment expenses for the nine months ended September 30, 2025, relate to the Company's January 2025 announcement to reduce its overall workforce by 55% and cease its lab operations in Hopewell, New Jersey. As a result, 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. Subsequent to recording the impairment, the Company entered into a sales agreement for $1.2 million for substantially all the laboratory equipment and certain other assets.

Leasing

The Company evaluates leases at their inception to determine if they are an operating lease or a finance lease. As of September 30, 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 did not recognize any impairment expenses for ROU assets for the three and nine months ended September 30, 2025. The Company recognized impairment expenses for ROU assets of $2.5 million for the three and nine months ended September 30, 2024.

Research and Development

Research and development costs are expensed as incurred and consist primarily of expenses incurred with the Trustees of the University of Pennsylvania's, or Penn's, Gene Therapy Program, or GTP, 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, and income from subleases.

The Company recorded $0.9 million to other income (expense), net for the three months ended September 30, 2025, which consisted of $0.5 million attributable to interest income and $0.4 million related to income from subleases.

The Company recorded $1.4 million to other income (expense), net for the three months ended September 30, 2024, which consisted of $1.1 million attributable to interest income and the amortization of premium and discount on the Company's marketable securities, and $0.3 million related to income from subleases.

The Company recorded $2.9 million to other income (expense), net for the nine months ended September 30, 2025, which consisted of $1.8 million attributable to interest income and the amortization of premium and discount on the Company's marketable securities, and $1.1 million related to income from subleases.

The Company recorded $4.1 million to other income (expense), net for the nine months ended September 30, 2024, which consisted of $3.5 million attributable to interest income and the amortization of premium and discount on the Company's marketable securities, and $0.6 million related to income from subleases.

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 ASC Topic 606, *Revenue from Contracts with Customer*s, 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.

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:

	Nine Months Ended September 30,	
	2025	2024
Stock options	669,558	600,473
Unvested restricted stock units	52,500	16,510
Employee stock purchase plan	1,973	5,220
	724,031	622,203

Recently Issued 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 is currently evaluating the impact of this guidance on its disclosures.

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.

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
September 30, 2025:				
Cash accounts in banking institutions	$ 2,490	$ —	$ —	$ 2,490
Money market funds	50,283	—	—	50,283
Total	$ 52,773	$ —	$ —	$ 52,773
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

As of September 30, 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 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)
September 30, 2025:			
Assets			
Cash equivalents:			
Money market funds	$ 50,283	$ —	$ —
Total cash equivalents	50,283	—	—
Total financial assets	$ 50,283	$ —	$ —
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	$ —

All of the marketable securities had contractual maturities less than one year as of December 31, 2024 and unrealized gains and losses on the marketable securities were de minimis as of December 31, 2024.

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. Assets remeasured in the nine months ended September 30, 2025 include the laboratory equipment and certain other assets which were sold prior to September 30, 2025 and are not included in the balance sheet as of September 30, 2025. The impairment related to the remeasurement of $2.6 million is included in the statement of operations for the nine months ended September 30, 2025.

6. Property and Equipment, Net

Property and equipment, net, consists of the following:

(in thousands)	September 30, 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	7,386	7,386
Total property and equipment	8,900	19,055
Accumulated depreciation and amortization	(3,741)	(9,724)
	$ 5,159	$ 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 entered into a sales agreement for $1.2 million for substantially all of the laboratory equipment and certain other assets. As a result, the Company did not record any depreciation on the impaired and disposed laboratory equipment during the three and nine months ended September 30, 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 September 30, 2025.

Depreciation and amortization expense was $0.2 million and $0.8 million for the three months ended September 30, 2025 and 2024, respectively.

Depreciation and amortization expense was $0.6 million and $2.4 million for the nine months ended September 30, 2025 and 2024, respectively.

7. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

(in thousands)	September 30, 2025	December 31, 2024
Professional fees	$ 303	$ 406
Compensation and related benefits	2,985	4,405
Research and development	713	1,896
	$ 4,001	$ 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, 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 $5.0 million was previously received and $5.0 million of which was due in May 2025; (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 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 September 30, 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 is a newly-formed company with 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 September 30, 2025, the Company has received an initial payment 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 September 30, 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 nine months ended September 30, 2025. During the three months ended September 30, 2025, and the three and nine months ended September 30, 2024, the Company recorded no severance and termination-related costs in general and administrative expenses or in research and development expenses. As of September 30, 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 September 30, 2025. In 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 is focused on state-of-the-art analytical capabilities, assay development and validation, and clinical product testing to support both viral vector manufacturing and clinical development. 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 September 30, 2025.

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 value, 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 it 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. The impairment charge was recorded as of the sublease execution date.

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. The Company is pursuing additional opportunities to sublease additional space to further offset portions of its financial obligations under the Laboratory Lease and additional impairments to ROU assets and leasehold improvements could occur based on the economic terms included in such agreements.

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)	
2025	$ 918
2026	3,757
2027	3,863
2028	3,973
2029	4,085
Thereafter	21,621
Total undiscounted lease payments	38,217
Less: imputed interest	(13,880)
Total lease liabilities	$ 24,337

The following table summarizes lease expense by lease type that was recognized during the three and nine months ended September 30, 2025 and 2024:

($ in thousands)	Three Months Ended		Nine Months Ended	
	September 30, 2025	September 30, 2024	September 30, 2025	September 30, 2024
Operating lease cost	$ 871	$ 904	$ 2,628	$ 2,644
Variable lease cost	503	530	1,584	1,644
	$ 1,374	$ 1,434	$ 4,212	$ 4,288

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

($ in thousands)	Nine Months Ended	
	September 30, 2025	September 30, 2024
Weighted-average discount rate	9.7%	9.7%
Weighted-average remaining lease term (years)	9.5	10.4

The cash paid for amounts included in the measurement of the Company's operating lease liabilities for the nine months ended September 30, 2025 and 2024 were $3.0 million and $2.8 million, respectively, recorded in operating cash flows.

The following table summarizes sublease income that was recognized in other income (expense), net during the three and nine months ended September 30, 2025 and 2024:

($ in thousands)	Three Months Ended		Nine Months Ended	
	September 30, 2025	September 30, 2024	September 30, 2025	September 30, 2024
Sublease rental income	$ 371	$ 332	$ 1,101	$ 632

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 IND-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. The outlicense of GM1 to Gemma under the Outlicense Transaction Agreements, and subsequent business decisions implemented by Gemma in their sole discretion, could be considered an event related to the divesture of GM1 under the Amended Catalent Agreements and require the Company to make payment of certain fees to Catalent, which fees are immaterial.

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 September 30, 2025.

The Company is a 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 his 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. The Company is awaiting a decision on whether the Superior Court of Pennsylvania will review the case and 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. Stockholder's Equity and Share-Based Compensation

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.

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 September 30, 2025 was 947,598. Additionally, 200,621 shares previously issued under the 2018 Plan which were forfeited are available for issuance under the Incentive Plan. As of September 30, 2025, 423,039 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 155,155 and 137,361 shares in January 2025 and 2024, 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 September 30, 2025 was 125,000. Of this amount, 87,166 shares were available for future grants as of September 30, 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:

	Three Months Ended September 30,		Nine Months Ended September 30,	
(in thousands)	2025	2024	2025	2024
Research and development	$ 170	$ 535	$ 662	$ 2,078
General and administrative	441	865	1,730	2,495
	$ 611	$ 1,400	$ 2,392	$ 4,573

The following table summarizes stock option activity for the nine months ended September 30, 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	(114,941)	48.96	
Expired	(41,290)	175.24	
Outstanding at September 30, 2025	669,558	$ 50.58	8.0
Vested and exercisable at September 30, 2025	341,557	$ 84.77	7.1
Vested or expected to vest at September 30, 2025	669,558	$ 50.58	8.0

The weighted average grant date fair value of options granted was $6.02 and $20.60 for the nine months ended September 30, 2025 and 2024, respectively. As of September 30, 2025, the total unrecognized compensation expense related to unvested stock option awards was $3.5 million, which the Company expects to recognize over a weighted average period of 2.2 years.

The aggregate intrinsic value of options outstanding was $0.1 million at September 30, 2025 and was de minimis at September 30, 2024. The aggregate intrinsic value of options exercised and options exercisable were each de minimis during the three and nine months ended September 30, 2025 and 2024.

The fair value of each option was estimated on the date of grant using the weighted average assumptions in the table below:

	Nine Months Ended September 30,	
	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 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 price 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 nine months ended September 30, 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	(14,325)	27.56
Forfeited	(268)	90.40
Unvested balance at September 30, 2025	52,500	$ 11.44

As of September 30, 2025, the total unrecognized expense related to all RSUs was $0.4 million, which the Company expects to recognize over a weighted-average period of 1.2 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, 60,703 were available for future grants as of September 30, 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, 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.

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 three and nine months ended September 30, 2025 and 2024.

13. 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 in the Company's 2024 Annual Report filed on Form 10-K. 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)	Three Months Ended September 30, 2025	Three Months Ended September 30, 2024	Nine Months Ended September 30, 2025	Nine Months Ended September 30, 2024
Research and development				
Wages, benefits and other payroll	$ 1,147	$ 2,957	$ 6,038	$ 9,312
Third-party costs	2,880	4,492	10,828	17,171
Share-based compensation	170	535	662	2,078
Depreciation and amortization	110	672	330	2,060
Total research and development expenses	4,307	8,656	17,858	30,621
General and administrative				
Wages, benefits and other payroll	1,416	2,346	6,004	6,886
Third-party costs	2,421	3,952	6,998	10,592
Share-based compensation	441	865	1,730	2,495
Depreciation and amortization	70	88	221	303
Total general and administrative expenses	4,348	7,251	14,953	20,276
Impairment of long-lived assets	—	4,795	2,637	5,233
Loss from operations	8,655	20,702	35,448	56,130
Other (income) expense, net	(906)	(1,362)	(2,909)	(4,088)
Net loss	$ 7,749	$ 19,340	$ 32,539	$ 52,042

14. Subsequent Events

None.

Item 2. 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 Quarterly Report on Form 10-Q. 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 Part II, Item 1A below.

Overview and Pipeline

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.

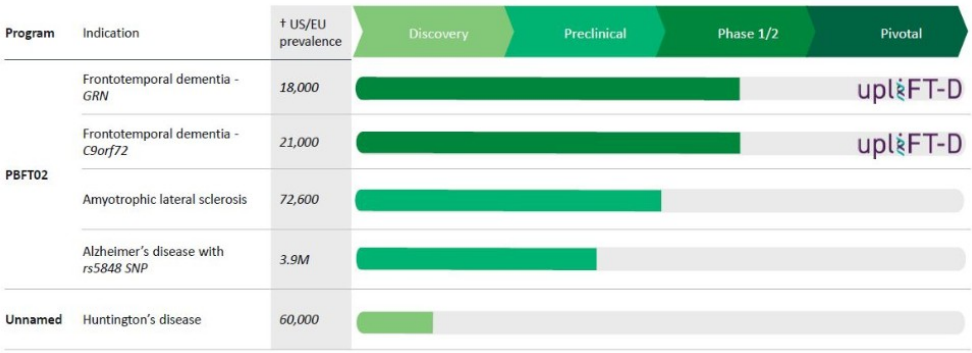
Our lead clinical product candidate, PBFT02, seeks to elevate progranulin levels to enhance lysosomal function and slow disease progression across a variety of neurodegenerative diseases. PBFT02 is a gene replacement therapy that utilizes an adeno-associated virus serotype 1, or AAV1, capsid to deliver 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 are proceeding with clinical development of PBFT02 in FTD-*C9orf72* patients, and have opened enrollment in the upliFT-D study for this population.

We are party to a series of sublicense agreements, as amended, with Gemma Biotherapeutics, Inc., or Gemma, a newly formed genetic medicines company co-founded by Dr. James Wilson in connection with the outlicensing of PBGM01 for the treatment of GM1 gangliosidosis, or GM1, PBKR03 for the treatment of Krabbe disease, and PBML04 for the treatment of metachromatic leukodystrophy, or MLD, collectively the Outlicensed Programs, and such agreements, the Amended Gemma Sublicenses. In addition, we have entered into a Transition Services Agreement, as amended, and a research, collaboration and license agreement, or the Gemma Collaboration Agreement, 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 progressed four product candidates from preclinical to clinical stage development and had one active preclinical program in Huntington's disease 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.

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

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 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=7), 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 June 2025, interim safety highlights from PBFT02 in FTD-*GRN* patients (n=8) included:

- In five of eight patients, all treatment emergent adverse events were mild to moderate in severity.
- Three of eight patients experienced a total of four serious adverse events, or SAEs. Patient 1 experienced the asymptomatic SAEs of venous sinus thrombosis, or VST, and hepatotoxicity. Patient 7 also experienced the SAE of VST, which was asymptomatic and completely resolved prior to day 30 following treatment with anticoagulants. The first Dose 2 patient (Patient 8) experienced the SAE of pulmonary embolism in the setting of a concurrent systemic infection six weeks after receiving PBFT02. The patient responded to treatment with anticoagulants, and the SAE was assessed as possibly related to treatment.
- No evidence of 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.

As of November 2025, we have completed dosing of Cohorts 1 and 2 in the upliFT-D study. 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.

We have amended the upliFT-D clinical trial protocol to introduce a short course of low dose prophylactic anticoagulation, a decision supported by study investigators and the Independent Data Monitoring Committee, or IDMC.

We have implemented the amended protocol at initial trial sites and are currently enrolling Cohort 3, which is expected to consist of five to ten FTD-GRN patients receiving Dose 2 of PBFT02.

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 our high-productivity, suspension-based PBFT02 manufacturing process.

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 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 received positive regulatory feedback on the clinical pathway to treating FTD-*C9orf72* with PBFT02 in the ongoing upliFT-D trial and revised the study to include two cohorts. Cohorts 4 and 5 will consist of three to five symptomatic FTD patients with *C9orf72* gene mutations who will initially receive Dose 2 PBFT02. There are no disease modifying therapies approved for the treatment of FTD-*C9orf72*. Based on available literature, we estimate the prevalence of FTD-*C9orf72* in the United States and Europe is approximately 21,000. We have implemented the amended protocol at initial trial sites and are currently enrolling Cohort 4.

Similarly, we received positive regulatory feedback on the clinical pathway to treating ALS with PBFT02.

PBFT02 for the treatment of AD

We 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.

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 study in FTD-*GRN*.

Active Research Programs

We have one unnamed preclinical research program through the Gemma Collaboration Agreement and are exploring multiple potential treatment targets for Huntington's disease.

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

Paused Research Programs

We also have a research program through the Gemma Collaboration Agreement for Temporal Lobe Epilepsy, or TLE, which was previously conducted under the research, collaboration and licensing agreement with Penn, as amended, previously the Penn Agreement and now referred to as the Penn License Agreement. In order to reduce operating expenses, we have paused development of this program.

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 the accompanying 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.

Business Overview

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 $7.7 million and $19.3 million for the three months ended September 30, 2025 and 2024, respectively, and $32.5 million and $52.0 million for the nine months ended September 30, 2025 and 2024, respectively. As of September 30, 2025, we had an accumulated deficit of $691.8 million. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures, and to a lesser extent, 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 September 30, 2025, we had cash and cash equivalents of $52.8 million. We expect our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2027.

Financial Operations Overview

License Agreement

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 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, 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 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-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, on 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 $5.0 million was previously received and $5.0 million of which was due in May 2025; (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 September 30, 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.

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. The outlicense of GM1 to Gemma under the Outlicense Transaction Agreements, and subsequent business decisions implemented by Gemma in their sole discretion, could be considered an event related to the divesture of GM1 under the Amended Catalent Agreements and require us to make payment of certain fees to Catalent, which fees are immaterial.

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 and amortization;
- 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 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 study 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 that 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 nine months ended September 30, 2025, we recognized impairment expenses related to property and equipment and certain other assets in connection with the announcement to reduce our workforce by 55% and cease our lab operations in Hopewell, New Jersey. We reassessed asset groups at the lab in Hopewell, New Jersey, 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.

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, and income from subleases.

Results of Operations

Comparison of the three months ended September 30, 2025 and 2024

The following table sets forth our results of operations for the three months ended September 30, 2025 and 2024:

	Three months ended September 30,		
(in thousands)	**2025**	**2024**	**Change**
Operating expenses:			
Research and development	$ 4,307	$ 8,656	$ (4,349)
General and administrative	4,348	7,251	(2,903)
Impairment of long-lived assets	—	4,795	(4,795)
Loss from operations	(8,655)	(20,702)	12,047
Other income (expense), net	906	1,362	(456)
Net loss	$ (7,749)	$ (19,340)	$ 11,591

Research and Development Expenses

Research and development expenses decreased by $4.4 million to $4.3 million for the three months ended September 30, 2025 from $8.7 million for the three months ended September 30, 2024. The decrease was primarily due to the following:

- a decrease of $1.8 million in wages and benefits due to a lower headcount following our restructuring in January 2025;
- a decrease of $0.8 million in facility and other expenses related to decreased depreciation expenses in connection with the disposal of our laboratory equipment;
- a decrease of $0.4 million in clinical operations expenses due to decreased activity in the GM1 program partially offset by increased activity supporting the FTD program;
- a decrease of $0.4 million in share-based compensation expense related to reductions in headcount;
- a decrease of $0.4 million in professional fees;
- a decrease of $0.3 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; and
- a decrease of $0.3 million in preclinical research expenses primarily related to reduced Huntington's disease program expenses.

General and Administrative Expenses

General and administrative expenses decreased by $3.0 million to $4.3 million for the three months ended September 30, 2025 from $7.3 million for the three months ended September 30, 2024. The decrease was primarily due to the following:

- a decrease of $1.3 million in facility and other expenses primarily due to accruals for litigation matters in the three months ended September 30, 2024 which were subsequently reversed;
- a decrease of $1.0 million and $0.4 million in wages and benefits and share-based compensation expense, respectively, related to reductions in headcount; and
- a decrease of $0.3 million in professional fees.

Impairment of Long-Lived Assets

During the three months ended September 30, 2025, we did not record any impairment expense.

During the three months ended September 30, 2024, we recorded $4.8 million of impairment expense 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.

Other Income (Expense), Net

Other income (expense), net decreased by $0.5 million to $0.9 million for the three months ended September 30, 2025 from $1.4 million for the three months ended September 30, 2024. The decrease was primarily due to the following:

- a decrease of $0.6 million in the amortization of premium and discount on our marketable securities.

The decrease was partially offset by:

- an increase of $0.1 million attributable to income from subleases.

Comparison of the nine months ended September 30, 2025 and 2024

The following table sets forth our results of operations for the nine months ended September 30, 2025 and 2024:

	Nine months ended September 30,		
(in thousands)	**2025**	**2024**	**Change**
Operating expenses:			
Research and development	$ 17,858	$ 30,621	$ (12,763)
General and administrative	14,953	20,276	(5,323)
Impairment of long-lived assets	2,637	5,233	(2,596)
Loss from operations	(35,448)	(56,130)	20,682
Other income (expense), net	2,909	4,088	(1,179)
Net loss	$ (32,539)	$ (52,042)	$ 19,503

Research and Development Expenses

Research and development expenses decreased by $12.7 million to $17.9 million for the nine months ended September 30, 2025 from $30.6 million for the nine months ended September 30, 2024. The decrease was primarily due to the following:

- 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 $3.3 million in wages and benefits due to a lower headcount from our restructuring in January 2025;
- a decrease of $1.9 million in facility and other expenses related to decreased depreciation expenses in connection with the disposal of our laboratory equipment;
- a decrease of $1.4 million in share-based compensation expense related to reductions in headcount;
- a decrease of $1.2 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 $1.1 million in professional fees; and
- a decrease of $0.1 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 $5.3 million to $15.0 million for the nine months ended September 30, 2025 from $20.3 million for the nine months ended September 30, 2024. The decrease was primarily due to the following:

- a decrease of $2.1 million in professional fees;
- a decrease of $1.5 million in facility and other expenses primarily due to accruals for litigation matters in the nine months ended September 30, 2024 which were subsequently reversed; and
- a decrease of $0.9 million and $0.8 million in wages and benefits and share-based compensation expense, respectively, related to reductions in headcount.

Impairment of Long-Lived Assets

During the nine months ended September 30, 2025, we recorded $2.6 million of impairment expense related to laboratory equipment and certain other assets which were revalued and subsequently sold from the Hopewell Laboratory Space.

During the nine months ended September 30, 2024, we recorded $5.2 million of impairment expense primarily consisting of $2.5 million and $2.3 million recorded to the ROU assets and property and equipment, net, respectively, related to the Hopewell Laboratory Space. In addition, we recorded $0.4 million of impairment expenses related to property and equipment for a construction in progress asset we no longer planned to deploy.

Other Income (Expense), Net

Other income (expense), net decreased by $1.2 million to $2.9 million for the nine months ended September 30, 2025 from $4.1 million for the nine months ended September 30, 2024. The decrease was primarily due to the following:

- a decrease of $1.7 million in the amortization of premium and discount on our marketable securities.

The decrease was partially offset by:

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

Liquidity and Capital Resources

Overview

As of September 30, 2025, we had $52.8 million in cash and cash equivalents and had an accumulated deficit of $691.8 million. We expect our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into 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 6,000,000 shares (300,000 shares adjusted for the Reverse Stock Split) 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. We are limited in our capacity to offer and sell shares of our common stock under this sales agreement pursuant to the prospectus supplement to our shelf registration statement on Form S-3, filed on March 5, 2025. As of September 30, 2025, $15.8 million of capacity remains available to be sold under the ATM Facility.

Cash Flows

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

	Nine months ended September 30,	
(in thousands)	**2025**	**2024**
Cash provided by (used in) operating activities	$ (25,030)	$ (39,512)
Cash provided by (used in) investing activities	40,216	41,268
Cash provided by (used in) financing activities	14	8,827
Net increase (decrease) in cash and cash equivalents	$ 15,200	$ 10,583

Net Cash Provided by (Used in) Operating Activities

During the nine months ended September 30, 2025, we used $25.0 million of net cash in operating activities. Cash used in operating activities reflected a net loss of $32.5 million and a decrease in our operating assets of $1.8 million and non-cash charges of $5.7 million related to depreciation, amortization, share-based compensation, amortization of premium and discount, net, impairment of long-lived assets, and other non-cash items. The primary use of cash was to fund our operations related to the development of our product candidates.

During the nine months ended September 30, 2024, we used $39.5 million of net cash in operating activities. Cash used in operating activities reflected a net loss of $52.0 million, partially offset by a net decrease in our operating assets of $1.5 million, and net non-cash charges of $11.0 million related to depreciation, amortization, share-based compensation, amortization of premium and discount, net, and impairment of long-lived assets. The primary use of cash was to fund our operations related to the development of our product candidates.

Net Cash Provided by (Used in) Investing Activities

During the nine months ended September 30, 2025, we had sales and maturities of $39.0 million in marketable securities and received cash proceeds of $1.2 million related to the sale of property and equipment and certain other assets. We did not make any purchases of property and equipment for the nine months ended September 30, 2025.

During the nine months ended September 30, 2024, we purchased $72.6 million in marketable securities, and had sales and maturities of $113.9 million in marketable securities. Purchases of property and equipment were de minimis for the nine months ended September 30, 2024.

Net Cash Provided by (Used in) Financing Activities

During the nine months ended September 30, 2025, we received de minimis proceeds from the issuance of common stock under the ESPP.

During the nine months ended September 30, 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 $0.1 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 and sublease are $38.2 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. The outlicense of GM1 to Gemma under the Outlicense Transaction Agreements, and subsequent business decisions implemented by Gemma in their sole discretion, could be considered an event related to the divesture of GM1 under the Amended Catalent Agreements and require us to make payment of certain fees to Catalent, which fees are immaterial.

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

During the nine months ended September 30, 2025, there were no material changes to our critical accounting policies and estimates from those described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates" in our 2024 Annual Report filed on Form 10-K.

JOBS Act Accounting Election

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies.

We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until December 31, 2025.

We are also 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 may 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. If we are a smaller reporting company at the time we cease to be an emerging growth company, 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, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Recent Accounting Pronouncements

See Note 3 to our unaudited interim financial statements included elsewhere in this Quarterly Report on Form 10-Q for a description of recent accounting pronouncements applicable to our financial statements.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

Not applicable.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

As of September 30, 2025, management, with the participation of our Principal Executive Officer and Principal Financial and Accounting Officer, performed an evaluation of the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including the Principal Executive Officer and Principal Financial and Accounting Officer, to allow timely decisions regarding required disclosures. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Principal Executive Officer and Principal Financial and Accounting Officer concluded that, as of September 30, 2025, our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended September 30, 2025 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II-OTHER INFORMATION

Item 1. Legal Proceedings

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 his 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. We are awaiting a decision on whether the Superior Court of Pennsylvania will review the case and 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 1A. 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 quarterly 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.

Summary of Risk Factors

Our business is subject to a number of risks and uncertainties, including those immediately following this summary. 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;
- 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.

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 our 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 $32.5 million and $52.0 million for the nine months ended September 30, 2025 and 2024, respectively. As of September 30, 2025, we had an accumulated deficit of $691.8 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 September 30, 2025, our cash and cash equivalents were $52.8 million. We expect that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into 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 $50.0 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 our 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 study 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, three patients in our upliFT-D trial, have experienced a total of four serious adverse events. As a result of the immune response observed in the first patient dosed, who received a low initial level of immunosuppression (60 mg oral prednisone daily for 60 days), we amended the protocol to increase the steroid regimen. Subsequent to the SAE experienced by the seventh patient, we introduced a new dose (Dose 2), which is half the dose used in patients one through seven (Dose 1). Subsequent to the SAE experienced by the eighth patient, we amended the upliFT-D trial protocol 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 also serves 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 study 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 study 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 Biologics License Application, or 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 disagree with our interpretation of data from preclinical programs or clinical trials;
- 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 new 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 the current or 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 new 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 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 new 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. If Dr. Wilson were to leave Gemma or to otherwise no longer be meaningfully involved with us, our preclinical research and development capabilities may be substantially reduced. Additionally, as a newly formed company, 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. 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.

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. 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 to produce clinical supply of our product candidates, and we have not entered into binding agreements with any such manufacturers to support commercialization. The competition for gene therapy contract development, manufacturing and testing services is intense. Additionally, these manufacturers do not have experience producing our product candidates at commercial scale and may not achieve the necessary regulatory approvals or produce our product candidates at the quality, quantities, locations and timing needed to support commercialization.

While we are in the process of establishing manufacturing capability for certain clinical manufacturing activities, we do not currently plan to independently manufacture most of the drug material for our planned clinical programs. We currently rely, and expect to continue to rely, on third parties for the production of our preclinical study and planned clinical trial materials, including the materials used to administer our product candidates and, therefore, we can control only certain aspects of their activities. The landscape for gene therapy contract development, manufacturing, and testing is competitive. Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves, including but not limited to potential competition from other genetic biotechnology companies for the use of such third-party manufacturers. For example, we currently rely on Catalent to manufacture our clinical supply. However, following the recently announced acquisition of Catalent by Novo Holdings A/S, we may face delays or other risks to our manufacturing process depending on any changes implemented as result of such transaction.

While we have secured an agreement with Catalent to manufacture clinical supply of our product candidates, we have not yet secured manufacturing capabilities for commercial quantities of our product candidates. We may be unable to negotiate binding agreements with the manufacturers to support our potential commercialization activities at commercially reasonable terms. 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 or 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 we 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 and suppliers can begin to commercially manufacture our product candidates, including the materials used to administer our product candidates, they must demonstrate to regulatory authorities that the planned chemistry, manufacturing and controls for our gene therapy product candidates meet certain requirements. Manufacturing of product candidates for clinical and commercial purposes must comply with the cGMP and applicable ex-U.S. regulatory requirements. The cGMP requirements govern quality control and documentation policies and procedures. Complying with cGMP and ex-U.S. regulatory requirements will require that we expend time, money and effort in production, recordkeeping and quality control to assure that our product candidates meet applicable specifications and other requirements. Our third-party manufacturers also must demonstrate to the FDA and ex-U.S. regulators that they can make the product candidate in accordance with the cGMP requirements as part of a pre-approval inspection prior to FDA or similar ex-U.S. regulatory approval of the product candidate. Failure to pass a pre-approval inspection might significantly delay our ability to begin trials in the respective jurisdiction and FDA and ex-U.S. regulatory approval of our product candidates. If any of our third-party manufacturers fail to comply with these requirements, we would be subject to possible regulatory action, which could limit the jurisdictions in which we are permitted to sell our products. As a result, our business, financial condition and results of operations may be materially harmed.

In addition, our third-party manufacturers may fail to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

Even if our third-party manufacturers comply with applicable regulatory requirements, we cannot assure that they will be able to successfully manufacture additional product candidates at a larger scale in a timely or economical manner, or at all. If they are unable to successfully increase our manufacturing scale or capacity, the development, testing, and clinical trials of our product candidates may be delayed or 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 competitors with respect to PBFT02 for the treatment of FTD-*GRN* to be Prevail Therapeutics Inc. (part of Eli Lilly & Co), which is conducting a Phase 1/2 clinical trial for a gene therapy treatment for FTD-*GRN*, and 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 is conducting a Phase 1/2 study 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 Arkuda Therapeutics small molecule progranulin enhancer program which entered 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., is conducting 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 preclinical programs targeting the TDP-43 pathway. There are also numerous pre-IND stage programs exploring TDP-43 and other targets for the treatment of FTD.

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 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, to methods of treating those diseases with rAAV, as well as to certain aspects of our manufacturing capabilities and related technologies. 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-*C9orf72* and ALS and an assay for measuring potency of our rAAV product candidate.

We also 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 will 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 U.S. Patent and Trademark Office, or USPTO, challenging the validity of one or more claims of our own or licensed patents, once issued. Such submissions may also be made prior to a patent's issuance, precluding the granting of a patent based on one of our pending licensed 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 have licensed, once issued. Furthermore, patents that we 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. As a result, 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. 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 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, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. 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 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 product 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 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, 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 in specific indications, we may not be the first to obtain marketing approval of these product candidates for the orphan-designated indication 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 indication 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 indication 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.

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 approved 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 approved 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 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 2031, 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 may, in some cases, require 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. The FDA released a final rule in September 2020 providing guidance for states to build and submit importation plans for drugs from Canada, and the FDA authorized the first such plan in Florida in January 2024.

Recently, several healthcare reform initiatives culminated in the enactment of the Inflation Reduction Act, or IRA, in August 2022, which allows, among other things, 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. 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. Negotiations for Medicare Part D products began in 2024 with the negotiated price taking effect in 2026, and negotiations for Medicare Part B products begin in 2026 with the negotiated price taking effect in 2028. In August 2023, HHS announced the ten Medicare Part D drugs and biologics that it selected for negotiations, and by October 1, 2023, each manufacturer of the selected drugs signed a manufacturer agreement to participate in the negotiations. HHS announced the negotiated maximum fair prices on August 15, 2024, and these price caps, which cannot exceed the statutory ceiling price, will come into effect on January 1, 2026. 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. 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 also extended enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through the year 2025. 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.

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. 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. We also benefit from the research expertise of Dr. Wilson. In his capacity as a Scientific Advisor, Dr. Wilson is not involved in day-to-day operations and does not have the ability to control or significantly influence the management or operating policies of the Company. Although we have entered into a consulting agreement with Dr. Wilson, he may terminate his relationship with us at any time. 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 believe that we take reasonable steps that are designed to protect the security, integrity and confidentiality of the information we collect, use, store, and disclose, but inadvertent or unauthorized data access may occur despite our efforts. For example, our system protections may be ineffective or inadequate, or we could be impacted by software bugs or other technical malfunctions, as well as employee error or malfeasance. Additionally, privacy and data protection laws are evolving, and it is possible that these laws may be interpreted and applied in a manner that is inconsistent with our data handling safeguards and practices that could result in fines, lawsuits, and other penalties, and significant changes to our or our third-party partners business practices and products and service offerings. To the extent that the measures we or our third-party business partners have taken prove to be insufficient or inadequate, we may become subject to litigation, breach notification obligations, or regulatory or administrative sanctions, which could result in significant fines, penalties, damages, harm to our reputation or loss of patients. 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, 2024, we had federal and state net operating loss, or NOL, carryforwards of $339.1 million, and local NOL carryforwards of $218.8 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 2044, and our local NOL began to expire in 2024 and expire through 2044.

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 Controls, 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, the current 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.

Our executive officers, directors, principal stockholders and their affiliates exercise significant influence over our company, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

As of September 30, 2025, our executive officers, directors, beneficial owners of 5% or more of our capital stock and their respective affiliates beneficially owned shares representing a substantial portion of our capital stock.

This group of stockholders may have the ability to control us through this ownership position and may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

The liquidity of our common stock may be adversely affected by our Reverse Stock Split.

On July 14, 2025, we effected the Reverse Stock Split in order to regain compliance with the continued listing requirements of the Nasdaq Capital Market. The liquidity of our common stock may be adversely affected by the Reverse Stock Split given the reduced number of shares that are outstanding following the Reverse Stock Split, which may lead to reduced trading and a smaller number of market makers for our common stock. In addition, the Reverse Stock Split may have increased the number of stockholders who own "odd lots" of less than 100 shares of our common stock. Odd lot shares may be more difficult to sell, and brokerage commissions and other costs of transactions in odd lots may be higher than the costs of transactions in "round lots" of even multiples of 100 shares.

Despite the Reverse Stock Split, the resulting per-share trading price of our common stock may nevertheless fail to attract institutional investors and may not satisfy the investing guidelines of such investors and, consequently, the trading liquidity of our common stock may be adversely affected. Accordingly, the Reverse Stock Split may not achieve the desired results of increasing marketability of our common stock.

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 either a small reporting or emerging growth 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 expect to 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, particularly after we are no longer an "emerging growth 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 an "emerging growth company" and "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until December 31, 2025. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- being permitted to present only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Form 10-Q;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some, but not all, of the available exemptions. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company, which would allow us to take

advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period to comply with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will not be subject to the same adoption timelines for new or revised accounting standards as other public companies that are not emerging growth companies.

We are also 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. If we are a smaller reporting company at the time we cease to be an emerging growth company, 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, similar to emerging growth companies, smaller reporting companies 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 rule 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.

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 recently 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, in 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 users, and affords such users 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 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 the 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. German and Irish supervisory authorities have indicated, and enforced in recent rulings, that the standard contractual clauses alone provide inadequate protection for EU-U.S. data transfers. 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 Officer 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 strive to comply with all applicable laws, policies, legal obligations and industry codes of conduct relating to privacy and data protection to the extent possible. 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 the ongoing conflicts in Ukraine and the Middle East, the possibility of a wider European or global conflict, global sanctions imposed in response thereto, and potential recessions. Moreover, there has been recent 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, as they did with Silicon Valley Bank, or SVB, depositors, in the event of further 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 prevented us from using all or a significant portion of our headquarters, 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 2. Unregistered Sales of Equity Securities, Use of Proceeds, and Issuer Purchases of Equity Securities.

Unregistered Sales of Equity Securities

None.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

10b5-1 Trading Plans

During the three months ended September 30, 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 Regulations S-K, Item 408.

Item 6. Exhibits.

The exhibits filed or furnished as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index below.

Exhibit Number	Description	Form	File No.	Exhibit Filing Date	Filed/Furnished Herewith
3.1	Amended and Restated Certificate of Incorporation of Passage Bio, Inc, as amended.				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
101.INS	Inline XBRL Instance Document				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document				X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)				X

* 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.

SIGNATURES

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

PASSAGE BIO, INC.

Date: November 10, 2025

By: /s/ William Chou, M.D.
William Chou, M.D.
President and Chief Executive Officer

Date: November 10, 2025

By: /s/ Kathleen Borthwick
Kathleen Borthwick
Chief Financial Officer

Exhibit 3.1

CERTIFICATE OF AMENDMENT TO THE
RESTATED CERTIFICATE OF INCORPORATION
OF
PASSAGE BIO, INC.

Passage Bio, Inc. (the "***Corporation***"), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "***DGCL***"), does hereby certify as follows:

1. This Certificate of Amendment (this "Certificate of Amendment") amends the provisions of the Corporation's Restated Certificate of Incorporation filed with the Delaware Secretary of State on May 30, 2023 (the "Certificate of Incorporation").

2. Pursuant to Section 242 of the DGCL, the Board of Directors of the Corporation has duly adopted this Certificate of Amendment, and the Corporation's stockholders have duly approved this Certificate of Amendment.

3. Section 1 of Article IV of the Certificate of Incorporation is hereby amended by adding the following paragraph to the end of such section:

> "Effective at 12:01 a.m. Eastern Daylight Time on July 14, 2025 (the "***Effective Time***"), each twenty (20) shares of Common Stock then issued and outstanding, or held in treasury of the Corporation, immediately prior to the Effective Time shall automatically be reclassified and converted into one (1) share of Common Stock, without any further action by the Corporation or the respective holders of such shares (the "***Reverse Stock Split***"). No fractional shares shall be issued in connection with the Reverse Stock Split. A holder of Common Stock who would otherwise be entitled to receive a fractional share of Common Stock as a result of the Reverse Stock Split will receive one whole share of Common Stock in lieu of such fractional share."

4. The foregoing terms and provisions of this Certificate of Amendment shall be effective as of the Effective Time.

5. Except as herein amended, the Certificate of Incorporation shall remain in full force and effect.

[Signature appears on the following page.]

IN WITNESS WHEREOF, the Corporation has caused this Certificate of Amendment to be signed by its duly authorized officer this 11th day of July, 2025.

PASSAGE BIO, INC.

By: /s/ William Chou
Name: William Chou
Title: Chief Executive Officer

PASSAGE BIO, INC.

RESTATED CERTIFICATE OF INCORPORATION

Passage BIO, Inc., a Delaware corporation, hereby certifies as follows:

1. The name of the corporation is "Passage BIO, Inc." The date of the filing of its original Certificate of Incorporation with the Secretary of State was July 26, 2017.

2. The Restated Certificate of Incorporation of the corporation attached hereto as Exhibit "A", which is incorporated herein by this reference, and which restates, integrates and further amends the provisions of the Certificate of Incorporation of this corporation as previously amended and/or restated, has been duly adopted by this corporation's Board of Directors and by the stockholders in accordance with Sections 242 and 245 of the General Corporation Law of the State of Delaware, with the approval of the corporation's stockholders having been given by written consent without a meeting in accordance with Section 228 of the General Corporation Law of the State of Delaware.

IN WITNESS WHEREOF, this corporation has caused this Restated Certificate of Incorporation to be signed by its duly authorized officer and the foregoing facts stated herein are true and correct.

Dated: May 30, 2023

PASSAGE BIO, INC.

By: /s/ William Chou, M.D.
Name: William Chou, M.D.
Title: Chief Executive Officer and President

EXHIBIT "A"

PASSAGE BIO, INC.

RESTATED CERTIFICATE OF INCORPORATION

ARTICLE I: NAME

The name of the corporation is Passage BIO, Inc. (the "***Corporation***").

ARTICLE II: AGENT FOR SERVICE OF PROCESS

The address of the Corporation's registered office in the State of Delaware is 1209 North Orange Street, Wilmington, Delaware 19801 in the County of New Castle. The name of the registered agent of the Corporation at that address is The Corporation Trust Company.

ARTICLE III: PURPOSE

The purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of the State of Delaware (the "***General Corporation Law***").

ARTICLE IV: AUTHORIZED STOCK

1. **Total Authorized**. The total number of shares of all classes of stock that the Corporation has authority to issue is 310,000,000 shares, consisting of two classes: 300,000,000 shares of Common Stock, $0.0001 par value per share ("***Common Stock***"), and 10,000,000 shares of Preferred Stock, $0.0001 par value per share ("***Preferred Stock***").

2. **Designation of Additional Series**.

2.1 The Board of Directors of the Corporation (the "***Board***") is authorized, subject to any limitations prescribed by the law of the State of Delaware, to provide for the issuance of the shares of Preferred Stock in one or more series, and, by filing a Certificate of Designation pursuant to the applicable law of the State of Delaware ("***Certificate of Designation***"), to establish from time to time the number of shares to be included in each such series, to fix the designation, powers (including voting powers), preferences and relative, participating, optional or other special rights, if any, of the shares of each such series and any qualifications, limitations or restrictions thereof, and, except where otherwise provided in the applicable Certificate of Designation, to thereafter increase (but not above the total number of authorized shares of the Preferred Stock) or decrease (but not below the number of shares of such series then outstanding) the number of shares of any such series. The number of authorized shares of Preferred Stock may also be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of two-thirds of the voting power of all of the then-outstanding shares of capital stock of the Corporation entitled to vote thereon, without a separate vote of the holders of the Preferred Stock, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law, unless a separate vote of the holders of one or more series is required pursuant to the terms

of any Certificate of Designation; *provided*, *however*, that if two-thirds of the Whole Board (as defined below) has approved such increase or decrease of the number of authorized shares of Preferred Stock, then only the affirmative vote of the holders of a majority of the voting power of all of the then-outstanding shares of the capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, without a separate vote of the holders of the Preferred Stock (unless a separate vote of the holders of one or more series is required pursuant to the terms of any Certificate of Designation), shall be required to effect such increase or decrease. For purposes of this Restated Certificate of Incorporation (as the same may be amended and/or restated from time to time, including pursuant the terms of any Certificate of Designation designating a series of Preferred Stock, this "***Certificate of Incorporation***"), the term "***Whole Board***" shall mean the total number of authorized directors whether or not there exist any vacancies in previously authorized directorships.

2.2 Except as otherwise expressly provided in any Certificate of Designation designating any series of Preferred Stock pursuant to the foregoing provisions of this Article IV, any new series of Preferred Stock may be designated, fixed and determined as provided herein by the Board without approval of the holders of Common Stock or the holders of Preferred Stock, or any series thereof, and any such new series may have powers, preferences and rights, including, without limitation, voting powers, dividend rights, liquidation rights, redemption rights and conversion rights, senior to, junior to or pari passu with the rights of the Common Stock, any series of Preferred Stock or any future class or series of capital stock of the Corporation.

2.3 Each outstanding share of Common Stock shall entitle the holder thereof to one vote on each matter properly submitted to the stockholders of the Corporation for their vote; *provided, however*, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation.

ARTICLE V: AMENDMENT OF BYLAWS

The Board shall have the power to adopt, amend or repeal the Bylaws of the Corporation (as the same may be amended and/or restated from time to time, the "***Bylaws***"). Any adoption, amendment or repeal of the Bylaws by the Board shall require the approval of a majority of the Whole Board. The stockholders shall also have power to adopt, amend or repeal the Bylaws; *provided*, *however*, that notwithstanding any other provision of this Certificate of Incorporation or any provision of law that might otherwise permit a lesser or no vote, but in addition to any vote of the holders of any class or series of stock of the Corporation required by applicable law or by this Certificate of Incorporation, the affirmative vote of the holders of at least two-thirds of the voting power of all of the then-outstanding shares of the capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required for the stockholders to adopt, amend or repeal any provision of the Bylaws; *provided further*, that, in the case of any proposed adoption, amendment or repeal of any provisions of the Bylaws that is approved by the Board and submitted to the stockholders for adoption thereby, if two-thirds of the Whole Board has approved such adoption, amendment or repeal of any provisions of the Bylaws, then only the affirmative vote of the holders of a majority of the voting power of all of the then-

outstanding shares of the capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to adopt, amend or repeal any provision of the Bylaws.

ARTICLE VI: MATTERS RELATING TO THE BOARD OF DIRECTORS

1. **Director Powers**. Except as otherwise provided by the General Corporation Law or this Certificate of Incorporation, the business and affairs of the Corporation shall be managed by or under the direction of the Board.

2. **Number of Directors**. Subject to the special rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, the total number of directors constituting the Whole Board shall be fixed from time to time exclusively by resolution adopted by a majority of the Whole Board.

3. **Classified Board**. Subject to the special rights of the holders of one or more series of Preferred Stock to elect additional directors under specified circumstances, the directors shall be divided, with respect to the time for which they severally hold office, into three classes designated as Class I, Class II and Class III, respectively (the "***Classified Board***"). The Board may assign members of the Board already in office to the Classified Board. The number of directors in each class shall be as nearly equal as is practicable. At each annual meeting of stockholders, directors elected to succeed those directors of the class whose terms then expire shall be elected for a term of office expiring at the third succeeding annual meeting of stockholders after their election.

4. **Term and Removal**. Each director shall hold office until the annual meeting at which such director's term expires and until such director's successor is duly elected and qualified, or until such director's earlier death, resignation, disqualification or removal. Any director may resign by delivering a resignation in writing or by electronic transmission to the Corporation at its principal office or to the Chairperson of the Board, the Chief Executive Officer, or the Secretary. Subject to the special rights of the holders of any series of Preferred Stock, no director may be removed from the Board except for cause and only by the affirmative vote of the holders of at least two-thirds of the voting power of the then-outstanding shares of capital stock of the Corporation entitled to vote thereon, voting together as a single class. In the event of any increase or decrease in the authorized number of directors, (a) each director then serving as such shall nevertheless continue as a director of the class of which he or she is a member and (b) the newly created or eliminated directorships resulting from such increase or decrease shall be apportioned by the Board among the classes of directors so as to make all classes as nearly equal in number as is practicable, provided that no decrease in the number of directors constituting the Board shall shorten the term of any director.

5. **Board Vacancies and Newly Created Directorships**. Subject to the special rights of the holders of any series of Preferred Stock, any vacancy occurring in the Board for any cause, and any newly created directorship resulting from any increase in the authorized number of directors, shall be filled only by the affirmative vote of a majority of the directors then in office, even if less than a quorum, or by a sole remaining director, and shall not be filled by the stockholders. Any director elected in accordance with the preceding sentence shall hold office for

a term expiring at the annual meeting of stockholders at which the term of office of the class to which the director has been assigned expires and until such director's successor shall have been duly elected and qualified, or until such director's earlier death, resignation, disqualification or removal.

6. **Vote by Ballot**. Election of directors need not be by written ballot unless the Bylaws shall so provide.

7. **Preferred Directors**. If and for so long as the holders of any series of Preferred Stock have the special right to elect additional directors, then upon commencement and for the duration of the period during which such right continues: (i) the then otherwise total authorized number of directors of the Corporation shall automatically be increased by such specified number of directors, and the holders of such Preferred Stock shall be entitled to elect the additional directors so provided for or fixed pursuant to said provisions, and (ii) each such additional director shall serve until such director's successor shall have been duly elected and qualified, or until such director's right to hold such office terminates pursuant to said provisions, whichever occurs earlier, subject to his or her earlier death, resignation, retirement, disqualification or removal. Except as otherwise provided by the Board in the resolution or resolutions establishing such series, whenever the holders of any series of Preferred Stock having such right to elect additional directors are divested of such right pursuant to the provisions of such stock, the terms of office of all such additional directors elected by the holders of such stock, or elected to fill any vacancies resulting from the death, resignation, disqualification or removal of such additional directors, shall forthwith terminate and the total authorized number of directors of the Corporation shall be reduced accordingly.

ARTICLE VII: DIRECTOR AND OFFICER LIABILITY

1. **Limitation of Liability**. To the fullest extent permitted by law, neither a director of the Corporation nor an officer of the Corporation shall be personally liable for monetary damages for breach of fiduciary duty as a director or officer, as applicable. Without limiting the effect of the preceding sentence, if the General Corporation Law is hereafter amended to authorize the further elimination or limitation of the liability of a director or officer, then the liability of a director of the Corporation or officer of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law, as so amended.

2. **Change in Rights**. Neither any amendment nor repeal of this Article VII, nor the adoption of any provision of this Certificate of Incorporation inconsistent with this Article VII, shall eliminate, reduce or otherwise adversely affect any limitation on the personal liability of a director of the Corporation or officer of the Corporation existing at the time of such amendment, repeal or adoption of such an inconsistent provision.

ARTICLE VIII: MATTERS RELATING TO STOCKHOLDERS

1. **No Action by Written Consent of Stockholders**. Subject to the rights of any series of Preferred Stock then outstanding, no action shall be taken by the stockholders of the Corporation except at a duly called annual or special meeting of stockholders and no action shall be taken by the stockholders of the Corporation by written consent in lieu of a meeting.

2. **Special Meeting of Stockholders.** Special meetings of the stockholders of the Corporation may be called only by the Chairperson of the Board, the Chief Executive Officer, the Lead Independent Director (as defined in the Bylaws), the President, or the Board acting pursuant to a resolution adopted by a majority of the Whole Board and may not be called by the stockholders or any other person or persons.

3. **Advance Notice of Stockholder Nominations and Business Transacted at Special Meetings**. Advance notice of stockholder nominations for the election of directors of the Corporation and of business to be brought by stockholders before any meeting of stockholders of the Corporation shall be given in the manner provided in the Bylaws. Business transacted at special meetings of stockholders shall be limited to the purpose or purposes stated in the notice of meeting.

ARTICLE IX: CHOICE OF FORUM

Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware, to the fullest extent permitted by law, shall be the sole and exclusive forum for: (a) any derivative action or proceeding brought on behalf of the Corporation; (b) any action asserting a claim of breach of a fiduciary duty owed by, or other wrongdoing by, any director, officer, stockholder, employee or agent of the Corporation to the Corporation or the Corporation's stockholders; (c) any action asserting a claim against the Corporation arising pursuant to any provision of the General Corporation Law, this Certificate of Incorporation or the Bylaws or as to which the General Corporation Law confers jurisdiction on the Court of Chancery of the State of Delaware; (d) any action to interpret, apply, enforce or determine the validity of this Certificate of Incorporation or the Bylaws; or (e) any action asserting a claim against the Corporation governed by the internal affairs doctrine.

Any person or entity purchasing or otherwise acquiring or holding any interest in shares of capital stock of the Corporation shall be deemed to have notice of and to have consented to the provisions of this Article IX.

ARTICLE X: AMENDMENT OF CERTIFICATE OF INCORPORATION

If any provision of this Certificate of Incorporation shall be held to be invalid, illegal, or unenforceable, then such provision shall nonetheless be enforced to the maximum extent possible consistent with such holding and the remaining provisions of this Certificate of Incorporation (including without limitation, all portions of any section of this Certificate of Incorporation containing any such provision held to be invalid, illegal, or unenforceable, which is not invalid, illegal, or unenforceable) shall remain in full force and effect.

The Corporation reserves the right to amend or repeal any provision contained in this Certificate of Incorporation in the manner prescribed by the laws of the State of Delaware and all rights conferred upon stockholders are granted subject to this reservation; *provided, however*, that, notwithstanding any provision of this Certificate of Incorporation or any provision of law that might otherwise permit a lesser vote or no vote (but subject to Section 2 of Article IV hereof), but in addition to any vote of the holders of any class or series of the stock of the Corporation required by law or by this Certificate of Incorporation, the affirmative vote of the holders of at least two-thirds of the voting power of all of the then-outstanding shares of the capital stock of the

Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to amend or repeal any provision of this Certificate of Incorporation; *provided*, *further*, that if two-thirds of the Whole Board has approved such amendment or repeal of any provisions of this Certificate of Incorporation, then only the affirmative vote of the holders of at least a majority of the voting power of all of the then-outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class (in addition to any other vote of the holders of any class or series of stock of the Corporation required by law of by this Certificate of Incorporation), shall be required to amend or repeal such provisions of this Certificate of Incorporation.

* * * * * * * * * * *

Exhibit 31.1

CERTIFICATION PURSUANT TO RULE 13a-14(a) OR 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, William Chou, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Passage Bio, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
    a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 10, 2025

/s/ William Chou
William Chou
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO RULE 13a-14(a) OR 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Kathleen Borthwick, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Passage Bio, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
    a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 10, 2025

/s/ Kathleen Borthwick
Kathleen Borthwick
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

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

I, William Chou, President and Chief Executive Officer of Passage Bio, Inc. (the "Company"), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

1. the Quarterly Report on Form 10-Q of the Company for the fiscal quarter ended September 30, 2025 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: November 10, 2025

/s/ William Chou
William Chou
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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

I, Kathleen Borthwick, Chief Financial Officer of Passage Bio, Inc. (the "Company"), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

1. the Quarterly Report on Form 10-Q of the Company for the fiscal quarter ended September 30, 2025 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: November 10, 2025

/s/ Kathleen Borthwick
Kathleen Borthwick
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)