UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2025

OR

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

Commission File Number 001-38886

TREVI THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**45-0834299**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
195 Church Street, 16th Floor New Haven, Connecticut	**06510**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (203) 304-2499

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	**TRVI**	**The Nasdaq Stock Market LLC**

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

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

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

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

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

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

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

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

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

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

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

As of June 30, 2025, the last business day of the Registrant's most recently completed second fiscal quarter, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Stock Market, was $588.4 million.
The number of shares of the Registrant's Common Stock outstanding as of March 12, 2026 was 128,397,271.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the registrant's 2026 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues and profitability, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- our plans to develop and, if approved, subsequently commercialize Haduvio for the treatment of chronic cough in patients with idiopathic pulmonary fibrosis, or IPF, non-IPF interstitial lung disease, or non-IPF ILD, and refractory chronic cough, or RCC;
- our clinical trials, including our planned Phase 3 trials of Haduvio for the treatment of chronic cough in patients with IPF, our planned adaptive design Phase 2b clinical trial of Haduvio for the treatment of chronic cough in patients with non-IPF ILD, our planned Phase 2b trial of Haduvio for the treatment of patients with RCC, and our planned Phase 1 NDA supportive studies;
- our expectations regarding the timing for the initiation of clinical trials and the reporting of data from such trials;
- the timing of and our ability to submit applications for and to obtain and maintain regulatory approvals for Haduvio;
- our expectations regarding our ability to fund our operating expenses, including our ongoing and planned clinical trials, with our cash, cash equivalents and marketable securities;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- the impact of government laws and regulations;
- our competitive position; and
- our ability to establish and maintain collaborations.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the section titled "Risk Factors," that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may differ materially from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

This report includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates. All of the market data used in this report involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for Haduvio include several key assumptions based on our industry knowledge, industry publications, third-party research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

We own or have rights to trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. We own the trademarks Trevi® and Haduvio™. Other trademarks, service marks and trade names appearing in this Annual Report on Form 10-K are the property of their respective owners. Solely for convenience, some of the trademarks, service marks and trade names referred to in this Annual Report on Form 10-K are listed without the ® and ™ symbols, but we will assert, to the fullest extent under

applicable law, our rights to our trademarks, service marks and trade names. We intend to propose Haduvio as the trade name for our oral nalbuphine ER investigational product.

RISK FACTOR SUMMARY

The following is a summary of the principal factors that make an investment in our company speculative or risky. This summary does not address all of the risks and uncertainties that we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Additional discussion of the risks summarized in this summary and other risks that we face, can be found in the "Risk Factors" section of this Annual Report on Form 10-K, and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the Securities and Exchange Commission, before making an investment decision regarding our common stock. The forward-looking statements discussed above are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

- We have incurred significant losses since inception and expect to continue to incur significant and increasing losses for the foreseeable future. We may never achieve or maintain profitability.
- We will need substantial additional funding. If we are unable to raise sufficient capital when needed on acceptable terms or at all, we could be forced to delay, reduce or abandon our product development programs or commercialization efforts.
- We are dependent on the successful development and commercialization of Haduvio, our sole product candidate. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize Haduvio or if we experience significant delays in doing so, our business would be substantially harmed.
- We are in the process of designing future clinical trials of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC. Before commencing these trials, we plan to submit the protocols to regulatory authorities to obtain any feedback they may have. Changes in the design of the planned trials or regulatory delays may affect the timing and costs of these trials and may affect our ability to complete these trials with our existing cash resources.
- The outcome of clinical trials of a product candidate may not be predictive of the success of later clinical trials of such product candidate or of clinical trials of such product candidate for different indications. For instance, Haduvio may fail to show the desired safety and efficacy results in our planned trials of Haduvio despite demonstrating positive results in earlier Phase 2 clinical trials.
- We have experienced delays and difficulties in the enrollment of patients in our clinical trials in the past. If we experience delays or difficulties in the enrollment of patients in future clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented. Other companies are conducting clinical trials or have announced plans for future clinical trials that are seeking or are likely to seek to enroll patients with IPF, non-IPF ILD, and RCC, and patients are generally only able to enroll in a single trial at a time. In addition, many patients use various treatments not specifically approved to treat chronic cough and these patients and their physicians may be reluctant to forgo, discontinue or otherwise alter their use of such treatments to participate in our clinical trials.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome. Even if we complete the necessary nonclinical studies and clinical trials, the regulatory approval process is uncertain, which may prevent us from obtaining approvals for the commercialization of Haduvio or any future product candidate on a timely basis or at all.
- Adverse events or undesirable side effects caused by, or other unexpected properties of, Haduvio or any future product candidate may be identified during development and could delay or prevent the marketing approval or limit the use of Haduvio or any future product candidate.
- The drug label for nalbuphine, the active ingredient in Haduvio, carries an opioid class label warning for serious, life-threatening or fatal respiratory depression and Haduvio, if approved for marketing in any indication, will likely carry a similar opioid class label.
- Many currently approved mu-opioid receptor agonist products are subject to restrictive marketing and distribution regulations which, if applied to Haduvio, could potentially restrict its use and harm our ability to generate profits.
- If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing Haduvio or any future product candidates if and when they are approved.

- We face competition, which may result in others developing or commercializing products before or more successfully than we do.
- We contract with third parties to conduct our clinical trials and for the manufacture, storage, packaging and distribution of Haduvio for clinical trials, including with a single supplier for the active ingredient in Haduvio. We expect to continue to rely on third parties for these services in connection with our future development and commercialization efforts for Haduvio. If they do not perform satisfactorily, our business could be harmed.
- If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, including our license with Keenova Therapeutics plc, we could lose license rights that are critical to our business or owe damages to the licensor of such intellectual property.
- If we are unable to obtain and maintain sufficient patent protection for Haduvio or any future product candidate and the disease indications for which we are developing or may in the future develop Haduvio or any other product candidate, or if the scope of the patent protection is not sufficiently broad, competitors could develop and commercialize products similar or identical to such product candidate and our ability to successfully commercialize such product candidate may be adversely affected.
- The number of shares of common stock underlying our outstanding warrants is significant in relation to our currently outstanding common stock, which could have a negative effect on the market price of our common stock and make it more difficult for us to raise funds through future equity financings.

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PART I

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of the investigational therapy Haduvio (oral nalbuphine ER) for the treatment of chronic cough in patients with idiopathic pulmonary fibrosis, or IPF, non-IPF interstitial lung disease, or non-IPF ILD, and refractory chronic cough, or RCC.

Haduvio is an oral extended-release formulation of nalbuphine. Haduvio acts on the cough reflex arc both centrally and peripherally as a kappa receptor agonist and a mu receptor antagonist ("KAMA"), targeting opioid receptors that play a key role in controlling chronic cough. The kappa- and mu-opioid receptors are known to be critical mediators of cough. Nalbuphine has been approved and marketed as an injectable for pain indications for decades in the United States, or the U.S., and Europe. Nalbuphine's mechanism of action also mitigates the risk of abuse associated with mu-opioid agonists because it antagonizes, or blocks, the mu-opioid receptor. Parenteral nalbuphine is not scheduled as a controlled substance by the U.S. Drug Enforcement Agency and in most of Europe. We believe this makes Haduvio a promising potential therapy for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC.

IPF-related Chronic Cough Program. We are developing Haduvio for the treatment of IPF-related chronic cough, which is a progressive fibrosing interstitial lung disease associated with high mortality rates. After an IPF diagnosis, the median survival is 3 to 5 years, during which time patients suffer from chronic cough, dyspnea, and fatigue. IPF-related chronic cough is a condition with high unmet need and no therapies approved by the U.S. Food and Drug Administration, or FDA. There are approximately 150,000 U.S. patients with IPF, and two-thirds of these patients have uncontrolled chronic cough. The impact of chronic cough is significant, with patients coughing up to 1,500 times per day. This consistent cough, and any associated damage, may lead to a higher risk of morbidity and mortality, including worsening disease, a higher risk of progression, increased respiratory hospitalizations, and a decline in patients' physical, psychological, and social quality of life.

In June 2025, we announced positive topline results from our Phase 2b CORAL trial, which was a dose-ranging study evaluating the efficacy, safety and tolerability of Haduvio for IPF-related chronic cough. The Phase 2b CORAL trial was a randomized, double-blind, placebo-controlled, parallel-arm design that evaluated three different dose groups of Haduvio (108 mg BID, 54 mg BID and 27 mg BID) as compared to placebo. The primary efficacy endpoint for the trial was the relative change in 24-hour cough frequency (coughs per hour) for the modified intent-to-treat, or mITT, population at the end of Week 6 versus Baseline for Haduvio compared to placebo, as measured via an objective cough monitor. The mITT population consists of all randomized patients who received at least one dose of study drug or placebo (n=165). The primary efficacy endpoint in the Phase 2b CORAL trial was achieved, demonstrating statistically significant reductions in 24-hour cough frequency across all dose groups at Week 6. The 108 mg BID, 54 mg BID and 27 mg BID dose groups achieved statistically significant reductions from Baseline of 60.2% ($p<0.0001$), 53.4% ($p<0.0001$), and 47.9% ($p<0.01$), respectively, compared to a placebo reduction from Baseline of 16.9%.

We have completed an End-of-Phase 2 meeting with the FDA. At the meeting, we gained overall alignment on the plan for the remaining clinical studies to potentially support an NDA submission for nalbuphine ER, including two pivotal Phase 3 clinical trials and agreement on the remaining Phase 1 clinical studies. The Phase 3 trials will run in parallel, and we remain on track to initiate the first Phase 3 trial in the second quarter of 2026 and the second Phase 3 trial in the second half of 2026. The first of the two Phase 3 trials is planned to enroll approximately 300 patients and have 52 weeks of fixed dosing with nalbuphine ER 54 mg twice-a-day (BID), with the primary endpoint at 24 weeks of fixed dosing. The second Phase 3 trial is planned to enroll approximately 130 patients with and have 12 weeks of fixed dosing with nalbuphine ER 54 mg BID. The primary efficacy endpoint for both trials will be the relative change from Baseline in 24-hour cough frequency (coughs per hour), as determined by an objective cough monitor, for nalbuphine ER compared with placebo. These trial designs are subject to final review of the protocols by the FDA.

Non-IPF ILD-related Chronic Cough Program. We also plan to develop Haduvio for the treatment of non-IPF ILD-related chronic cough. Many patients diagnosed with non-IPF ILD suffer from a dry, non-productive chronic cough that is as disruptive as the cough associated with IPF. Cough may be an independent predictor of disease progression in non-IPF ILDs, and therefore we believe chronic cough may contribute to the progression of the underlying disease and worsening health outcomes.

Approximately 228,000 adults in the U.S. and greater than 1 million adults worldwide are believed to have ILDs other than IPF. In addition, up to 50%-60% of non-IPF ILD patients are reported to suffer from an uncontrolled chronic cough. There are no approved therapies for the treatment of non-IPF ILD-related chronic cough. We plan to initiate an

adaptive design Phase 2b clinical trial for the treatment of patients with non-IPF ILD-related chronic cough in the second half of 2026, subject to review of the protocol for the trial by the FDA.

RCC Program. We are developing Haduvio for the treatment of RCC, which affects approximately 2-3 million adults in the U.S. and is related to biological changes in the central and peripheral nervous systems that lower the threshold of the cough reflex. It is highly disruptive and accompanied by a wide range of complications, ranging from urinary incontinence in females to sleep disruption and social embarrassment that causes significant social and economic burden for patients and those around them.

In March 2025, we announced positive topline data from our Phase 2a clinical trial of Haduvio in patients with RCC, which we refer to as the Phase 2a RIVER trial. The Phase 2a RIVER trial was a randomized, double-blind, placebo-controlled, two-treatment, two-period, crossover study that was designed to evaluate the efficacy, safety, tolerability and dosing of Haduvio for the treatment of patients with RCC. The primary endpoint of the trial was the mean change in 24-hour cough frequency, as determined by an objective cough monitor, for the full analysis set population. In the trial, Haduvio met the primary endpoint at Day 21 with a statistically significant reduction in the objective 24-hour cough frequency of 67% from Baseline and 57% from Baseline on a placebo-adjusted basis ($p<0.0001$). Planned analyses of all pre-specified secondary endpoints, including patient reported endpoints, at the end of treatment were also statistically significant. The safety results of the trial were generally consistent with the known safety profile of Haduvio from previous trials in other patient populations and there were no serious adverse events reported in the trial.

We expect to initiate a Phase 2b trial of Haduvio for the treatment of patients with RCC in the second quarter of 2026, which we are planning to conduct in the United Kingdom, Canada, and possibly other European countries. We expect the primary efficacy endpoint of the trial will be the mean change in 24-hour cough frequency, as determined by an objective cough monitor, and we plan to use the trial to determine the doses to be evaluated in the Phase 3 clinical trial as well as to further characterize safety in this specific patient population. The trial is subject to final review of the protocol by regulatory authorities.

Other NDA Supportive Studies. We also plan to continue to progress and advance NDA supportive studies necessary for regulatory approval, including Phase 1 clinical studies such as completing our respiratory safety study, and conducting drug-drug interaction, food effect, and hepatic and renal impairment studies.

Commercialization of Haduvio. We have retained worldwide commercial rights for Haduvio.

Nalbuphine Mechanistic Rationale

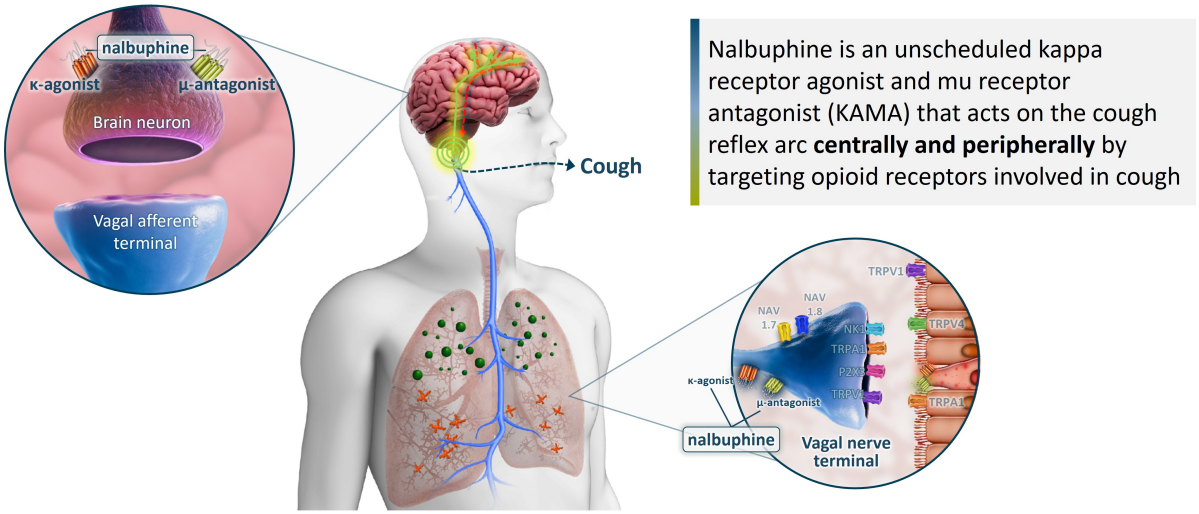
Nalbuphine is a mixed kappa-opioid receptor agonist and a mu-opioid receptor antagonist. The kappa- and mu-opioid receptors are known to be critical mediators of cough. Nalbuphine has been approved and marketed as an injectable for pain indications for decades in the U.S. and Europe. Nalbuphine's mechanism of action also mitigates the risk of abuse associated with mu-opioid agonists because it antagonizes, or blocks, the mu-opioid receptor.

Modulation of opioid receptors in the central and peripheral nervous systems, either naturally or with drugs, results in multiple signaling actions at the cellular level. The receptor dynamics are complex and receptor signaling differs depending on whether the receptor is being exposed to an agonist or antagonist opioid drug. Agonists activate the receptors to which they bind, and antagonists bind to receptors, and can block the activity of agonists. In addition, opioid drugs of the same class may have different effects depending on their pharmacological properties.

In addition to the individual cellular dynamics, published research also supports the phenomena of network interaction dynamics, where activation of one type of opioid receptor type at one anatomical location can influence the activity of a different type of opiate receptor located at a different anatomical location. For example, published research has shown evidence of signaling between cell groups where kappa-opioid receptor activation on specific cells can antagonize mu-opioid receptor activation on other cells. As a result of these apparent network interaction dynamics between the kappa- and mu-opioid receptors, we believe that simultaneously modulating both kappa- and mu-opioid receptors with a single drug offers significant therapeutic potential in diseases that are mediated through these receptors.

Published research suggests that in certain diseases the concentration and expression of opioid receptors is different for people with the disease as compared to healthy individuals. We believe these differences in opioid receptor concentration and expression between healthy individuals and people with disease suggest that opioid drugs targeting these receptors have the potential to offer therapeutic benefit to people suffering from these diseases.

As shown in the diagram below, kappa- and mu-opioid receptors are naturally concentrated in several areas of the body, including in the forebrain, brain stem, spinal cord, and peripheral nerves innervating the lung, which are the areas of the body involved in the physiology of chronic cough.



κ-agonist, kappa opioid receptor agonist; μ-antagonist, mu opioid receptor antagonist; ER, extended release; NAV 1.7, voltage-gated sodium channel, subtype 1.7; NAV 1.8, voltage-gated sodium channel, subtype 1.8; NK1, neurokinin 1 receptor; NMDA, N-methyl-D-aspartate receptor; P2X3, P2X purinoceptor 3; Pannexin 1, pannexin-1 channel; TRPA1, transient receptor potential ankyrin 1; TRPV1, transient receptor potential vanilloid 1; TRPV4, transient receptor potential vanilloid 4.
1. Chung KF et al. *Nat Rev Dis Primers*. 2022;8(1):45. 2. Krajnik M et al. *Curr Opin Support Palliat Care*. 2014;8(3)191-199.
Haduvio (NAL ER / nalbuphine ER) is an investigational drug

With respect to cough, kappa- and mu-opioid receptors in the forebrain, brain stem, lungs and the peripheral nerves innervating the lung are believed to be involved in mediating respiration and the cough reflex. While there are no approved opioid therapeutics for suppression of cough in humans, mu-agonist opioids have been used clinically to suppress cough.

Haduvio

Haduvio is an oral extended-release formulation of nalbuphine, a small molecule and is in the opioid mixed agonist-antagonist class of drugs. Nalbuphine is a marketed drug currently available only as nalbuphine hydrochloride for injection, a generic equivalent to Nubain, which has been approved in the U.S. and Europe for use in the relief of moderate to severe pain for decades. Nalbuphine is not currently classified as a controlled substance in the U.S. or most of Europe and is not commercially available in an oral dosage form.

We have leveraged the known mechanism and proven biological activity of nalbuphine in pain to expedite the clinical development of Haduvio. We have also drawn on the safety and tolerability data from eight prior clinical trials of Haduvio conducted by Penwest Pharmaceuticals Co., which subsequently merged into Endo, Inc. and which has since merged with Mallinckrodt plc which was then renamed Keenova Therapeutics plc, or Keenova, for which we have licensed rights from Keenova, including two Phase 2 clinical trials of Haduvio for the treatment of pain, to support our clinical development efforts.

Our Haduvio Development Programs

IPF-related Chronic Cough Program

Overview

IPF is a progressive fibrosing interstitial lung disease associated with high mortality rates. After IPF diagnosis, the median survival is 3 to 5 years, during which time patients suffer from chronic cough and dyspnea. IPF-related chronic cough is a condition with high unmet need and no FDA-approved therapies. There are approximately 150,000 U.S. patients with IPF, and two-thirds of these patients are faced with uncontrolled chronic cough. The impact of chronic cough is significant, with patients coughing up to 1,500 times per day. A higher cough severity, and any associated damage, may lead to a higher risk of morbidity and mortality, including worsening disease, a higher risk of progression, increased respiratory hospitalizations, and a decline in patients' physical, psychological, and social quality of life.

The opioid class of drugs has demonstrated the ability to suppress cough and is used in the clinical management of cough. There is also preclinical and clinical evidence that mixed agonist-antagonist drugs can also be effective in treating cough.

Clinical Development

We have conducted two Phase 2 trials of Haduvio for IPF-related chronic cough and plan to initiate our Phase 3 trials consisting of two Phase 3 trials, the first of which we expect to initiate in the second quarter of 2026.

Phase 2b CORAL Clinical Trial

In June 2025, we announced positive topline results of our Phase 2b CORAL trial, which was a dose-ranging study evaluating the efficacy, safety and tolerability of Haduvio for IPF-related chronic cough. The Phase 2b CORAL trial (N=165) was conducted at multiple sites in ten countries and used a randomized, double-blind, placebo-controlled, parallel-arm design, which evaluated three doses of Haduvio as compared to placebo. The primary efficacy endpoint for the trial was the relative change in 24-hour cough frequency (coughs per hour) for the modified intent-to-treat, or mITT, population at the end of Week 6 versus Baseline for Haduvio compared to placebo, as measured via an objective cough monitor. The mITT population consists of all randomized patients who received at least one dose of study drug or placebo. The primary efficacy endpoint in the Phase 2b CORAL trial was achieved, demonstrating statistically significant reductions in 24-hour cough frequency across all dose groups at Week 6. The 108 mg BID, 54 mg BID and 27 mg BID dose groups achieved statistically significant reductions from Baseline of 60.2% ($p<0.0001$), 53.4% ($p<0.0001$), and 47.9% ($p<0.01$), respectively, compared to a placebo reduction from Baseline of 16.9%[1].

The table below shows the data for the primary endpoint – Relative Change from Baseline in 24-hour Cough Frequency (coughs per hour) at Week 6:

	Placebo[1] (N=39)	**Haduvio 27 mg BID (N=42)**	**Haduvio 54 mg BID (N=43)**	**Haduvio 108 mg BID (N=40)**
Baseline 24-hour Cough Frequency (coughs/hour)	29.4	24.6	28.0	31.5
Relative Change from Baseline in 24-hour Cough Frequency at Week 6	-16.9%	-47.9% ($p<0.01$)	-53.4% ($p<0.0001$)	-60.2% ($p<0.0001$)
Placebo-adjusted difference	-	-30.9%	-36.5%	-43.3%

[1]One placebo patient with an extreme outlier value at Week 6 was excluded from the modified intent-to-treat ("mITT") population. Inclusion of the patient in the placebo group would have resulted in an increased cough frequency from Baseline in the placebo group and much greater placebo-adjusted differences.

Additional Trial Results

- A rapid reduction was seen in 24-hour cough frequency as early as Week 2 with Haduvio, the first time point measured.
- A 50% reduction in 24-hour cough frequency at Week 6 vs Baseline was seen in 65% of patients on 108 mg BID Haduvio ($p<0.001$), 63% of patients on 54 mg BID Haduvio ($p<0.001$) and 60% of patients on 27 mg BID Haduvio ($p<0.001$) dose groups, compared to 19% of placebo patients.
- A statistically significant response was observed on the cough-severity numerical rating scale (CS-NRS), a secondary endpoint, at Week 6 on Haduvio in both the 108 mg BID and 54 mg BID dose groups. There was a mean reduction on a 0 – 10 scale of 3.0 points on the 108 mg BID ($p<0.05$), 3.2 points on the 54 mg BID ($p<0.01$) and 2.0 points on the 27 mg BID ($p=0.46$) dose groups compared to a 1.5-point reduction on placebo at Week 6.
- The 108 mg BID and 54 mg BID dose groups were statistically significant ($p<0.01$) on the patient-reported outcome E-RS®: IPF Cough Subscale, a secondary endpoint, with mean relative change from Baseline of -42.4% and -43.1%, respectively at Week 6, compared to -23% for those on placebo at Week 6. The 27 mg BID dose group was not statistically significant with a mean relative change from Baseline of –31.6%.
- Discontinuation rates due to adverse events were similar in the combined Haduvio groups (5.6%) and placebo group (5.0%). The safety profile observed in the trial was generally consistent with the known safety profile of Haduvio from previous trials. The most common adverse events experienced included: nausea, vomiting, constipation, dizziness, headache, fatigue, somnolence, and dry mouth. Serious adverse events (all non-fatal) were reported for four patients (10.0%) in the placebo group and for two patients (1.6%) across all Haduvio

doses combined.

- The trial showed positive results with Haduvio on the Leicester Cough Questionnaire (LCQ) Total Score for the 108 mg BID and 54 mg BID dose groups, increasing the LCQ score by 3.4 points (p=0.01) and 3.7 points (p=0.01), respectively. A 1.3-point increase from Baseline is considered clinically meaningful.

Phase 2a CANAL Clinical Trial

Prior to our Phase 2b CORAL trial, we conducted our Phase 2a CANAL trial. The Phase 2a CANAL trial was a randomized, double-blind, placebo-controlled, two-treatment, two-period, crossover study that was designed to evaluate the efficacy, safety, and tolerability of Haduvio for IPF-related chronic cough that we conducted at multiple sites in the United Kingdom. Patients were randomized into one of two treatment arms. The patients in the first treatment arm received escalating doses of Haduvio for three weeks, which was followed by a two-week washout period and then a three-week treatment period during which they received placebo. The patients in the second treatment arm received placebo during the first three-week treatment period, followed by a two-week washout period, then received escalating doses of Haduvio during the second three-week treatment period. During the active treatment periods, Haduvio was studied over a dosing range starting at 27 mg once daily and titrated in steps to 162 mg twice daily. The primary efficacy endpoint of the trial was mean percent change in daytime cough frequency for Haduvio treatment compared to placebo treatment. Secondary endpoints in the trial included assessments of fatigue, dyspnea or shortness of breath and cough frequency and severity.

In total, 42 patients in the trial received Haduvio. In the full analysis data set, Haduvio demonstrated statistically significant results for the primary efficacy endpoint of daytime cough frequency reduction ($p<0.0001$) and for key secondary endpoints on patient and clinician reported outcomes. The trial results comparing patients randomized to Haduvio or placebo showed that:

- On the primary efficacy endpoint, Haduvio patients had a 75.1% reduction in daytime cough frequency at end of treatment period vs. study Baseline compared to placebo patients who had a 22.6% reduction, a 52.5% placebo-adjusted change ($p<0.0001$);
- Haduvio patients had a 76.1% reduction in 24-hour cough frequency at end of treatment period vs. study Baseline compared to placebo patients who had a 25.3% reduction, a 50.8% placebo-adjusted change ($p<0.0001$);
- In a post-hoc analysis, 97% of Haduvio patients had at least a 30% reduction in 24-hour cough frequency compared to 35% of placebo patients, signifying a clinically meaningful reduction in cough ($p<0.0001$);
- Patients on Haduvio experienced a statistically significant improvement as measured by their patient reported outcomes compared to placebo over the three-week treatment period in the EXACT2: Cough Frequency Score (p=0.001) and Cough Severity Numerical Rating Scale (p=0.0001); and
- Based on the Clinical Global Impression of Change rating measuring clinicians' view of change since the start of the trial, 62% of Haduvio patients improved vs. Baseline compared to 19% of placebo patients (p=0.01).

The safety results of the trial were generally consistent with the known safety profile of Haduvio from previous trials in other patient populations. There were two SAEs reported during the trial, neither of which was considered by the investigator to be treatment related. Adverse events most commonly observed during the trial were nausea, fatigue, constipation, dizziness, somnolence, vomiting, headache, anxiety and depression.

Next Steps

Based on the results of these trials, and discussions with the FDA at our End-of-Phase 2 meeting, we expect to initiate our Phase 3 trials in the second quarter of 2026 and will include two Phase 3 trials. The Phase 3 trials will run in parallel, and we remain on track to initiate the first Phase 3 trial in the second quarter of 2026 and the second Phase 3 trial in the second half of 2026. The first of the two Phase 3 trials is planned to enroll approximately 300 patients and have 52 weeks of fixed dosing with nalbuphine ER 54 mg twice-a-day (BID), with the primary endpoint at 24 weeks of fixed dosing. The second Phase 3 trial is planned to enroll approximately 130 patients and have 12 weeks of fixed dosing with nalbuphine ER 54 mg BID. The primary efficacy endpoint for both trials will be the relative change from Baseline in 24-hour cough frequency (coughs per hour), as determined by an objective cough monitor, for nalbuphine ER compared with placebo. These trial designs are subject to final review of the protocols by the FDA.

Non-IPF ILD-related Chronic Cough Program

Similar to IPF, non-IPF ILDs are characterized by fibrosis of lung tissue leading to a loss of lung function and reduced life expectancy. Many patients diagnosed with non-IPF ILD also suffer from a dry, non-productive chronic cough.

Approximately 228,000 adults in the U.S. and greater than 1 million adults worldwide are believed to have ILDs other than IPF. In addition, up to 50%-60% of non-IPF ILD patients are reported to suffer from uncontrolled chronic cough. There are no approved therapies for the treatment of non-IPF ILD-related chronic cough.

We plan to initiate an adaptive design Phase 2b clinical trial for the treatment of patients with non-IPF ILD-related chronic cough in the second half of 2026, subject to review of the protocol for the trial by the FDA.

RCC Program

Overview

Chronic cough affects up to 10% of the adult population and is defined as a persistent cough lasting more than eight weeks, despite treatment for an underlying condition. RCC affects approximately 2-3 million adults in the U.S. and is related to biological changes in the central and peripheral nervous systems that lower the threshold of the cough reflex. It is highly disruptive and accompanied by a wide range of complications, ranging from urinary incontinence in females to sleep disruption and social embarrassment that causes significant social and economic burden for patients and those around them. When a cause for RCC is identifiable, it is most commonly asthma, gastroesophageal reflux disease, or GERD, non-asthmatic eosinophilic bronchitis, and upper airway cough syndrome or post-nasal drip. The RCC population is generally considered to also include those with unexplained chronic cough where no cough-associated conditions can be identified.

Phase 2a RIVER Clinical Trial

In March 2025, we announced positive topline data from our Phase 2a clinical trial of Haduvio for the treatment of patients with RCC, which we refer to as the Phase 2a RIVER trial. The Phase 2a RIVER trial was a randomized double-blind, placebo-controlled, two-treatment, two-period, crossover study that was designed to evaluate the efficacy and safety, tolerability and dosing of Haduvio for the treatment of patients with RCC. Each treatment period lasted 21 days, separated by a 21-day washout period, and patients on Haduvio had their dose titrated from 27 mg once a day (QD) up to 108 mg twice a day (BID) across the 21-day dosing period. We conducted this trial at multiple sites in the United Kingdom and Canada. The primary endpoint of the study was a mean change in 24-hour cough frequency using an objective cough monitor in the overall population.

In total, 66 patients received Haduvio. In the full analysis data set, Haduvio demonstrated statistically significant results for the primary endpoint of 24-hour cough frequency reduction ($p<0.0001$) and for secondary endpoints on patient and clinician reported outcomes. The trial results comparing patients randomized to Haduvio or placebo showed that:

- On the primary endpoint, Haduvio patients had a 67% reduction in 24-hour cough frequency at end of treatment period compared to placebo patients who had a 10% reduction, with a 57% placebo-adjusted change from Baseline ($p<0.0001$);
- Haduvio demonstrated a statistically significant reduction in 24-hour cough frequency of 66% in the severe cough (20+ coughs/hour) subgroup (N=40) ($p<0.0001$) and 68% in the moderate cough (10-19 coughs/hour) subgroup (N=13) ($p<0.0001$);
- 84% of Haduvio patients had at least a 30% reduction in 24-hour cough frequency vs. Baseline, as compared to 29% of placebo patients, a difference of 55% ($p<0.0001$); and
- A statistically significant reduction in 24-hour cough frequency, as measured by an objective cough monitor, was seen as early as Day 7 (27 mg BID) for patients on Haduvio ($p<0.0001$).

Patients on Haduvio experienced a statistically significant improvement in patient reported outcomes compared to placebo as early as Day 7 (27 mg BID) in the Cough Severity Visual Analog Scale and the Patient-Reported Cough Frequency. The safety results of the trial were generally consistent with the known safety profile of Haduvio from previous trials in other patient populations. Adverse events most commonly observed during the trial were constipation, nausea, somnolence, headache, dizziness and fatigue and there were no treatment emergent SAEs.

Next Steps

Based on these results, we plan to initiate a Phase 2b trial of Haduvio for the treatment of patients with RCC in the second quarter of 2026, which we are planning to conduct in the United Kingdom, Canada, and possibly other European countries. We expect the objectives for the trial will be to determine the doses to be evaluated in the Phase 3 clinical trial as

well as to further characterize safety in this specific patient population. The trial is subject to final review of the protocol by regulatory authorities.

Other Haduvio Development Work

We have agreed to the remaining Phase 1 studies required for a submission of an NDA for IPF-related chronic cough. These include studies such as drug-drug interaction, hepatic, renal and food effect studies.

Human Abuse Potential Study

In December 2024, we announced positive topline results from our human abuse potential, or HAP, study which compared the abuse potential of oral nalbuphine to IV butorphanol. The injectable version of nalbuphine is currently unscheduled in the U.S. by the Drug Enforcement Agency. The study was a randomized, double-blind, active and placebo-controlled five-way crossover design. The study was conducted in two parts. The first part of the study characterized various IV butorphanol doses in order to select a dose to be studied. The second part of the study was designed to utilize the selected dose and compare oral nalbuphine relative to IV butorphanol using the study metrics. The study demonstrated a statistically significant lower "Drug Liking" for the clinical doses of oral nalbuphine (81mg and 162mg) compared to 6mg IV butorphanol. The supratherapeutic dose of oral nalbuphine (486mg) was numerically lower than the 6mg IV butorphanol for “Drug Liking” but the results were not statistically significant.

Primary Endpoint*

	Placebo (N=52)	IV butorphanol 6mg (N=52)	Oral nalbuphine 81mg (N=52)	Oral nalbuphine 162mg (N=52)	Oral nalbuphine 486mg (N=52)
Mean E_{max} for "Drug Liking"	51.8	82.3	71.2	74.5	81.1
P-value difference vs IV butorphanol 6mg	p<0.0001	—	p<0.0001	p=0.0008	p=0.3221

*All analyses performed were on the Modified Completer Population, which was prespecified in the statistical analysis plan for the primary endpoint.

Secondary endpoints included pharmacodynamic markers and patient reported outcomes, which were generally consistent with the primary endpoint. No SAEs were reported in the study.

Secondary Endpoints

	Placebo (N=52)	IV butorphanol 6mg (N=52)	Oral nalbuphine 81mg (N=52)	Oral nalbuphine 162mg (N=52)	Oral nalbuphine 486mg (N=52)
Mean E_{max} for "Take Drug Again"	53.4	62.8	71.0	67.3	64.2
Mean E_{max} for "I Feel High"	3.4	77.6	35.6	39.3	59.2
Mean E_{max} for "I Feel Good"	2.7	71.9	40.3	40.8	61.0

The results of the HAP study will be included in the 8-factor analysis of the abuse potential of nalbuphine for nalbuphine ER that would be submitted as part of any NDA submission to inform scheduling considerations.

Drug-Drug Interaction Study

In October 2025, we completed our Phase 1 drug-drug interaction study to evaluate the co-administration of Haduvio with pirfenidone or nintedanib in healthy adult subjects. Pirfenidone and nintedanib are prescribed as anti-fibrotic therapies in a significant portion of patients with IPF. The results of the study concluded coadministration of Haduvio with pirfenidone and nintedanib showed no clinically meaningful pharmacokinetic findings for nalbuphine ER or either of the antifibrotics when given in combination. No dose adjustments for any of the drugs will be required if Haduvio is administered concomitantly with these agents.

Respiratory Safety

We are also conducting a Phase 1 respiratory function and safety study, which we refer to as TIDAL, in the U.K. and U.S. and we have screened and enrolled patients. TIDAL is a multi-center, open-label, in-clinic, fixed-sequence placebo to nalbuphine ER dose escalation study assessing overnight respiratory function and safety in patients with IPF. We expect to enroll approximately ten patients who will be in-clinic for ten days. The goal of the study is to assess the safety and tolerability of Haduvio as well as the effect on respiratory function and safety in subjects with IPF based on assessment of end tidal partial pressure of carbon dioxide by capnography (PetCO2), oxygen saturation (SpO2), and respiratory rate. The study is intended to better characterize the physiological effects of administering nalbuphine ER at the intended therapeutic doses on parameters of respiration important for patients with IPF. The safety review committee met to review data for the sentinel cohort of patients and concluded there were no safety signals and gave approval to complete enrollment. We expect to complete this study in mid-2026.

We also anticipate conducting additional standard pharmacokinetic, pharmacodynamic and other studies as needed to support marketing applications for regulatory approval in the U.S. and Europe.

Competition

The biopharmaceutical industry is intensely competitive and is subject to rapid and significant change. While we believe that our technology, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies. If we are able to successfully develop and commercialize Haduvio, it would compete with existing therapies and new therapies that may become available in the future.

Chronic Cough in Patients with Idiopathic Pulmonary Fibrosis and Non-IPF Interstitial Lung Diseases

If Haduvio is approved for the treatment of chronic cough in patients with IPF and non-IPF ILD, we expect that it may compete with product candidates that may be developed for the treatment of chronic cough in patients with IPF or ILD. Development of BI 1839100, a TRPA1 antagonist by Boehringer Ingelheim for the treatment of IPF-related chronic cough and progressive pulmonary fibrosis, was terminated in September 2025. It is possible that product candidates currently in development for the treatment of fibrosis in patients with IPF and ILD could, if approved, reduce the need for therapies to treat chronic cough in patients with IPF and non-IPF ILD. We expect that Haduvio might also compete with other product candidates currently in development, for the treatment of patients with RCC that might be used off-label to treat IPF-related chronic cough.

RCC

If Haduvio is approved for the treatment of patients with RCC, we expect that it may compete with product candidates in clinical development for the treatment of patients with RCC such as camlipixant, a P2X3 antagonist, which is being developed by GSK plc. Gefapixant, a P2X3 antagonist, which was developed by Merck & Co., Inc., or Merck, is approved for refractory or unexplained chronic cough in Japan, the United Kingdom, Switzerland, and the E.U. The application filed with the FDA was withdrawn and Merck indicated it does not plan to refile. Other product candidates that are currently in development for the treatment of patients with RCC include taplucainium (formerly NTX-1175), a charged sodium channel blocker, which is being developed by Nocion Therapeutics Inc.

We also expect that Haduvio would compete with a number of therapeutics that are not specifically approved to treat chronic cough including benzonatate, opioids, corticosteroids, proton-pump inhibitors, and neuromodulators.

Many of our competitors and potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and commercializing approved products than we do. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials.

We expect that Haduvio, if approved for marketing, will compete on the basis of, among other things, efficacy, safety, health-economic benefit, convenience of administration and delivery, price, the level of generic competition and the availability of adequate reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than Haduvio. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for Haduvio, which could result in our competitors establishing a strong market position before we are able to enter the market.

License Agreements

Exclusive License Agreement with Keenova Therapeutics plc

In May 2011, we entered into an agreement with Keenova, for an exclusive worldwide sublicensable license under certain patent rights and know-how controlled by Keenova to develop and commercialize products incorporating nalbuphine hydrochloride in any formulation, including an extended-release formulation such as Haduvio, in all fields and for any use.

Under the license agreement, we paid Keenova a non-creditable, non-refundable upfront license fee. We may also become obligated to make milestone payments to Keenova of $0.3 million, which would become due upon the successful completion of the first Phase 3 clinical trial of a licensed product candidate, and $0.8 million, which would become due upon the marketing approval of a licensed product in the U.S., and to pay royalties based on net sales of the licensed

products by us, our affiliates and sublicensees. In addition, we are obligated to pay Keenova a low-to-mid double-digit percentage of certain income we receive from sublicensees, based on the date of the definitive agreement under which the sublicense was granted.

Our royalty obligation with respect to each licensed product in each country commences upon the first commercial sale of the product in that country and extends until the later of the expiration, unenforceability or invalidation of the last valid claim of any licensed patent or application covering the licensed product in the country or the expiration of 10 years after the first commercial sale of the licensed product in the country, which period is referred to as the royalty term. Upon the expiration of the royalty term for a product in a country, we are thereafter obligated to pay a low single-digit know-how and trademark royalty.

Under the agreement, we have granted Keenova a non-exclusive, royalty-free (except for pass-through payments to third parties), sublicensable license under our relevant patent rights, to use any improvement we make to Endo's controlled release technology, for any product other than the products under which we are licensed by Endo.

Both we and Keenova have the right to terminate the agreement if the other party materially breaches the agreement and fails to cure the breach within specified cure periods. Keenova also has the right to terminate in the event we undergo specified bankruptcy, insolvency or liquidation events. We have the right to terminate the agreement at our convenience at any time on 180 days' notice to Keenova. Additionally, if we or any of our sublicensees challenge the validity or enforceability of any licensed patent rights covering a licensed product, and that challenge is not terminated within a specified period, the agreement will immediately terminate and all licenses granted under the agreement shall be revoked.

Upon termination of the agreement, we must transfer to Keenova all regulatory filings and approvals relating to the development, manufacture or commercialization of the licensed products and all trademarks, other than our corporate trademarks, then being used in connection with the licensed products. If the agreement is terminated under certain specified circumstances, we will be deemed to have granted Keenova a perpetual, royalty-free (except for pass-through payments to third parties), worldwide, exclusive, sublicensable license, under any improvements we made to the licensed know-how, and any related patent rights we have, to manufacture and commercialize the licensed products.

Manufacturing

We currently contract with third parties for the supply of nalbuphine hydrochloride drug substance and the manufacture of Haduvio tablets for clinical trials and intend to do so for clinical and commercial supply in the future. We do not own or operate facilities for the production of clinical or commercial quantities of drug substance or drug product. At present, we have no plans to initiate our own clinical or commercial scale manufacturing capabilities. Although we rely on contract manufacturers, we have personnel with experience to oversee our relationships with contract manufacturers.

We rely, and plan to continue to rely, on a single supplier, Par Health, which was spun off as an independent company after the merger between Mallinckrodt plc and Endo, Inc., for nalbuphine hydrochloride drug substance. We do not have agreements in place with Par Health that guarantee supply quantities or pricing. Any significant delay in acquisition, increase in cost or decrease in availability of nalbuphine hydrochloride drug substance could considerably delay the manufacture of Haduvio, which could adversely impact the timing of our current and planned clinical trials and potential regulatory approval and commercialization of Haduvio. Although we are evaluating alternate sources of supply that could satisfy our clinical and commercial requirements for nalbuphine drug substance, we have not qualified any alternate sources and cannot assure you that we would be able to establish relationships with any such sources in a timely fashion, on commercially reasonable terms or at all.

Haduvio is manufactured from readily available starting materials using established, scalable processes that do not require any special equipment or technology. Nalbuphine hydrochloride drug substance is commercially available and manufactured at production scale. Haduvio tablets are currently manufactured at a scale adequate to support clinical trials and initial commercial supply. Further scale-up assessment is also being planned.

We believe that our current suppliers and manufacturers have the capacity to support commercial scale production of Haduvio, however we have no formal agreements with them to cover commercial production and we may seek to pursue supply or manufacturing arrangements with additional or alternative parties in the future. While we believe there are alternate sources of supply that can satisfy our clinical requirements and any future commercial requirements, replacing or adding a supplier or manufacturer at the present time could result in additional cost or delay.

Commercial Operations

We have retained worldwide commercial rights for Haduvio. If Haduvio were to receive marketing approval from the FDA for IPF-related chronic cough or non-IPF ILD-related chronic cough, we would plan to market and commercialize Haduvio in the U.S. with our own focused, specialty sales force and target pulmonologists who specialize in treating IPF and non-IPF ILD patients, as well as ILD centers of excellence, as applicable. If Haduvio were to receive marketing

approval from the FDA for RCC, we would plan to market and commercialize Haduvio in the U.S. with our own focused sales force and target pulmonologists and other specialists, such as allergists, who treat RCC patients who have failed other chronic cough therapies. We also expect to utilize a variety of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize Haduvio outside the U.S.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for Haduvio and our manufacturing and process discoveries and other know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position.

As of December 31, 2025, we owned six U.S. patents, 22 foreign patents and multiple pending U.S. and foreign patent applications that include claims relating to methods of use of Haduvio, including a U.S. patent covering the use of Haduvio for the treatment of IPF-related chronic cough. The issued patents expire between 2032 and 2041 and the patent applications, if issued as patents, would expire between 2032 and 2045. In February 2025, we received a notice of allowance for a U.S. patent application with claims covering the use of Haduvio for the treatment of chronic cough in IPF in patients with hepatic impairment. The patent issuing from this application will expire in 2042.

In addition, we are party to an exclusive license agreement with Keenova under which we have licensed patent rights and know-how to develop and commercialize products incorporating nalbuphine hydrochloride in any formulation, including Haduvio. As of December 31, 2025, the intellectual property in-licensed under this agreement included six U.S. patents and four foreign patents, which include granted European patent rights that have been validated in various European Union, or E.U., member states. The licensed patents from Keenova include claims relating to the formulation of Haduvio. These patents expire between 2026 and 2029.

In addition, we have in-licensed three issued U.S. patents, one issued European patent, one issued Japanese patent, and one issued Canadian patent. These patents relate to the use of nalbuphine in various movement disorders. The U.S. patents expire in 2032. The Japanese, European and Canadian patents expire in 2032.

We do not own or exclusively license any composition of matter patents for Haduvio.

The terms of individual patents depend upon the legal term for patents in the countries in which they are granted. In most countries, including the U.S., the patent term is generally 20 years from the earliest claimed filing date of a nonprovisional patent application in the applicable country. In the U.S., a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date.

Provisions are available in the E.U. and certain other non-U.S. jurisdictions to extend the term of a patent that covers an approved drug. The expiration dates referred to above are without regard to potential patent term extension or other market exclusivity that may be available to us. However, we cannot provide any assurances that any such patent term extension of a non-U.S. patent will be obtained and, if obtained, the duration of such extension. We also protect our proprietary technology and processes, in part, by confidentiality and invention assignment agreements with our employees, consultants, scientific advisors and other contractors. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants, scientific advisors or other contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, alter our processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize Haduvio or any future product candidate may have a material adverse impact on us. If third parties prepare and file patent applications in the U.S. that also claim technology to which we have rights, we may have to participate in interference or derivation proceedings in the USPTO to determine priority of invention.

Government Regulation and Product Approvals

Government authorities in the U.S., at the federal, state and local levels, and in other countries and jurisdictions, including the E.U., extensively regulate, among other things, the research, development, testing, manufacture, sales,

pricing, reimbursement, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the U.S. and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources and may have a significant impact on our business.

Approval and Regulation of Drugs in the U.S.

In the U.S., drug products are regulated under the Federal Food, Drug, and Cosmetic Act, or FDCA, and applicable implementing regulations and guidance. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. The failure of a sponsor to comply with the applicable regulatory requirements at any time during the product development process, including nonclinical testing, clinical testing, the approval process or the post-approval process, may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions.

A sponsor seeking approval to market and distribute a new drug in the U.S. generally must satisfactorily complete each of the following steps before the FDA will consider approving the product candidate:

- preclinical testing including laboratory tests, animal studies and formulation studies, which must be performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards;
- completion of the manufacture, under current Good Manufacturing Practices, or cGMP, conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- design of a clinical protocol and submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication, in accordance with current good clinical practices, or cGCP;
- preparation and submission to the FDA of an NDA for a drug product which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacturing and controls, or CMC, for the product candidate and proposed labelling for one or more proposed indication(s);
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of any FDA audits of the nonclinical and clinical trial sites to assure compliance with cGCPs and the integrity of clinical data in support of the NDA;
- payment of user application and program fees pursuant to the Prescription Drug User Fee Act, or PDUFA;
- securing FDA approval of the NDA to allow marketing of the new drug product for a particular indication in the U.S.; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS and the potential requirement to conduct any post-approval studies required by the FDA.

Preclinical Studies

Before a sponsor begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. These studies are generally referred to as IND-enabling studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may

continue after the IND is submitted. With passage of the FDA's Modernization Act 2.0 in December 2022, Congress eliminated provisions in both the FDCA and the Public Health Service Act that required animal testing in support of an NDA. While animal testing may still be conducted, the FDA was authorized to rely on alternative nonclinical tests, including cell-based assays, microphysiological systems, or bioprinted or computer models. In April 2025, the FDA released a roadmap to replace animal testing in preclinical safety studies with scientifically validated new approach methodologies.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research patients will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. The FDA may also place a hold or partial hold on a clinical study based on CMC issues involving the investigational product. In either case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

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

Once an IND application takes effect, the sponsor of the IND may amend the application as needed to ensure that the clinical investigations are conducted according to protocols included in the IND. The FDA has indicated that sponsors are expected to submit amendments for new protocols or changes to existing protocols before implementation of the respective changes. New studies may begin, however, when the sponsor has submitted the change to the FDA for its review and the new protocol or changes to the existing protocol have been approved by the IRB with the responsibility for review and approval of the studies. In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB, which must operate in compliance with FDA regulations, must review and approve, among other things, the study protocol and informed consent information to be provided to study patients. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data monitoring committee, or DMC. This group provides authorization as to whether or not a trial may move forward at designated checkpoints based on review of available data from the study, to which only the DMC maintains access. Suspension or termination of development during any phase of a clinical trial can occur if the DMC determines that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or Cures Act, passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests, it must make that policy publicly available. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the investigational drug receives designation as a breakthrough therapy, fast-track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product candidate to human patients under the supervision of a qualified investigator in accordance with cGCP requirements which include, among other things, the requirement that all research patients provide their informed consent in writing before they participate in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

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

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

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

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

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

In September 2025, the FDA issued final guidance with updated recommendations for cGCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The final guidance is adopted from the International Council for Harmonisation's recently updated E6(R3) final guideline that was developed to enable the incorporation of rapidly

developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued final guidance outlining recommendations for the implementation of decentralized clinical trials.

In October 2025, the FDA issued final guidance that focuses on patient-focused drug development. The guidance outlines how stakeholders, such as patients, caregivers, researchers and medical product developers, can submit patient experience data in support of the development and approval of drug products. To that end, the guidance provides an overview of clinical outcome assessments, or COAs, in clinical trials, and the role that COAs may play in in evaluating the clinical benefit of a medical product.

In February 2026, the Commissioner of the FDA and the Director of Center for Biologics Evaluation and Research published an editorial in the New England Journal of Medicine in which they declared that, in most cases, the new default requirement for FDA approval of a new product will be one adequate and well-controlled pivotal clinical trial plus confirmatory evidence, rather than two pivotal clinical trials. In determining whether to rely on one trial, the FDA will focus on the single trial's quality, including magnitude of effect, appropriateness of control arms, endpoint selection, statistical power, blinding, handling of missing data, biological plausibility and alignment with intermediate biomarkers. At this point, it is unclear how this new policy will be implemented by the FDA. Based on the guidance from the FDA at our End-of-Phase 2 meeting, we plan to conduct two pivotal Phase 3 clinical trials for IPF-related chronic cough but it is not clear how the FDA's new policy will apply to any other indication for which we develop Haduvio and how, if at all, it will affect our clinical development programs.

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

A development and safety update report, or DSUR, detailing the results of clinical trials must be submitted at least annually to the FDA. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. The FDA will typically inspect one or more clinical sites to assure compliance with cGCP and the integrity of the clinical data submitted.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The FDA has historically not enforced these reporting requirements due to the long delay of the Department of Health and Human Services, or HHS, in issuing final implementing regulations. With those regulations now in place, the FDA has issued, as of January 31, 2026, eight notices of non-compliance, thereby signaling the government's willingness to begin enforcing these requirements against non-compliant clinical trial sponsors. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Violations may also result in injunctions and/or criminal prosecution or disqualification from federal grants.

Clinical Studies Outside the United States in Support of FDA Approval

In connection with our clinical development program, we may conduct trials at sites outside the United States. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with cGCP, including undergoing review and receiving approval by an independent ethics committee and seeking and receiving informed consent from subjects. cGCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

The acceptance by the FDA of study data from clinical trials conducted outside the United States in support of U.S. approval may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical

practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to cGCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or, if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

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

Interactions with the FDA During the Clinical Development Program

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

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

Pediatric Studies

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

For investigational products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the End-of-Phase 1 meeting for serious or life-threatening diseases and by no later than ninety days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete. The FDA is required to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, and have failed to seek or obtain a deferral or deferral extension. Unless otherwise required by regulation, the pediatric data requirements generally do not apply to products with orphan designation, although FDA has taken steps to limit what it considers abuse of this statutory exemption in PREA. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

Submission and Review of an NDA

In order to obtain approval to market a drug product in the U.S., a marketing application must be submitted to the FDA that provides sufficient data establishing the safety and efficacy of the drug product for its intended indication. The application must include all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product candidate's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of the use of a product candidate, or from a number of alternative sources, including studies initiated by independent investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the drug product to the satisfaction of the FDA.

The NDA is a vehicle through which sponsors formally propose that the FDA approve a new product for marketing and sale in the U.S. for one or more indications. Every new drug product candidate must be the subject of an approved NDA before it may be commercialized in the U.S. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2026 is $4,682,003 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for federal fiscal year 2026 is $442,213. Certain exceptions and waivers are available for some of these fees, such as a waiver for certain small businesses.

Following submission of an NDA, the FDA conducts a preliminary review of the application within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the sponsor. The FDA may request additional information rather than accept the application for filing. In this event, the application must be resubmitted with the requested additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective for its intended use, whether it has an acceptable purity profile and whether the product is being manufactured in accordance with cGMP. The FDA has agreed to specified performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within 10 months from the date on which the FDA accepts the application for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date.

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

In connection with its review of an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

Moreover, the FDA will review a sponsor's financial relationship with the principal investigators who conducted the clinical trials in support of the NDA. That is because, under certain circumstances, principal investigators at a clinical trial site may also serve as scientific advisors or consultants to a sponsor and receive compensation in connection with such services. Depending on the level of that compensation and any other financial interest a principal investigator may have in a sponsor, the sponsor may be required to report these relationships to the FDA. The FDA will then evaluate that financial relationship and determine whether it creates a conflict of interest or otherwise affects the interpretation of the trial or the integrity of the data generated at the principal investigator's clinical trial site. If so, the FDA may exclude data from the clinical trial site in connection with its determination of safety and efficacy of the investigational product.

Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP and the integrity of the data submitted in support of the application. In 2022, Congress clarified FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and nonclinical studies submitted to FDA as well as other persons holding study records or involved in the study process.

In addition, as a condition of approval, the FDA may require a sponsor to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events and whether the product is an NME.

The FDA may also refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Expedited Review Programs

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

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

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

Priority Review. A product candidate is eligible for Priority Review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. The FDA aims to complete its review of Priority Review applications within six months as opposed to 10 months for standard review.

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

Commissioner's National Priority Voucher Program. In June 2025, the FDA announced the creation of the "Commissioner's National Priority Voucher, or CNPV, Program. Vouchers issued under this program can reportedly be redeemed by sponsors to shorten the review time of an NDA from approximately 10-12 months to 1-2 months. The FDA has indicated that the new CNPV process will convene experts from the FDA's offices for a team-based review rather than using the standard review system. Clinical information will be reviewed by a multidisciplinary team of physicians and scientists who will pre-review the submitted information and convene for a 1-day meeting. Vouchers under this program will reportedly be given to companies aligned with U.S. national priorities.

Rare Disease Evidence Principles. In September 2025, the FDA introduced a framework intended to streamline the approval of new therapies for ultrarare diseases. The Rare Disease Evidence Principles, or RDEP, is intended to allow sponsors to rely on a single-arm trial in support of approval of biologics that treat rare diseases with very small patient populations and where the disease is linked to a known genetic defect and characterized by progressive functional

deterioration leading to disability or death in a short period of time. The targeted diseases should also lack adequate alternative therapies.

Accelerated approval. In addition to programs that allow for expedited review of applications, the FDA is authorized to approve new products through an accelerated approval pathway. Under this pathway, a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well controlled post-marketing studies or clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of all promotional materials.

In 2022, Congress directed the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to FDA every six months until the study is completed. Moreover, the FDA was authorized to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval study of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner of Food and Drugs, or the Commissioner, or the Commissioner's designee and a written appeal, among other things.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of an NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter, or CRL. To reach this determination, the FDA reviews an application to determine, among other things, whether the product is safe and effective for its intended use. The FDA must determine that the investigational product is effective and that its expected benefits outweigh its potential risks to patients. This assessment is informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks.

A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six month extension to respond. For those seeking to challenge FDA's CRL decision, the agency has indicated that sponsors may request a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution. While CRLs were previously treated by the FDA as confidential and were only disclosed in action packages for approved products, the agency announced in September 2025 that it will now release CRLs promptly after they are issued to sponsors. Since that announcement, the FDA has posted a number of CRLs on its website.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific conditions. The FDA may limit the approved indications for use of the product. The agency may also require testing and surveillance programs to monitor the product after the initiation of commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, such as REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

In the event that a sponsor wishes to make a change to a product that has been approved under an NDA, the sponsor must submit a supplemental application to the FDA. Such changes may include a revision of the labeling for the approved

product, the addition of a new indication, a change in the dosage, strength or formulation of the product, or a modification of the manner in which the drug is manufactured. Under the timelines established pursuant to PDUFA, the standard review time for a non-NME original NDA is generally 10 months from receipt of the application by the FDA.

Post-Approval Regulation

If regulatory approval for marketing of a product or a new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA may have imposed as part of the approval process. The sponsor will be required to report, among other things, certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

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

In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the

unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws. The Prescription Drug Marketing Act, or the PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. In November 2013, the federal Drug Supply Chain Security Act, or DSCSA, became effective in the U.S., mandating an industry-wide, electronic, interoperable system to trace prescription drugs through the pharmaceutical distribution supply chain with a ten-year phase-in process. Manufacturers were required by November 2023 to have such systems and processes. So as not to disrupt supply chains, the FDA has granted certain exemptions from enhanced drug distribution security requirements for eligible trading partners for particular periods of time. For wholesale drug distributors, the final DSCSA deadline was August 27, 2025, marking the date for mandatory transition to a fully electronic, interoperable system for tracking prescription drugs at the package level throughout the United States.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations that were previously conducted to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by or for the sponsor. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) sponsor can establish that reliance on the FDA's previous approval is scientifically appropriate, the sponsor may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) sponsor.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Act, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs.

In order for an abbreviated new drug application, or ANDA, to be approved, the FDA must find that the generic version is identical to the reference listed drug, or RLD, with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD.

Under the Hatch-Waxman Act, the FDA may not approve an ANDA until any applicable period of regulatory exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, an NCE is a drug that contains no active

moiety that has previously been approved by the FDA in any other NDA. This interpretation of the FDCA by the FDA was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the sponsor may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of regulatory exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the sponsor and are essential to the approval of the application.

Hatch-Waxman Act Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the sponsor's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. The FDA's regulations governing patient listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. When an ANDA sponsor files its application with the FDA, the sponsor is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA sponsor is not seeking approval. To the extent that the Section 505(b)(2) sponsor is relying on studies conducted for an already approved product, the sponsor is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA sponsor would.

Specifically, the sponsor must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, is unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the sponsor does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all of the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the sponsor is not seeking approval).

If the ANDA sponsor has provided a Paragraph IV certification to the FDA, the sponsor must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earliest of 30 months after the receipt of the Paragraph IV notice, expiration of the patent and a decision in the infringement case that is favorable to the ANDA sponsor.

To the extent that the Section 505(b)(2) sponsor is relying on studies conducted for an already approved product, the sponsor is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA sponsor would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of an NCE, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earliest of 30 months, settlement of the lawsuit and a decision in the infringement case that is favorable to the Section 505(b)(2) sponsor.

Pediatric Exclusivity

Pediatric exclusivity is a type of non-patent marketing exclusivity in the U.S. and, if granted, provides for the attachment of an additional six months of regulatory exclusivity to the term of any existing patent or regulatory exclusivity for drug products. This six month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months.

This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application for a similar product.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half of the time between the effective date of the IND and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Health Care Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements.

Restrictions under applicable federal and state health care laws and regulations, include the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, 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, in whole or in part, under a federal health care program such as Medicare and Medicaid; the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government; the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and the federal transparency requirements known as the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the HHS, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians, and their immediate family members.

Further, 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 in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. 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 the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Health Care Reform

In the U.S. and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the U.S. such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a

product could reduce physician utilization once the product is approved. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the U.S.

In March 2010, the U.S. Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. Other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013.

The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to four percent.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the Tax Act, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On June 17, 2021, the U.S. Supreme Court dismissed an action challenging the constitutionality of the ACA after finding that the plaintiffs do not have standing to bring the action. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Pharmaceutical Price Reforms

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In addition, the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program to import certain prescription drugs from Canada into the U.S. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue the HHS. Several states have passed laws allowing for the importation of products from Canada. On January 5, 2023, the FDA approved Florida's plan for Canadian product importation. That state now has authority to import certain products from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each product selected for importation, which must be approved by the FDA. The state will also need to relabel the products and perform quality testing of the products to meet FDA standards.

On May 21, 2025, the FDA announced that it would offer individual states the opportunity to submit a draft proposal for pre-review and meet with the agency to obtain initial feedback from FDA prior to formally submitting their Section 804 importation program (SIP) proposal. The intent of these meetings is to assist states in developing their proposals by further clarifying requirements, enhancing the quality of proposals submitted to the agency and ultimately shortening the review timeline. Further, the HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would also eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage of the Inflation Reduction Act of 2022, or the IRA, has been delayed by Congress to January 1, 2032.

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

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain single-source drug products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS was directed to negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least nine years. Drugs that have been approved for a single rare disease or condition were originally categorically excluded from price negotiation but, with the passage of the One Big Beautiful Bill Act, or OBBBA, on July 3, 2025, Congress extended this exemption to drugs with multiple orphan drug designations.

The IRA subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. In addition, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023, with the negotiated prices for ten selected drug products becoming effective on January 1, 2026. The second cycle of negotiations with participating drug companies will occurred during 2025, and the negotiated prices for this second set of fifteen drugs will become effective on January 1, 2027. On January 27, 2026, CMS published the list of fifteen drugs selected for the third cycle of negotiations. These negotiated prices will become effective on January 1, 2028.

On June 6, 2023, Merck filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties also filed lawsuits in various courts with similar constitutional claims. HHS has generally won the substantive disputes in these cases or succeeded in getting claims dismissed for lack of standing or on the merits. For example, on May 8, 2025, the U.S. Court of Appeals for the Third Circuit rejected AstraZeneca L.P.'s challenge to the Medicare price negotiation program, finding that the program did not violate the company's due process rights under the Constitution. Litigation involving these and other provisions of the IRA will continue with unpredictable and uncertain results.

Since adoption of the IRA, the Trump Administration has taken a number of actions to reduce the costs of pharmaceutical products. For example, on April 15, 2025, President Trump issued an Executive Order which directs HHS to take steps to reduce the prices of pharmaceutical products. Further, on May 12, 2025, President Trump issued an additional Executive Order calling on pharmaceutical manufacturers to voluntarily reduce the prices of medicines in the United States. The Order provides that if such actions do not lower the costs of pharmaceuticals, the Secretary of HHS would pursue other actions, including proposing a rulemaking that imposes most favored nation, or MFN, pricing in the United States. Thereafter, on July 31, 2025, the President issued letters to 17 pharmaceutical companies reiterating the requirements of the May 12, 2025, Executive Order and demanding that such companies extend MFN pricing to Medicaid patients. Virtually all of these pharmaceutical companies have entered into agreements with the administration to provide for lower prices on certain pharmaceuticals.

Federal and State Data Privacy and Security laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the healthcare industry generally, under HIPAA, HHS has issued regulations to protect the privacy and security of protected health information used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them.

Our clinical trials will be regulated by HIPAA's Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal

penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

In 2018, California passed into law the California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or the GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, a number of other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation in 2024. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

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

Review and Approval of Medicinal Products in the E.U.

In order to market any product outside of the U.S., a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, a sponsor will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the E.U. generally follows the same lines as in the U.S. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA and granting of a marketing authorization, or MA, by these authorities before the product can be marketed and sold in the E.U.

Nonclinical Studies

Nonclinical studies are performed to demonstrate the health or environmental safety of new chemical substances. Nonclinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in E.U. Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, nonclinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP

principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for nonclinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical Trial Approval

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014, or CTR, became effective in the E.U. and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the E.U. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the E.U., or E.U. Member State, will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the E.U. Member States and the public.

Beyond streamlining the process, the new regulation includes a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all E.U. Member States in which an application for authorization of a clinical trial has been submitted, which we refer to as the Member States concerned. Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Member State concerned. However, overall related timelines will be defined by the CTR.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the E.U. Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different E.U. Member States, the competent authorities in each of these E.U. Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion. As of January 31, 2025, all clinical trials in the E.U. (including those which are ongoing) are subject to the CTR.

As in the U.S., clinical trial information must be posted in the E.U. at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the E.U.

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or the Committee for Advanced Therapies, or CAT, is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Marketing Authorization

To obtain an MA for a product under E.U. regulatory systems, a sponsor must submit an MAA either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in the E.U. Member States (either a decentralized procedure, national procedure or mutual recognition procedure). An MA may be granted only to a sponsor established in the E.U. Regulation (EC) No 1901/2006 provides that prior to obtaining an MA in the E.U., sponsors have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (i) a product-specific waiver, (ii) a class waiver or (iii) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single MA by the European Commission that is valid across the European Economic Area, or the EEA (i.e. the E.U., as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that

are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may also be used in certain other cases at the request of the sponsor. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. Under the centralized procedure in the E.U., the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the sponsor in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not an MA should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for an MA. This draft decision must take the opinion and any relevant provisions of E.U. law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use, or the Standing Committee. The Standing Committee is composed of representatives of the E.U. Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard". The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant an MA.

Exceptional Circumstances

The European Commission may grant a so-called "marketing authorization under exceptional circumstances". Such authorization is intended for products for which the sponsor can demonstrate that it is unable to provide comprehensive data on efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the sponsor cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, an MA under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the sponsor must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

An MA under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the MA being suspended or revoked. The renewal of an MA of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" MA. Thus, an MA under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

Conditional Marketing Authorization

The European Commission may also grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full MA. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies and the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each E.U. Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for

authorization through the centralized procedure. The reference E.U. Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned E.U. Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned E.U. Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all E.U. Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the E.U. Member States of the MA of a medicinal product by the competent authorities of other E.U. Member States. The holder of a national MA may submit an application to the competent authority of an E.U. Member State requesting that this authority recognize the MA delivered by the competent authority of another E.U. Member State.

Regulatory Data Protection in the E.U.

In the E.U., innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents sponsors for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic MAA can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the E.U. market until the expiration of the market exclusivity. The overall 10-year period will be extended to a maximum of 11 years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be an NCE so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

In November 2020, the European Commission launched a review of the E.U.'s pharmaceutical legislation, including its provisions governing regulatory exclusivity. The EC's proposal for revision of several legislative measures was published in April 2023 and includes, among other things, provisions that would potentially reduce the duration of regulatory exclusivity protection. On December 11. 2025, the European Parliament and Council reached a provisional political agreement on the legislation, which is expected to be adopted by mid-2026. Key changes include updating regulatory exclusivity to a new system with eight years of data exclusivity and a reduced market exclusivity period to one year, which can be extended if specific conditions are fulfilled up to a maximum of eleven years. This measure, and others, are expected to be adopted by mid-2026 and, following a transition period of 24 months, will likely take effect in mid-2028.

Patent Term Extensions in the E.U. and Other Jurisdictions

The E.U. also provides for patent term extension through Supplementary Protection Certificates, or SPCs. The rules and requirements for obtaining a SPC are similar to those in the U.S. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. These periods can be extended for six additional months if pediatric exclusivity is obtained, which is described in detail below. Although SPCs are available throughout the E.U., sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the E.U.

Periods of Authorization and Renewals

An MA has an initial validity for five years in principle. The MA may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the E.U. Member State. To this end, the MA holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the MA was granted, at least six months before the MA ceases to be valid. The European Commission or the competent authorities of the E.U. Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of MA. Once subsequently definitively renewed, the MA shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the E.U. market (in case of centralized procedure) or on the market of the authorizing E.U. Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Pediatric Studies and Exclusivity

Prior to obtaining an MA in the E.U., sponsors must demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all MA procedures are laid down in Regulation (EC) No 1901/2006, the so-called Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not

needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing MA can be amended, the EMA must determine that a company actually complied with the agreed studies and measures listed in each relevant PIP. If a sponsor obtains an MA in all E.U. Member States, or an MA granted in the Centralized Procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate.

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the E.U. is obtained, the holder of the MA is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the E.U.'s stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable E.U. laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice, or E.U. cGMP. These requirements include compliance with E.U. cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the E.U. with the intention to import the active pharmaceutical ingredients into the E.U.
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the E.U. notably under Directive 2001/83EC, as amended, and E.U. Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the E.U.

Review and Approval of Medical Products in the U.K.

The U.K.'s withdrawal from the E.U., commonly referred to as Brexit, took place on January 31, 2020. The E.U. and the U.K. reached an agreement on their new partnership in the Trade and Cooperation Agreement, which entered into force on May 1, 2021. As of January 1, 2025, the Medicines and Healthcare Products Regulatory Agency, or the MHRA, is responsible for approving all medicinal products destined for the United Kingdom market (Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. The MHRA relies on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of E.U. law instruments governing medicinal products that pre-existed prior to the U.K.'s withdrawal from the E.U. On April 28, 2025, the Parliament adopted amendments to improve and strengthen the clinical trials regulatory regime in the United Kingdom. These revisions will take effect on April 28, 2026, and were needed since the then existing requirements in the United Kingdom were based upon the now-repealed Clinical Trials Directive, which has been replaced by the CTR. Since the U.K. left the E.U. prior to the date on which the E.U. CTR took effect, the legal framework in the U.K. did not benefit from the same revisions as occurred at the E.U. level.

As of January 1, 2024, a new international recognition procedure, or IRP, applies which intends to facilitate approval of pharmaceutical products in the U.K. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the EEA member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). The RR assessment must have undergone a full and standalone review. RR assessments based on reliance or recognition cannot be used to support an IRP application. A CHMP positive opinion or an MRDC positive end of procedure outcome is an RR authorization for the purposes of IRP.

General Data Protection Regulation

The collection, use, disclosure, transfer or other processing of personal data regarding individuals in the E.U., including personal health data, is subject to the GDPR. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the E.U., including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or four percent of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data patients and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the E.U.-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. Following this decision, the European Commission adopted an adequacy decision for the E.U.-U.S. Data Privacy Framework in July 2023. This adequacy decision permits U.S. companies who self-certify under the E.U.-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the European Union to the United States. However, some privacy advocacy groups have already suggested that they will be challenging the E.U.-U.S. Data Privacy Framework, and there is currently one pending litigation against the EU-U.S. Data Privacy Framework before the Court of Justice of the European Union (CJEU), C-703/25 P – Latombe v Commission. If these challenges are successful, they may not only impact the E.U.-U.S. Data Privacy Framework, but also further limit the viability of the so-called standard contractual clauses and other data transfer mechanisms.

In October 2022, President Biden signed an executive order to implement the E.U.-U.S. Data Privacy Framework, which would serve as a replacement to the E.U.-U.S. Privacy Shield. The European Commission initiated the process to adopt an adequacy decision for the E.U.-U.S. Data Privacy Framework in December 2022, and has now adopted an adequacy decision to permit data transfers from the E.U. to the U.S. going forward. This development permits data transfers under the E.U.-U.S. Data Privacy Framework and more broadly has made international data transfers more straightforward, but these provisions are being challenged in court. The continuing uncertainty around this issue may further impact our business operations in the E.U. We may, however, incur liabilities, expenses, costs, and other operational losses under the GDPR and the laws of applicable E.U. Member States and the U.K. privacy laws in connection with any measures we take to comply with them.

Following the withdrawal of the United Kingdom from the E.U., the U.K. Data Protection Act applies to the processing of personal data that takes place in the United Kingdom and includes parallel obligations to those set forth by GDPR. The United Kingdom government has determined that it considers all EU member states and European Economic Area, or EEA, member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the E.U./EEA remain unaffected. Further, the European Commission decided in June 2021 that the level of data protection in the United Kingdom is "essentially adequate" for purposes of data transfer from the EU to the United Kingdom. On December 19, 2025, the European Commission renewed this decision until December 27, 2031. The United Kingdom and the U.S. have also agreed to a U.S.- U.K. "Data Bridge," which functions similarly to the E.U.-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer personal data from the United Kingdom to the United States.

Beyond the GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow the GDPR as a model, other laws contain different or conflicting provisions. These laws may impact our ability to conduct our business activities, including both our clinical trials and any eventual sale and distribution of commercial products.

Pricing Decisions for Approved Products

In the E.U., pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the E.U. provides options for the E.U. Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. E.U. Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other E.U. Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the E.U. have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the E.U. The downward pressure on health care costs in general, particularly with respect to prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various E.U. Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced E.U. Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Employees and Human Capital Resources

As of December 31, 2025, we had 34 employees, with 21 employees engaged in research and development and the remaining 13 engaged in general management and administration, including finance and commercial. None of our employees are represented by labor unions or covered by collective bargaining agreements. We believe that we maintain good relations with our employees.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and future employees. The principal purposes of our equity incentive plans are to attract, retain and

motivate employees, selected consultants and directors through the granting of stock-based compensation awards in ways that are aligned with the interests of our stockholders. We value our employees and regularly benchmark total rewards we provide, such as short- and long-term compensation, 401(k) contributions, health, welfare and quality of life benefits, paid time off and personal leave, against our industry peers to ensure we remain competitive and attractive to potential new hires.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on March 17, 2011 under the name Trevi Therapeutics, Inc. Our principal executive offices are located at 195 Church Street, 16th Floor, New Haven, Connecticut 06510, and our telephone number is (203) 304-2499. Our website address is www.trevitherapeutics.com. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

Item 1A. Risk Factors.

Our business is subject to numerous risks. The following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Annual Report on Form 10-K and other filings with the Securities and Exchange Commission, or SEC, press releases, communications with investors, and oral statements. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events, or otherwise.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception, expect to incur significant and increasing losses for the foreseeable future and may never achieve or maintain profitability.

We have incurred significant annual net losses every year since our inception. We expect to continue to incur significant and increasing net losses for at least the next several years. Our net losses were $42.8 million and $47.9 million for the years ended December 31, 2025 and 2024, respectively. As of December 31, 2025, we had an accumulated deficit of $329.8 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations to date primarily through private placements of our convertible preferred stock and convertible notes prior to our initial public offering, or IPO, proceeds from our IPO, sales of our common stock and warrants to purchase our common stock, and borrowings from term loans. We have devoted substantially all our financial resources and efforts to the clinical development of our product candidate Haduvio and related activities. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials of Haduvio, including our planned Phase 3 trials of Haduvio for the treatment of chronic cough in patients with idiopathic pulmonary fibrosis, or IPF, our planned adaptive design Phase 2b clinical trial of Haduvio for the treatment of chronic cough in patients with non-IPF interstitial lung disease, or non-IPF ILD, our planned Phase 2b clinical trial of Haduvio for the treatment of patients with refractory chronic cough, or RCC, and our planned Phase 1 NDA supportive studies;
- complete other development work required for the filing of a new drug application, or NDA, with the U.S. Food and Drug Administration, or FDA, and the filing of marketing authorization applications, or MAAs, with the European Medicines Agency, or EMA and the Medicines and Healthcare Products Regulatory Agency in the United Kingdom, or MHRA, or other government agencies, for Haduvio;
- seek regulatory and marketing approvals for Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD or RCC or for any future product candidate that successfully completes clinical trials, if any;
- negotiate and execute pediatric development plans and complete any post-approval commitments;
- establish sales, marketing, distribution and other commercial infrastructure to commercialize any products for which we may obtain marketing approval;
- require the manufacture of larger quantities of Haduvio or any future product candidate for clinical development and, potentially, commercialization;
- acquire or in-license rights to other potential product candidates or technologies;

- initiate and conduct research, preclinical and clinical development efforts for any future product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel, such as clinical, regulatory and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our commercialization efforts and to help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our development program for Haduvio and for any future product candidates.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we are able to obtain marketing approval for and successfully commercialize Haduvio or any future product candidate. Successful commercialization will require achievement of key milestones, including completing clinical trials of Haduvio or any future product candidate, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for any such product from private insurance or government payors. For example, based on guidance from the FDA at an End-of-Phase 2 meeting in order to successfully commercialize Haduvio for the treatment of IPF-related chronic cough, we plan to complete two Phase 3 clinical trials prior to submitting an NDA and MAA to regulatory authorities to obtain marketing approval. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues and if or when we might achieve profitability. We may never succeed in these activities and, even if we do, we may never generate revenues that are large enough for us 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, expand our business, maintain our development efforts, develop a pipeline of product candidates or continue our operations.

We have no products approved for commercial sale, which may make it difficult to evaluate the prospects for our future success and viability.

We were founded and commenced operations in 2011. Our operations to date have been limited to financing and staffing our company and conducting preclinical and clinical development of Haduvio. We have not yet demonstrated an ability to successfully complete clinical development of any product candidates, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third-party to do so on our behalf or conduct sales and marketing activities necessary for successful commercialization of any products. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by clinical-stage biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. If we obtain marketing approval for Haduvio or any future product candidate, we will need to transition from a company focused on clinical development to a company capable of supporting commercial activities. We may not be successful in effectuating such a transition.

We expect our financial condition and operating results will continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We will need substantial additional funding and if we are unable to raise sufficient capital when needed on acceptable terms or at all, we could be forced to delay, reduce or abandon our product development programs or commercialization efforts.

Developing pharmaceutical products, including conducting preclinical and nonclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We have consumed substantial amounts of cash since our inception. For example, in the years ended December 31, 2025 and 2024, we used net cash of $42.1 million and $38.3 million, respectively, in our operating activities, substantially all of which related to development activities for Haduvio. As of December 31, 2025, our cash, cash equivalents and marketable securities were $188.3 million. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue to develop Haduvio, including as and if we:

- conduct our planned Phase 3 trials and any additional trials of Haduvio for the treatment of IPF-related chronic cough;

- conduct our planned adaptive design Phase 2b clinical trial and any additional trials of Haduvio for the treatment of non-IPF ILD-related chronic cough; and
- conduct our planned Phase 2b clinical trial and any additional trials of Haduvio for the treatment of patients with RCC.

In addition, we may incur additional expenses:

- if we determine to conduct additional clinical trials of Haduvio for other indications; and
- if we acquire or in-license rights to or develop other potential product candidates or technologies and seek regulatory and marketing approvals for Haduvio or any future product candidate that successfully completes clinical trials.

In addition, if we obtain marketing approval for Haduvio or any future product candidate, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. For instance, we currently intend to commercialize Haduvio in the United States, ourselves by developing a focused, specialty sales, marketing and distribution organization. Furthermore, we expect to continue to incur significant costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise sufficient capital when needed on acceptable terms or at all, we may be forced to delay, reduce or abandon our development programs or any future commercialization efforts.

We plan to use our existing cash, cash equivalents and marketable securities to fund the development of Haduvio and for working capital and other general corporate purposes. We will be required to expend significant funds to advance the development of Haduvio in multiple indications, as well as any future product candidates we may seek to develop. Our existing cash, cash equivalents and marketable securities will not be sufficient to complete development of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, in RCC, or for any other condition or of any future product candidate. We do not have any committed external source of funds. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into 2028. We expect these resources will enable us to fund our planned Phase 3 trials of Haduvio for the treatment of IPF-related chronic cough, our planned adaptive design Phase 2b clinical trial of Haduvio for the treatment of non-IPF ILD-related chronic cough, our planned Phase 2b clinical trial of Haduvio for the treatment of RCC, and our planned Phase 1 NDA supportive studies. However, these resources will not be sufficient for us to fund Haduvio for any indication or any future product candidates through regulatory approval, and we will need to raise substantial additional capital to complete the development and commercialization of Haduvio and any future product candidates.

We have based our estimates as to how long we expect we will be able to fund our operations on assumptions that may prove to be wrong and we could use our available capital resources sooner than we currently expect, in which case we would be required to obtain additional financing. However, such a financing may not be available to us on acceptable terms, on a timely basis or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate and we may need to seek additional funds sooner than planned. Our future funding requirements, both short-term and long-term, will depend on many factors including:

- the scope, progress, timing, costs and results of clinical trials of Haduvio, including our planned Phase 3 trials of Haduvio for the treatment of chronic cough in patients with IPF, our planned adaptive design Phase 2b clinical trial of Haduvio for the treatment of chronic cough in patients with non-IPF ILD, our planned Phase 2b clinical trial for the treatment of patients with RCC, and our planned Phase 1 NDA supportive studies as well as trials for any future product candidates;
- the number and characteristics of indications for which we seek to develop Haduvio or any future product candidates and their respective development requirements;
- the outcome, timing and costs of clinical and nonclinical trials and of seeking regulatory approvals, including the costs of supportive clinical studies;

- the costs to manufacture necessary quantities of Haduvio or any future product candidate for clinical development in connection with regulatory submissions;
- the costs of commercialization activities for Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC or for any future product candidates that receive marketing approval, if any, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approvals, revenue, if any, received from commercial sales of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, or RCC, or from any future product candidates;
- our ability to identify potential collaborators for Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, or RCC, or for any future product candidates, and the terms and timing of any collaboration agreement that we may establish for the development and any commercialization of such product candidates;
- the extent to which we acquire or in-license rights to other potential product candidates or technologies and the terms and timing of any such acquisition or licensing arrangements;
- our potential obligation to make milestone payments to Keenova Therapeutics plc, or Keenova, which would become due upon the successful completion of the first Phase 3 clinical trial of a licensed product candidate and the marketing approval of a licensed product in the U.S., as well as our potential obligations to pay Keenova royalties on the net sales of the product;
- our headcount growth and associated costs as we expand our research and development activities and medical affairs activities and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining, expanding and protecting our intellectual property rights and defending against intellectual property-related claims;
- the effect of competing technologies and market developments;
- our ability to establish and maintain healthcare coverage and adequate reimbursement for our products; and
- the costs of operating as a public company.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our product candidates.

We expect our expenses to increase substantially in connection with our planned operations, particularly if and as we:

- conduct our planned Phase 3 trials of Haduvio for the treatment of IPF-related chronic cough;
- conduct our planned adaptive design Phase 2b clinical trial and any additional trials of Haduvio for the treatment of non-IPF ILD-related chronic cough;
- conduct our planned Phase 2b clinical trial and any additional trials of Haduvio for the treatment of patients with RCC;
- conduct our planned Phase 1 NDA supportive studies; and
- seek regulatory and marketing approvals for Haduvio.

Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to fund these expenses. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder.

Debt financing, if available, would result in fixed payment obligations and may involve agreements that include grants of security interests on our assets and restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, granting liens over our assets, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business.

Securing financing could also require a substantial amount of time from our management and may divert a disproportionate amount of their attention away from daily activities, which may adversely affect our management's ability to oversee the development of Haduvio or that of any future product candidates. If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

Risks Related to the Development and Commercialization of Haduvio and Any Future Product Candidates

We are dependent on the successful development and commercialization of Haduvio, our sole product candidate. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize Haduvio or if we experience significant delays in doing so, our business would be substantially harmed.

We currently have no products approved for sale and are investing substantially all our efforts and financial resources to fund the development and commercialization of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC. Our prospects are dependent on our ability to develop, obtain marketing approval for and successfully commercialize Haduvio in one or more indications as we currently have no other product candidates under development. We may acquire or in-license rights to other potential product candidates or technologies in the future, but we are currently not developing any other product candidates.

Our most advanced program is for the development of Haduvio for the treatment of IPF-related chronic cough. As a result, if our efforts to develop and commercialize Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC are unsuccessful or we experience significant delays in doing so, our business could also be substantially harmed.

The success of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC will depend on several factors, including the following:

- initiating and successfully recruiting, enrolling and retaining patients in and completing additional clinical and nonclinical trials of Haduvio, including the additional clinical trials we plan to conduct for the treatment of chronic cough in patients with IPF, non-IPF ILD and RCC;
- completing other Phase 1 NDA supportive clinical studies to support NDA submission;
- demonstrating safety, tolerability and efficacy profiles that are satisfactory to the FDA, EMA, MHRA and other comparable regulatory authorities for marketing approval;
- receiving timely marketing approvals from applicable regulatory authorities;
- managing any required post-marketing approval commitments to applicable regulatory authorities;
- establishing and maintaining arrangements with our third-party supplier of drug substance for Haduvio;
- establishing and maintaining arrangements with third-party manufacturers of Haduvio, including developing, validating and maintaining a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMPs;
- obtaining, maintaining and protecting our patents, trade secrets and regulatory exclusivity in the U.S. and other countries;
- establishing a focused, specialty sales organization in the U.S. and successfully launching commercial sales following any marketing approval;
- obtaining commercial acceptance of our products, if approved, by patients, the medical community and third-party payors and obtaining and maintaining healthcare coverage and adequate reimbursement;
- maintaining an acceptable safety profile following any marketing approval; and
- our ability to compete with other therapies.

Many of these factors are beyond our control, including the clinical development and regulatory approval process; potential threats to our intellectual property rights; and the manufacturing, marketing and sales efforts, respectively, of any current or future third-party contractors. If we are unable to develop, receive marketing approval for and successfully commercialize Haduvio or if we experience delays as a result of any of these factors or otherwise, our business would be substantially harmed.

Our approach to the development and commercialization of Haduvio to treat chronic cough is unproven.

We are currently focused on the development and commercialization of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC. Haduvio is an oral extended-release formulation of nalbuphine, the active drug ingredient in Haduvio. Haduvio acts on the cough reflex arc both centrally and peripherally as a kappa receptor agonist and a mu receptor antagonist, or KAMA, targeting opioid receptors that play a key role in controlling chronic cough. Nalbuphine has been approved and marketed as an injectable for pain indications for decades in the U.S. and Europe and is currently not commercially available in an oral dosage form. While we believe that nalbuphine's dual mechanism of

action, which targets both the central and peripheral nervous systems, makes Haduvio a promising potential therapy for the treatment of chronic cough and that Haduvio has the potential to be safe and well-tolerated, nalbuphine has not been approved in any indications other than pain and balanced anesthesia. No therapies have been approved for the treatment of chronic cough in patients with IPF or non-IPF ILD, and no therapies have been approved in the U.S. for the treatment of patients with RCC. Gefapixant has been approved in Japan, the United Kingdom, Switzerland, and the E.U. for the treatment of patients with RCC. We can provide no assurance that Haduvio or any other future product candidate that we may seek to develop for chronic cough indications will be effective or safe, obtain regulatory approval or be commercially successful.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome.

We are not permitted to commercialize, market, promote or sell any product candidate in the U.S. without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA and MHRA, impose similar requirements. We must complete extensive clinical trials to demonstrate the safety and efficacy of Haduvio and any future product candidate in humans and complete required regulatory submissions before we will be able to obtain these approvals. We may never receive such approvals.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. The clinical development of Haduvio and any future product candidate is susceptible to the risk of failure at any stage of product development and we may experience numerous unforeseen events during or as a result of, clinical trials that could delay or prevent clinical development, marketing approval or commercialization of Haduvio or any future product candidate, including:

- clinical trials may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to restructure clinical trials, conduct additional clinical and nonclinical trials or abandon product development programs;
- we may experience delays in obtaining authorization to commence a clinical trial from regulators, clinical sites and institutional review boards;
- the number of patients required for clinical trials may be larger than we anticipate;
- patient enrollment in clinical trials may be slower than we anticipate or participants may discontinue their participation in these clinical trials at a higher rate than we anticipate;
- the cost of planned clinical trials may be greater than we anticipate, such as if we are required to add additional sites, increase the target number of enrolled patients or use additional incentive strategies to address site activation and enrollment;
- our clinical trial sites may not have adequate staff and resources to support our trials on a timely basis;
- our third-party contractors, including any that may be manufacturing a product candidate or drug substance or conducting clinical trials on our behalf, may deviate from applicable trial protocols, fail to comply with regulatory requirements or fail to meet their contractual obligations to us in a timely manner or at all;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- patients who enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with applicable clinical trial protocols, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- we may have to delay, suspend or terminate clinical trials for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of a product candidate;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;

- the FDA or comparable foreign regulatory authorities may disagree with our clinical trial designs or our interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for clinical and commercial supplies;
- the supply or quality of drug substance for our product candidates or the manufactured product candidate or other materials or drug substances necessary to conduct clinical trials of the product candidate may be insufficient, inadequate or not available at an acceptable cost or we may experience interruptions in supply;
- regulation of the importation or handling of drug substance and study equipment necessary to conduct clinical trials of the product candidate may significantly differ between jurisdictions, which could cause delays or prohibit us in delivering drug substance or study equipment to clinical trial sites;
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change or the landscape of available, approved therapies could change in a manner rendering our clinical data insufficient to obtain marketing approvals; and
- the FDA or comparable foreign regulatory authorities may refuse to accept for review any NDA, MAA or other comparable foreign regulatory application that we submit for a product candidate or may conclude after review of our data that our application is insufficient to obtain marketing approval of a product candidate.

In addition to the above, the COVID-19 pandemic previously adversely affected our clinical trial operations worldwide, and other outbreaks of infectious disease could in the future adversely affect our clinical trial operations worldwide, including our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to infectious diseases. In the future, we may experience adverse impacts on our clinical trial activities, business operations, financial condition, and prospects as a result of outbreaks of infectious disease, among other factors.

If we are required to conduct additional clinical trials or other testing of Haduvio or any future product candidate beyond the trials and testing that we contemplate, we are unable to successfully and timely complete clinical trials or other testing of Haduvio or any future product candidate, the results of these trials or tests are unfavorable, uncertain or are only modestly favorable or there are unacceptable safety concerns associated with the product candidate, we may:

- incur additional unplanned costs, which may exceed the resources that we have available or are able to obtain on reasonable terms;
- experience delays in obtaining marketing approval for the applicable product candidate for several years or more, which could shorten the periods during which we may have the exclusive right to commercialize the product candidate or allow competitors to bring products to market before us;
- fail to obtain marketing approval at all;
- obtain marketing approval for indications or patient populations that are not as broad as we originally intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

Similarly, the regulatory landscape related to clinical trials in the European Union, or E.U., has been evolving. The E.U. Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the E.U. Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each Member State of the E.U., or E.U. Member State, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all Member States concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each Member State, leading to a single decision per Member State. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all Member States

concerned, and a separate assessment by each Member State with respect to specific requirements related to its own territory, including ethics rules. Each Member State's decision is communicated to the sponsor via the centralized E.U. portal. Once the CTA is approved, clinical study development may proceed. If we are not able to address these changes in existing requirements or the adoption of new requirements or policies governing clinical trials or there are difficulties with the implementation of the CTR process, our development plans may be impacted.

Our failure to successfully and timely complete clinical trials of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC or of any future product candidate and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any such product candidates would significantly harm our business and could result in the loss or impairment of our ability to generate revenues and effectuate our business strategy.

Our clinical trials may fail to demonstrate adequately the safety and efficacy of Haduvio or any future product candidates, which would likely prevent or delay regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of Haduvio or any future product candidate we must demonstrate through lengthy, complex and expensive clinical trials that the product candidate is both safe and effective for use in the target indication. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. It is possible that even if Haduvio or any future product candidate has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of Haduvio or any future product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of, or intolerability caused by, Haduvio or any future product candidate or mistakenly believe that Haduvio or any future product candidate is toxic or not well tolerated when that is not the case after the clinical evaluation is completed. Many pharmaceutical and biotechnology companies have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face setbacks as we continue our clinical development of Haduvio and develop any other product candidates. It is also possible that any of our development programs could be placed on full or partial clinical hold by regulatory authorities at any point, which would delay and possibly prevent further development of those programs.

In addition, even if the clinical trials we plan are successfully completed and Haduvio or any future product candidate achieves its specified endpoints in such trials, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we are able to submit product candidates for marketing approval.

Use of patient-reported outcome assessments, or PROs, in our clinical trials and high placebo response rates may delay or impair the development of Haduvio or adversely impact our clinical trials.

Although the primary endpoint in our current and planned clinical trials of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC will be measured using an objective cough monitor, we have PRO instruments as secondary endpoints, including the key secondary endpoint. There is currently no validated PRO instrument that has been accepted for chronic cough indications.

PROs have an important role in the development and regulatory approval of treatments for cough. However, PROs involve patients' subjective assessments of efficacy, and this subjectivity can increase the uncertainty of clinical trial outcomes assessing cough. Such assessments can be influenced by a number of factors and can vary widely from day to day for any particular patient and from patient to patient and site to site within a clinical trial, leading to high variability in PRO measurements.

In addition, PROs have historically been observed to have high placebo group response rates. We observed this in some of our clinical trials of Haduvio. The variability of PRO measures may be greater than other measures used for clinical trial assessments, and that variability can complicate clinical trial design, adversely impact the ability of a trial to show a statistically significant improvement and generally adversely impact a clinical development program by introducing additional uncertainties.

The variability of PRO measures and related high placebo response rates have adversely impacted clinical results of other therapies being tested and could adversely impact our clinical development of Haduvio. The FDA could also require changes in the PROs we are currently using or indicate that the PROs we are using are insufficient for demonstrating efficacy, potentially delaying clinical development of Haduvio, increasing our costs and making additional clinical trials necessary.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for Haduvio or any future product candidate if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of our clinical trials and is affected by many factors, including:

- the size and nature of the eligible patient population;
- the severity of the disease under investigation;
- the proximity of eligible patients to clinical sites;
- patient referral practices of physicians;
- the eligibility criteria for the clinical trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications under investigation.

In particular, the successful completion of our clinical development program for Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC is dependent upon our ability to enroll a sufficient number of patients with these severe conditions. We have experienced delays and difficulties in the enrollment of patients in certain of our clinical trials, including our Phase 2 CANAL trial, which delayed the completion of these trials.

Other companies are conducting clinical trials or have announced plans for future clinical trials that are seeking or are likely to seek to enroll patients with IPF, non-IPF ILD and patients with RCC, and patients are often only able to enroll in a single trial at a time. No therapies have been approved for the treatment of chronic cough in patients with IPF or non-IPF ILD and no therapies have been approved in the U.S. for the treatment of patients with RCC. However, patients with these conditions, as well as their physicians, may be reluctant to forgo, discontinue or otherwise alter their use of the therapeutic approaches they currently use in order to participate in our clinical trials.

Any inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for Haduvio or any future product candidate, delay or halt the development of and approval processes for such product candidate and jeopardize our ability to commence sales of and generate revenues from such product candidate, any of which could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

Adverse events or undesirable side effects caused by, or other unexpected properties of, Haduvio or any future product candidate may be identified during development and could delay or prevent the marketing approval or limit the use of Haduvio or any future product candidate.

Adverse events or undesirable side effects caused by or other unexpected properties of, Haduvio or any future product candidate could cause us, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of such product candidate and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. We cannot be certain that serious adverse events will not occur in future clinical trials, which could cause the FDA or comparable foreign regulatory authorities to interrupt, delay or halt clinical trials of such product candidate, approve a more restrictive label than we desire or delay or deny regulatory approval.

In addition, Haduvio, as a mixed agonist antagonist, may be susceptible to side effects associated with drugs having either of those mechanisms of action. Kappa-opioid receptor agonists have been associated with poorly tolerated psychiatric side effects, such as feelings of emotional and mental discomfort or dysphoria and hallucinations, at high doses. While we believe that the mixed kappa-opioid receptor agonist and mu-opioid receptor antagonist mechanism of action of nalbuphine reduces the likelihood of such psychiatric side effects, we have observed mild psychiatric side effects, including a few reported cases of mild euphoria, somnolence and feeling relaxed or feeling "high," in clinical trials of Haduvio to date. Mu-opioid receptor antagonists have the potential to precipitate withdrawal effects in patients who are currently on chronic doses of mu-agonist opiates. We cannot be certain that any of these side effects often associated with opioids, or other side effects, will not be observed or observed at more severe levels in the future or that the FDA will not require additional trials or impose more severe labeling restrictions due to these side effects or other concerns. Such drug-related side effects could also affect patient recruitment or the ability of enrolled patients to complete a trial or result in potential product liability claims.

In our Phase 2b CORAL trial of Haduvio for the treatment of IPF-related chronic cough, the most frequently reported treatment emergent adverse events associated with Haduvio were nausea, vomiting, constipation, dizziness, headache, fatigue, somnolence, and dry mouth. In our Phase 2a RIVER trial of Haduvio for the treatment of RCC, the most frequently

reported treatment emergent adverse events associated with Haduvio were constipation, nausea, somnolence, headache, dizziness, and fatigue.

If Haduvio or any future product candidate is associated with adverse events or undesirable side effects or demonstrates unexpected properties, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that have initially shown promise in clinical or earlier stage testing were later discovered to cause undesirable or unexpected side effects or raised other safety issues that delayed or prevented further development of the compound.

The drug label for nalbuphine, the active ingredient in Haduvio, carries an opioid class label warning for serious, life-threatening or fatal respiratory depression and Haduvio, if approved for marketing in any indication, will likely carry a similar opioid class label.

Mu-opioid receptor agonists as a class are associated with respiratory depression. The drug label for the currently marketed parenterally administered formulation of nalbuphine, the active ingredient in Haduvio, carries an opioid class label warning for serious, life-threatening or fatal respiratory depression and Haduvio, if approved for marketing in any indication, will likely carry a similar opioid class label. We are conducting our Phase 1 TIDAL study to evaluate the effect of Haduvio on respiratory function and safety in patients with IPF of varying disease severity. We cannot be certain that respiratory depression will not be observed or that the FDA will not require additional trials or impose more severe labeling restrictions related to respiratory depression. If there is a safety signal in the Phase 1 study, it could affect our ability to conduct a trial in this patient population.

Many currently approved mu-opioid receptor agonist products are subject to restrictive marketing and distribution regulations which, if applied to Haduvio, could potentially restrict its use and harm our ability to generate profits.

Many currently approved mu-opioid receptor agonists require a Risk Evaluation and Mitigation Strategy, or REMS, as part of their approval by the FDA. REMS programs may require medication guides for patients, special communication plans to healthcare professionals or elements to assure safe use, such as restricted distribution methods, patient registries and/or other risk minimization tools. We cannot predict whether a REMS program would be required as part of FDA approval of Haduvio and, if required, what requirements it might entail. Any limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensation of Haduvio, if approved. If a REMS program is required, depending on the extent of the REMS requirements, the program might significantly increase our costs to commercialize Haduvio. Furthermore, risks of Haduvio that are not adequately addressed through a proposed REMS program for Haduvio may also prevent or delay any approval for commercialization.

In addition, the parenteral formulation of nalbuphine is currently not scheduled as a controlled substance under the federal Controlled Substances Act of 1970 or the regulations of the U.S. Drug Enforcement Agency, or the DEA, in the U.S. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the U.S. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and carrying the greater level of regulatory control and Schedule V substances considered to present the lowest relative risk of abuse among such substances and, accordingly, the lowest level of regulatory control. Various states also independently regulate controlled substances. Though state-controlled substance laws often mirror federal law, because the states are separate jurisdictions, they may separately regulate drugs as well. While some states automatically classify a drug when the DEA does so, in other states there must be rulemaking or a legislative action. Regulatory authorities in foreign jurisdictions may also determine to classify Haduvio as a controlled substance under different, but potentially no less burdensome, regulations. In our HAP trial, we compared Haduvio with butorphanol, which is currently classified as a Schedule IV substance. Nalbuphine has been available for decades and was regularly kept unscheduled by the DEA. In addition, Haduvio was less likable than butorphanol in the HAP study and the DEA will evaluate the HAP results together with other elements of the 8-factor plan required to determine scheduling. However, it is possible that the DEA could determine that Haduvio, which is an oral, extended-release formulation, should be classified as a Schedule V or Schedule IV substance.

If Haduvio is classified as a controlled substance, the level of regulation would depend on how it is scheduled and we and our suppliers, manufacturers, contractors, distributors and any future customers would be required to obtain and maintain any applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with any applicable state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation, exportation and distribution of controlled substances. If Haduvio is classified as a controlled substance, there is a risk that it could limit our ability to produce and distribute Haduvio in the volume needed to meet potential commercial demand.

Regulations associated with controlled substances govern manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, record keeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs and the expense associated with development and commercialization of product candidates, including controlled substances. The DEA and some states conduct periodic inspections of registered establishments that handle

controlled substances. If Haduvio is classified as a controlled substance, failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing Haduvio and subject us to enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In some circumstances, violations could lead to criminal proceedings. Because of the restrictive nature of these regulations, if Haduvio is classified as a controlled substance, depending on how it is scheduled, its commercial prospects could be limited.

Results of preclinical studies and clinical trials may not be predictive of results of later clinical trials.

The outcome of preclinical studies and clinical trials may not be predictive of the success of later clinical trials and preliminary or interim results of clinical trials do not necessarily predict final results. For instance, Haduvio or any future product candidate may fail to show the desired safety and efficacy in patients with chronic cough with IPF, non-IPF ILD, and RCC in future clinical trials despite demonstrating positive results in earlier clinical trials. The results of our Phase 2b CORAL trial for the treatment of IPF-related chronic cough or our Phase 2a RIVER trial for the treatment of RCC may not be predictive of the results of future trials of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, or RCC. Many pharmaceutical and biotechnology companies have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier stages of clinical development and we could face similar setbacks. Similarly, the design of a clinical trial can determine whether its results will support marketing approval of a product and adjustments in the design of a clinical trial may not be possible once the clinical trial has commenced.

We have limited experience as a company in designing pivotal clinical trials and flaws in the design of a clinical trial could result in significant delays in completing the clinical trial or may require us to abandon the clinical trial altogether or conduct additional clinical trials. Preclinical and clinical data are also often susceptible to varying interpretations and analyses. Many pharmaceutical and biotechnology companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for those product candidates. Even if we believe that the results of clinical trials for Haduvio or any future product candidate warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of the product candidate.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of patient populations, changes in and adherence to dosing regimens and other clinical trial protocols, as well as the rate of discontinuation among clinical trial participants. If we fail to demonstrate positive results in clinical trials of Haduvio or any future product candidate, the development timeline and regulatory approval and commercialization prospects for those product candidates and, correspondingly, our business and financial prospects would be negatively impacted.

Even if Haduvio or any future product candidate receives marketing approval, we or others may later discover that the product is less effective than previously believed or that it causes undesirable side effects that were not previously identified, which could compromise our ability to market the product.

Clinical trials are conducted in carefully defined sets of patients who have agreed to participate in clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we or others discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of or the manufacturing processes for, the product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and

- our reputation may suffer.

Any of these events could harm our business and operations and could negatively impact our stock price.

Even if Haduvio or any future product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case the market opportunity for Haduvio may be smaller than we estimate and we may not generate significant revenues or become profitable.

We have never commercialized a product and even if Haduvio or any future product candidate is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market and may be reluctant to prescribe opioid-based therapies due to perceived risks of misuse, abuse and addiction. Further, patients often acclimate to their current therapies and do not want to switch unless their physicians recommend changing products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third-party payors on the benefits of Haduvio or any future product candidate may require significant resources and may not be successful. If Haduvio or any future product candidate is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of Haduvio or any future product candidate, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential and perceived advantages of the product compared to other therapies;
- the prevalence and severity of any side effects;
- the potential that the DEA could determine that Haduvio should be classified as a controlled substance;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability to offer the product for sale at competitive prices;
- the product's convenience and ease of administration;
- the willingness of the target patient population to try and of physicians to prescribe the product;
- limitations or warnings, including distribution or use restrictions contained in the product's approved labeling;
- the strength of sales, marketing and distribution support for the product;
- the approval of other new products for the same indications;
- the timing of market introduction of the product as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- potential product liability claims;
- changes in the standard of care for the targeted indications for the product; and
- availability and amount of coverage and reimbursement from government payors, managed care plans and other third-party payors.

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 intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. For example, we currently intend to focus our resources on the development of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC. However, the development of Haduvio for these indications may ultimately prove to be unsuccessful or less successful than another product candidate or other indications that we might have chosen to pursue with our limited resources.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future development programs and product candidates for specific indications may not yield any commercially viable product candidates. 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 the product candidate.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing Haduvio or any future product candidates if and when they are approved.

We do not currently have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. If Haduvio were to receive marketing approval from the FDA for IPF-related chronic cough or non-IPF ILD-related chronic cough, we would plan to market and commercialize Haduvio in the U.S. with our own focused, specialty sales force and target pulmonologists who specialize in treating IPF and non-IPF ILD patients, as well as ILD centers of excellence, as applicable. If Haduvio were to receive marketing approval from the FDA for RCC, we would plan to market and commercialize Haduvio in the U.S. with our own focused sales force and target pulmonologists and other specialists, such as allergists, who treat RCC patients who have failed other therapies for chronic cough. We also expect to utilize a variety of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize Haduvio outside the U.S.

We plan to build focused capabilities to commercialize development programs for certain indications where we believe that medical specialists are sufficiently concentrated to allow us to effectively promote products with a specialty sales team. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. We could prematurely or unnecessarily incur commercialization costs if the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason. This may be costly, and our business and financial prospects could be significantly affected if we could not retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the U.S. that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain an adequate sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

In certain indications and markets, we may seek to enter into collaborations that we believe may contribute to our ability to advance development and ultimately commercialize Haduvio or any future product candidate. We may also seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be substantially lower than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any product candidate that receives marketing approval.

We face competition, which may result in others developing or commercializing products before or more successfully than we do.

The development and commercialization of new products is highly competitive. We expect that we will face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to Haduvio or any future product candidate that we may seek to develop or commercialize. Our competitors may succeed in developing, acquiring or licensing technologies and products that are more effective, have fewer or more tolerable side effects or are more convenient or less costly than Haduvio or any future product candidate we may develop, which could render any product candidates obsolete and noncompetitive. Our competitors also may obtain FDA or other marketing approval for their products before we are able to obtain approval for ours, which could result in competitors establishing a strong market position before we are able to enter the applicable market.

If Haduvio is approved for the treatment of chronic cough in patients with IPF and non-IPF ILD, we expect that it may compete with product candidates that may be developed for the treatment of chronic cough in patients with IPF or ILD. Development of BI 1839100, a TRPA1 antagonist by Boehringer Ingelheim for the treatment of IPF-related chronic cough and progressive pulmonary fibrosis, was terminated in September 2025. It is possible that product candidates

currently in development for the treatment of fibrosis in patients with IPF and ILD could, if approved, reduce the need for therapies to treat chronic cough in patients with IPF and non-IPF ILD. We expect that Haduvio might also compete with other product candidates currently in development, for the treatment of patients with RCC that might be used off-label to treat IPF-related chronic cough.

If Haduvio is approved for the treatment of patients with RCC, we expect that it may compete with product candidates in clinical development for the treatment of patients with RCC such as camlipixant, a P2X3 antagonist, which is being developed by GSK plc. Gefapixant, a P2X3 antagonist, which was developed by Merck & Co., Inc., or Merck, is approved for refractory or unexplained chronic cough in Japan, the United Kingdom, Switzerland, and the E.U. The application filed with the FDA was withdrawn and Merck indicated it does not plan to refile. Other product candidates that are currently in development for the treatment of patients with RCC include taplucainium (formerly NTX-1175), a charged sodium channel blocker, which is being developed by Nocion Therapeutics Inc.

We also expect that Haduvio would compete with a number of therapeutics that are not specifically approved to treat chronic cough including benzonatate, opioids, corticosteroids, proton-pump inhibitors, and neuromodulators.

Many of our competitors and potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and commercializing approved products than we do. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials.

Even if we are able to commercialize a product candidate, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business.

The commercial success of any product we develop will depend substantially, both in the U.S. and other countries, on the extent to which the costs of the product will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize that product. Even if coverage is provided for the product, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investments. In the U.S., no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of any product we commercialize to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we may obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if those product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability to commercialize any product candidate will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the U.S. and other countries. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell products profitably. These payors may not view our products, if any, as cost-effective and coverage and reimbursement may not be available to our customers or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us to decrease the price we might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

The commercial potential of any products we are able to commercialize depends in part on reimbursement by government health administration authorities, private health insurers and other organizations. If we are unable to obtain

coverage or reimbursement for those products at the levels anticipated, our financial condition could be harmed. Additionally, if new compounds currently in development by potential competitors obtain marketing approval, there may be downward pressure on reimbursement levels for therapies in our target indications, which could have a negative impact on our ability to achieve and maintain profitability.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new therapies and are challenging the prices charged for new products. We cannot be sure that coverage will be available for any product candidate that we commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop or in-license.

We face an inherent risk of product liability claims as a result of our clinical trials, despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we commercialize any product that we may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any products that we may develop or in-license;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend resulting litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we maintain product and clinical trial liability insurance of at least $10.0 million in the aggregate, our insurance coverage may not fully cover potential liabilities that we may incur. The cost of any product or clinical trial liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if we commercialize any product that receives marketing approval. If we are unable to maintain sufficient insurance coverage at an acceptable cost or otherwise protect against potential clinical trial liability or product liability claims, the development and commercial production and sale of Haduvio or any future product candidate could be prevented or inhibited, which could harm our business, financial condition, results of operations and prospects.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials. If they do not perform satisfactorily, our business could be harmed.

We do not independently conduct clinical trials of our product candidate. We rely on and expect to continue to rely on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials of Haduvio and any future product candidate that we may develop. These third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural

transition period when a new CRO begins work on a clinical trial. As a result, delays would likely occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Further, although our reliance on these third parties for clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the approved protocol, as well as applicable legal, regulatory and scientific standards. Moreover, the FDA and/or other regulatory authorities require us to comply with standards, commonly referred to as current Good Clinical Practices, or cGCPs, for conducting, recording and reporting the results of 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. The FDA and other regulatory authorities enforce these cGCPs through periodic inspections of clinical trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA and other regulatory authorities may require us to perform additional clinical trials before approving the applicable product candidate, which would delay the marketing approval process. We cannot be certain that, upon inspection, the FDA and other regulatory authorities will determine that any of our clinical trials complies with cGCPs. Similar regulatory requirements apply outside the U.S., including the International Council for Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use, or ICH. We are also required to register our clinical trials and post the results of our completed clinical trials on a government-sponsored database, ClinicalTrials.gov, and other registries within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees and except for remedies available to us under our agreements with our contractors, we cannot control whether they devote sufficient time, skill and resources to our ongoing development programs. Additionally, these third parties may have relationships with other commercial entities, including potential competitors, for which they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. Third parties may not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our protocols. For example, we have terminated clinical investigators from our previous clinical trials due to suspected non-compliance with regulatory requirements. If the third parties on which we rely do not carry out their duties, meet their deadlines or comply with regulatory requirements, we will not be able to, or may be delayed in our efforts to, successfully commercialize Haduvio or any future product candidate. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and we may not be able to generate revenues or become profitable.

We contract with third parties for the manufacture, storage, packaging and distribution of Haduvio and other drug product for clinical trials, including a single supplier for the active ingredient in Haduvio and expect to continue to rely on third parties for these services in connection with our future development and commercialization efforts for Haduvio and any future product candidates.

We currently have no manufacturing facilities and a relatively small number of personnel with sufficient experience to oversee the manufacturing process. We rely and plan to continue to rely, on contract manufacturers and other third-party contractors to manufacture, store, package and distribute both drug substance and drug product for our clinical trials. If any of our product candidates receive regulatory approval, we plan to continue to rely upon contract manufacturers and, potentially, collaboration partners, to manufacture commercial quantities of such products. We may be unable to establish any further agreements with contract manufacturers or any other third-party contractors or may fail to do so on acceptable terms or when needed. Even if we are able to establish agreements with such third-party contractors, reliance on third-party contractors entails additional risks, including:

- manufacturing delays if our third-party contractors experience supply chain-related delays, prioritize the supply of other companies' products over Haduvio or any other drug product needed for our clinical trials or any future product candidates, or otherwise fail to satisfactorily perform according to the terms of the agreements between us and them or if unforeseen events in the manufacturing process arise;
- the possible termination or nonrenewal of agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the possible breach by third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and

- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have long-term supply agreements with any of our contract manufacturers. If any of our existing manufacturers should become unavailable to us for any reason or fail to supply us with the ordered quantities, we may incur delays in identifying or qualifying replacement manufacturers or in obtaining replacement supply. Any performance failure on the part of our contract manufacturers or the other third-party contractors that we use to store and distribute drug substance and drug product could be disruptive to our operations and delay clinical development or marketing approval of Haduvio or any future product candidates of ours or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

We rely, and plan to continue to rely, on a single supplier, Par Health, which was spun off as an independent company after the merger between Mallinckrodt plc and Endo, Inc., for nalbuphine hydrochloride drug substance. We do not have agreements in place with Par Health that guarantee supply quantities or pricing. Any significant delay in acquisition, increase in cost or decrease in availability of nalbuphine hydrochloride drug substance could considerably delay the manufacture of Haduvio, which could adversely impact the timing of our current and planned clinical trials and potential regulatory approval and commercialization of Haduvio. Although we are evaluating alternate sources of supply that could satisfy our clinical and commercial requirements for nalbuphine drug substance, we have not qualified any alternate sources and cannot assure you that we would be able to establish relationships with any such sources in a timely fashion, on commercially reasonable terms or at all.

If Haduvio or any future product candidates are approved by any regulatory agency, we will need to enter into agreements with third-party contract manufacturers for the commercial production and distribution of those products. In addition, we may face competition for access to manufacturing facilities as there may be a limited number of contract manufacturers operating under cGMPs that are able to manufacture any such product. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, in a timely manner or at all, which could delay our commercialization efforts.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the U.S., such as the ICH. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA and before potential approval of the applicable product candidate. Similar regulations apply to manufacturers of product candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of Haduvio. We expect that we would be similarly dependent on third-party manufacturers of Haduvio at commercial scale or any future product candidate. If our manufacturers cannot successfully manufacture drug substance or drug product that conforms to our specifications or the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate and any future commercialization efforts.

In addition, our manufacturers are subject to ongoing periodic inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements both prior to and following the receipt of marketing approval for any product candidate. Some of these inspections may be unannounced. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, seizures or recalls of product candidates, interruptions in supply and criminal prosecutions, any of which could significantly impact the available supplies of Haduvio or any future product candidate and harm our business, financial condition and results of operations.

Our current and anticipated future dependence upon others for the manufacture of Haduvio, any other drug product needed for our clinical trials or any future product candidate may harm our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We may seek to establish collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

While we have not entered into any collaborations to date, we may seek to establish one or more collaborations for the development and commercialization of Haduvio or any future product candidate. Potential collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and academic research institutions. We also expect to utilize a variety of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize Haduvio outside the U.S.

We face significant competition in seeking appropriate collaborators. There have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. 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 potential differentiation of our

product candidates from competing product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and existing or potential competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than a collaboration with us. Any collaboration agreements that we enter into in the future may also contain restrictions on our ability to enter into other potential collaborations or to develop specified product candidates. We may not be able to negotiate 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 the potential commercialization of such product candidate, 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.

If we establish one or more collaborations, all the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K would also apply to the activities of any such future collaborators.

If we enter into collaborations with third parties for the development or commercialization of Haduvio or any future product candidate, our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.

We may seek to enter into collaborations with third parties for the development or commercialization of Haduvio or any future product candidate. If we enter into any such collaborations, we would have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of any such product candidates. Our ability to generate revenues from these arrangements would depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving a product candidate would pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of the product candidates under the collaboration or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition of the collaborator, that divert resources or create competing priorities;
- collaborators may be involved in a business combination and could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed by us;
- 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 the product candidates under the collaboration;
- 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;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- 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 potential litigation;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability or misappropriate our intellectual property or other proprietary information;
- collaborators may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements;
- disputes may arise between the collaborators and us regarding ownership of or other rights in the intellectual property generated in the course of the collaborations; and
- 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.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

Risks Related to Our Intellectual Property

If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are critical to our business or owe damages to the licensor of such intellectual property.

We are party to an exclusive license agreement with Keenova under which we have licensed certain patent rights and know-how to develop and commercialize products incorporating nalbuphine hydrochloride in any formulation, including an extended-release formulation such as Haduvio. We may in the future seek additional licenses from others to develop and commercialize additional product candidates or technologies. These licenses may not provide exclusive rights to use the relevant intellectual property in all desired fields of use and in all territories in which we may wish to develop or commercialize product candidates in the future. It is also possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all.

Our existing license agreements impose and we expect that future license agreements will impose, various diligence, development and commercialization, milestone payment, royalty and other obligations on us. If we fail to comply with our material obligations under these agreements or if we are subject to a bankruptcy event, the licensor may have the right to terminate the license or convert the license to a non-exclusive license, in which event we may be required to negotiate a new or reinstated license with less favorable terms or would not be able to exclusively market or market at all, products covered by the license. Any termination of our license agreements could have a material adverse impact on our business.

Disputes may also arise regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our activities or product candidates may infringe the intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under any collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship or ownership of inventions and know-how resulting from joint creation or use of intellectual property by licensors and us; and
- the priority of invention of any patented technology.

If disputes over intellectual property that we license prevent or impair our ability to maintain those license arrangements on acceptable terms or at all, we may be unable to successfully develop and commercialize any affected product candidates.

If we are unable to obtain and maintain sufficient patent protection for Haduvio or any future product candidate and the disease indications for which we are developing or may in the future develop, Haduvio or if the scope of the patent protection is not sufficiently broad, competitors could develop and commercialize products similar or identical to such product candidate and our ability to successfully commercialize such product candidate may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the U.S. and other countries with respect to Haduvio and any future product candidates and their use for indications for which we are developing or may develop, them in the future. If we do not adequately protect our intellectual property rights, competitors may erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we have licensed exclusive rights under patents, prosecuted additional patents and filed patent applications in the U.S. and other countries related to methods of use and formulations of Haduvio.

The patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner or at all.

Agreements through which we license patent rights may not give us control over patent prosecution or maintenance, so that we may not be able to control which claims or arguments are presented and may not be able to secure, maintain or successfully enforce necessary or desirable patent protection from those patent rights. We may not have primary control over patent prosecution and maintenance for certain of the patents and patent applications we may license and therefore cannot guarantee that these patents and applications will be prosecuted in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors or other responsible third parties have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope or patent term adjustments, or PTA. If we, our licensors or any future partners, collaborators, licensors or licensees fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors or any future partners, collaborators, licensors or licensees disagree or do not fully cooperate with us as to the prosecution, maintenance or enforcement of any patent rights, those patent rights could be compromised. We, our licensors and any future partners, collaborators, licensors and licensees may also fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the U.S. or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which in recent years have been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the U.S., the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications or that we were the first to file for patent protection of such inventions. Similarly, we cannot be certain that parties from whom we do or may license or purchase patent rights were the first to make relevant claimed inventions or were the first to file for patent protection for them. If third parties have filed patent applications on inventions claimed in our patents or applications on or before March 15, 2013, an interference proceeding in the U.S. can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding in the U.S. can be initiated by such third parties to determine whether our invention was derived from theirs.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the U.S. and other countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it may be used to invalidate a patent or may prevent a patent from issuing from a pending patent application. For example, such patent filings may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or to other patent offices around the world. Alternatively or additionally, we may become involved in post-grant review procedures, oppositions, derivation proceedings, reexaminations, inter partes review or interference proceedings, in the U.S. or other countries, challenging patents or patent applications in which we have rights, including patents on which we rely to protect our business. An adverse determination in any such challenge may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical products or product candidates or limit the duration of the patent protection of Haduvio or any future product candidates of ours. In addition, 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. Furthermore, 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. As a result, the inventorship or ownership of our intellectual property may be challenged in the future.

Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the U.S. For example, patent laws in various

jurisdictions, including significant commercial markets such as Europe, restrict the patentability of methods of treatment of the human body more than U.S. law does.

Issued patents that we have, may obtain or license may not provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with any products that we are able to develop and commercialize. Alternatively, our competitors may seek to market generic versions of any approved products by submitting abbreviated new drug applications, or ANDAs, to the FDA claiming that patents owned or licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable or find that competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

Pursuant to the terms of our license agreements with third parties, we have the right, but not the obligation, to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents. Even if we pursue such enforcement or defense, we will require the cooperation of our licensors and cannot guarantee that we would receive it and on what terms. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. If we cannot obtain patent protection or enforce existing or future patents against third parties, our competitive position and our financial condition could suffer.

If we are unable to protect the confidentiality of our trade secrets, the value of our products could be negatively impacted and our business would be harmed.

In addition to the protection afforded by patents, we also rely on trade secret protection for certain aspects of our intellectual property. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, advisors, contract manufacturers, suppliers and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming and the outcome is unpredictable. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third-party or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

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

Our competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may 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. In any patent infringement proceeding, there is a risk that a court will decide that one of our patents 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 one or more of our patents could limit our ability to assert those 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. 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 adversely affect 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 and require substantial resources. 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.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time-consuming, its outcome would be uncertain and it could prevent or delay us from developing or commercializing Haduvio or any future product candidate.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell products without infringing the intellectual property and other proprietary rights of third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds and methods of use for the treatment of the disease indications for which we are developing or may in the future develop, Haduvio or any future product candidate. If any third-party patents or patent applications are found to cover Haduvio or any future product candidate or their methods of use, we may not be free to manufacture or market the product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries and we may become party to or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our Haduvio or any future product candidates, including interference proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to Haduvio or any future product candidate. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that Haduvio or any future product candidate may be accused of infringing. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the relevant patent claims are invalid or unenforceable and we may not be able to do this. Proving invalidity is difficult. For example, in the U.S., proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third-party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third-party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or product. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us; alternatively or additionally, it could include terms that impede or eliminate our ability to compete successfully in the commercial marketplace. 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 Haduvio or any future product candidate or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

Changes to the patent law in the U.S. and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time-consuming and inherently uncertain. Recent patent reform legislation in the U.S., including the Leahy-Smith America Invents Act, or the America Invents Act, could increase those uncertainties and costs. The America Invents Act was signed into law on September 16, 2011 and many of the substantive changes became effective on March 16, 2013. The America Invents Act reformed U.S. patent law in part by changing the U.S. patent system from a "first to invent" system to a "first inventor to file" system, expanding the definition of prior art and developing a post-grant review system. This legislation changes U.S. patent law in a way that may weaken our ability to obtain patent protection in the U.S. for those applications filed after March 16, 2013.

Further, the America Invents Act created new procedures to challenge the validity of issued patents in the U.S., including post-grant review and inter partes review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with an effective filing date of March 16,

2013 or later, a petition for post-grant review can be filed by a third-party in a nine-month window from issuance of the patent. A petition for inter partes review can be filed immediately following the issuance of a patent if the patent has an effective filing date prior to March 16, 2013. A petition for inter partes review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with an effective filing date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of invalidity, whereas inter partes review proceedings can only raise grounds of invalidity based on lack of novelty or obviousness using published prior art and patents. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third-party to have a U.S. patent invalidated in a USPTO post-grant review or inter partes review proceeding than invalidated in a litigation in a U.S. federal court. If any of our patents are challenged by a third-party in such a USPTO proceeding, there is no guarantee that we or our licensors or collaborators will be successful in defending the patent, which would result in a loss of the challenged patent right to us.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. For example, in Amgen Inc. v. Sanofi, the U.S. Supreme Court held that claims with functional language may pose high hurdles in fulfilling the enablement requirement. Additionally, there have been recent proposals for additional changes to the patent laws of the U.S. and other countries that, if adopted, could impact our ability to enforce our patents. 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 future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, 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, recent decisions, including by the U.S. Court of Appeals for the Federal Circuit, raise questions regarding the award of PTA for patents in families where related patents have issued without PTA. Thus, it cannot be said with certainty how PTA will/will not be viewed in the future and whether patent expiration dates may be impacted.

Further, in Europe, a new unitary patent system took effect June 1, 2023, which significantly impacts European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court, or the UPC. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long-term effects of any potential changes.

We may not be able to enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive and our intellectual property rights in some countries outside the U.S. are less extensive than those in the U.S. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products. Our competitors may export otherwise infringing products to territories where we have no patent protection or where we may obtain patent protection, but where patent enforcement is not as strong as that in the U.S. and our issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the U.S. and Europe do not afford intellectual property protection to the same extent as the laws of the U.S. and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the U.S. and Europe.

In addition, geopolitical actions and dynamics, including the imposition of tariffs and responses to tariffs, may impact our ability to obtain and enforce patents or may increase the costs surrounding the prosecution or maintenance of our patent applications or maintenance, enforcement or defense of our issued patents in particular jurisdictions. If we are unable to obtain and enforce patents as needed in particular markets, our ability to exclude competitors in those markets may be reduced.

Agreements through which we license patent rights may not give us sufficient rights to permit us to pursue enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents (or control of enforcement or defense) of such patent rights in all relevant jurisdictions as requirements may vary.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Moreover, such proceedings 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. Furthermore, while we intend to protect our intellectual property rights in major markets for any products that we are able to develop, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market any such products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property or claiming ownership of what we regard as our own intellectual property.

Many of our employees and our licensors' employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including some which may be competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure, non-competition and non-solicitation agreements or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third-party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third-party and we could be required to obtain a license from such third-party to commercialize Haduvio or any future product candidate. Such a license may not be available on commercially reasonable terms or at all. 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 we typically require our employees, consultants and contractors who may be involved in the 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 develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

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.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside of the U.S. in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. While an inadvertent 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 non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, the 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 fail to maintain the patents and patent applications covering Haduvio or any future product candidate, our competitive position would be adversely affected.

If we are unable to obtain licenses from third parties on commercially reasonable terms, our business could be harmed.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize Haduvio or any future product candidate, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation in connection with any sales we make. Even if we are able to obtain a license, it may be non-exclusive, which could enable our competitors to obtain access to the same technologies licensed to us.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

If the FDA does not conclude that Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, or RCC, or any other development program satisfies the requirements under Section 505(b)(2) of the FDCA or if the requirements for such programs are not as we expect, the approval pathway for these programs will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated and in any case may not be successful.

We intend to pursue FDA approval of Haduvio for the treatment of IPF-related chronic cough under the FDA's Section 505(b)(2) regulatory pathway. The Drug Price Competition and Patent Term Restoration Act of 1984 or the Hatch-Waxman Act, added Section 505(b)(2) to the FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies that were not conducted by or for the sponsor and for which the sponsor has not received a right of reference, which could expedite the development program for Haduvio by potentially decreasing the amount of preclinical and clinical data that we would need to generate in order to obtain FDA approval. However, while we believe that Haduvio is a reformulation of an existing drug and, therefore, its active moiety will not be treated as a new chemical entity, or NCE, the submission of an NDA under the Section 505(b)(2) regulatory pathway does not preclude the FDA from determining that Haduvio contains an active moiety that is an NCE and, therefore, is not eligible for review under such regulatory pathway.

If the FDA does not allow us to pursue the Section 505(b)(2) or similar regulatory pathway as anticipated, we may need to conduct additional preclinical experiments and clinical trials, provide additional data and information and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for Haduvio for the treatment of IPF-related chronic cough and any future product candidates and complications and risks associated with these product candidates, would likely increase significantly. Moreover, our inability to pursue the Section 505(b)(2) regulatory pathway could result in new competitive products reaching the market more quickly than our product candidates, which would likely harm our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, our product candidates may not receive the requisite approvals for commercialization.

In addition, notwithstanding the approval of a number of products by the FDA under Section 505(b)(2) over the last few years, certain competitors and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, the FDA may be required to change its 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2). In addition, the pharmaceutical industry is highly competitive and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of our potential future NDAs for up to 30 months depending on the outcome of any litigation. It is not uncommon for a manufacturer of an approved product to file a citizen petition with the FDA seeking to delay approval of or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay or even prevent the approval of the new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if we are able to utilize the Section 505(b)(2) regulatory pathway for our product candidates, there is no guarantee this would ultimately lead to faster product development or earlier approval.

Moreover, even if our product candidates are approved under the Section 505(b)(2) pathway, the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

Even if we complete the necessary nonclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of Haduvio or any future product candidate on a timely basis or at all. As a result, we cannot predict when or if and in which territories, we will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. We are not permitted to market Haduvio or any other product candidate in the U.S. until we receive approval of an NDA from the FDA or in other countries until we receive marketing approval from the applicable regulatory authorities outside the U.S. We have not submitted an application for or received marketing approval for any product candidate in the U.S. or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the U.S. and other countries, is lengthy, expensive and uncertain. It may take 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. 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 relevant regulatory authorities. The FDA or other regulatory authorities may determine that Haduvio or any future product candidate is not safe and effective, only moderately effective or has undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Moreover, under certain circumstances, we may be required to report some of our financial relationships with clinical investigators to the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. 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. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

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

Any delay in obtaining or failure to obtain required approvals and clearances could negatively impact our ability to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

We have conducted, are conducting and intend in the future to conduct clinical trials for Haduvio and may conduct clinical trials for any future product candidates, at sites outside the U.S. The FDA may not accept data from trials conducted in such locations and the conduct of trials outside the U.S. could subject us to additional delays and expense.

We have conducted, are conducting and intend in the future to conduct clinical trials for Haduvio, and may conduct clinical trials for any future product candidates, at trial sites that are located outside the U.S. Although the FDA may accept data from clinical trials conducted outside the U.S., acceptance of these data is subject to certain conditions imposed by the FDA.

The FDA will not accept foreign study data as support for an application for marketing approval unless the study satisfies certain conditions. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with cGCPs. The FDA must be able to validate the data from the trial, including, if necessary, through an onsite inspection. The trial population must also have a similar profile to the U.S. population and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, except to the extent the disease being studied does not typically occur in the U.S. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the U.S. If the FDA does not accept the data from any trial that we conduct outside the U.S., it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of Haduvio or the applicable future product candidate.

In addition, the conduct of clinical trials outside the U.S. could have a significant adverse impact on us. Risks inherent in conducting international clinical trials include:

- clinical practice patterns and standards of care that vary widely among countries;
- non-U.S. regulatory authority requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple non-U.S. regulatory authority schema;
- foreign exchange rate fluctuations; and
- diminished protection of intellectual property in some countries.

Failure to obtain marketing approval in foreign jurisdictions would prevent Haduvio or any future product candidate from being marketed in other countries. Any marketing approval we are granted in the U.S. would not assure marketing approval in foreign jurisdictions.

In order to market and sell products in the E.U. and other foreign jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U.S., a product must be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the U.S. on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions and approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may file for marketing approvals but not receive necessary approvals to commercialize any products in any market. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of any product candidates in any country. In addition, if we fail to obtain the non-U.S. approvals required to market products outside the U.S. or if we fail to comply with applicable non-U.S. regulatory requirements, our target markets will be reduced and our ability to realize the full market potential of Haduvio or any future product candidate will be harmed and our business, financial condition, results of operations and prospects may be adversely affected.

Further, we could face heightened risks with respect to obtaining marketing authorization in the U.K. as a result of the withdrawal of the U.K. from the E.U., commonly referred to as Brexit. The U.K. is no longer part of the European Single Market and EU Customs Union. As of January 1, 2025, MHRA is responsible for approving all medicinal products destined for the U.K. market (i.e., Great Britain and Northern Ireland).

At the same time, a new international recognition procedure ("IRP") will apply, which intends to facilitate approval of pharmaceutical products in the U.K. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators ("RRs"). The RRs notably include EMA and regulators in the E.U./European Economic Area ("EEA") member states for approvals in the E.U. centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the U.K. for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the E.U. pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. On June 4, 2025, after almost two years of negotiations among the E.U. Member States, the Council of the European Union adopted its position on the proposed overhaul of the E.U. general pharmaceutical legislative framework, which is known as the new Pharma Package. Thereafter, on December 11, 2025, the European Parliament and Council reached a provisional political agreement on the legislation which is expected to be adopted by mid-2026. The revisions may have a significant impact on the pharmaceutical industry and our business. They would, among other things, set a baseline period of eight years of data exclusivity and one year of market exclusivity with possible extensions for new indications up to a maximum of eleven years total. There will likely be a transition period of 24 months, with the changes taking effect in mid-2028.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the U.S., including tariffs, trade barriers and regulatory requirements; economic weakness,

including inflation or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the U.S.

A Fast Track designation, grant of Priority Review status or Breakthrough Therapy status by the FDA or the receipt of a priority voucher from the FDA is not assured and, in any event, may not actually lead to a faster development or regulatory review or approval process and, moreover, would not assure FDA approval of Haduvio or any future product candidate.

We may be eligible for Fast Track designation, Priority Review or Breakthrough Therapy status for specific indications for the product candidates we may develop. If a product candidate is intended for the treatment of a serious or life-threatening disease or condition and the product candidate demonstrates the potential to address unmet medical needs for this disease or condition, the product candidate sponsor may apply for FDA Fast Track designation. If a product candidate offers major advances in treatment, the product candidate sponsor may apply for FDA Priority Review status. Additionally, a product candidate may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The FDA has broad discretion whether or not to grant these designations, so even if we believe a particular product candidate is eligible for such designation or status, the FDA could decide not to grant it. If we receive Fast Track designation or a different designation, such as Priority Review or Breakthrough Therapy status, for a product candidate of ours in the future, it may not result in our experiencing a faster development process, review or approval compared to conventional FDA procedures and there is no assurance that the product candidate will be approved by the FDA.

In addition, in June 2025, the FDA announced the creation of the "Commissioner's National Priority Voucher, or CNPV Program. Vouchers issued under this program can reportedly be redeemed by sponsors to shorten the review time of an NDA from approximately 10-12 months to 1-2 months. The FDA has indicated that the new CNPV process will convene experts from the FDA's offices for a team-based review rather than using the standard review system. Clinical information will be reviewed by a multidisciplinary team of physicians and scientists who will pre-review the submitted information and convene for a 1-day meeting. Vouchers under this program will reportedly be given to companies aligned with U.S. national priorities. As with the FDA's other programs for expediting review and approval of new drug products, even if we were to avail ourselves of this new program, there is no guarantee it would result in approval of our marketing applications or that such approval, if granted, would be on an expedited basis.

We may seek PRIME Designation in the E.U. for Haduvio but we might not receive such designations and, even if we do, such designations may not lead to a faster development or regulatory review or approval process.

In the E.U., we may seek PRIME designation for Haduvio in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the E.U. or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the E.U. and the sponsor intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims.

The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables a sponsor to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

Any regulatory approval to market Haduvio in the U.S. will be limited by indication. If we fail to comply or are found to be in violation of FDA regulations restricting the promotion of Haduvio for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

If our clinical trials are successful, we intend to seek approval to market Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD and RCC. If we obtain regulatory approval to market Haduvio with an indication statement for the treatment of chronic cough in patients with IPF, non-IPF ILD or RCC, we expect to be prohibited from marketing Haduvio using any promotional claims relating to treatment of cough generally. Marketing of Haduvio may also be limited by regulatory authorities based on use as a monotherapy or adjuvant, concomitant medications, severity of pruritus and other factors.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA, EMA, MHRA and other government agencies. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. While we have conducted, or may in the future conduct, clinical trials to evaluate the use of Haduvio to treat conditions other than chronic cough in patients with IPF, non-IPF ILD and RCC, Haduvio cannot be promoted for uses other than uses approved in the labeling by the FDA, EMA, MHRA or other applicable regulatory authorities. Physicians may nevertheless prescribe Haduvio off-label to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of Haduvio for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. For example, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product.

In recent years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, or the HHS, the FDA, the Federal Trade Commission, or the FTC, and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the False Claims Act, the Prescription Drug Marketing Act and anti-kickback laws and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement.

Many of these investigations originate as "*qui tam*" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim or caused a false claim to be submitted to the government for payment. The person bringing a *qui tam* suit is entitled to a share of any recovery or settlement. *Qui tam* suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a *qui tam* suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a *qui tam* suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

Any product for which we obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with any such product following approval.

Any product for which we obtain marketing approval, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market any product for an indication that is not approved, we may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with any product for which we may obtain marketing approval and its manufacturers or manufacturing processes or failure to comply with regulatory requirements, may yield various results, including:

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

Further, our ability to develop and market new drug products may be impacted by litigation challenging the FDA's approval of another company's drug product. In April 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021, were arbitrary and capricious. In June 2024, the U.S. Supreme Court reversed that decision after unanimously finding that the plaintiffs (anti-abortion doctors and organizations) did not have standing to bring this legal action against the FDA. On October 11, 2024, the Attorneys General of three states (Missouri, Idaho and Kansas) filed an amended complaint in the district court in Texas challenging FDA's actions. On January 16, 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge. Thereafter, on September 30, 2025, the district court declined to dismiss

the case and, instead, transferred it to federal district court in the Eastern District of Missouri. Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation.

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

Similar restrictions apply to the approval of our products in the E.U. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include: compliance with the E.U.'s stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the E.U. and are also subject to E.U. Member State laws. The failure to comply with these and other E.U. requirements can also lead to significant penalties and sanctions.

Disruptions at the FDA and other government agencies from funding cuts, personnel losses, regulatory reform, government shutdowns and other developments could hinder our ability to obtain guidance from the FDA regarding our clinical development program, progress development efficiently, and secure approval of our product candidates in a timely manner, which would negatively impact our business.

The FDA and comparable regulatory agencies in foreign jurisdictions, such as the EMA and Committee for Medicinal Products for Human Use, play an important role in the development of our product candidates by providing guidance on our clinical development programs and reviewing our regulatory submissions, including INDs, requests for special designations and marketing applications. If these oversight and review activities are disrupted, then correspondingly our ability to develop and secure timely approval of our product candidates could be impacted in a negative manner.

These actions and the resulting recent loss of FDA leadership and personnel could lead to disruptions and delays in FDA guidance, review and approval of our product candidate.

While the FDA's review of marketing applications and other activities for new drugs and biologics is largely funded through the user fee program established under the Prescription Drug User Fee Act, or PDUFA, it remains unclear how the administration's efforts to reduce the workforce of HHS and budget cuts will impact this program and the ability of the FDA to provide guidance and review our product candidates in a timely manner. For example, while the reduction in workforce did not reportedly specifically target FDA reviewers, many operations, administrative and policy staff that help support such reviews were affected and those losses could lead to delays in PDUFA reviews and related activities. In addition, while currently unclear, there is a risk that the reduction in workforce and budget cutbacks could threaten the integrity of the PDUFA program itself. That is because, for the FDA to obligate user fees collected under PDUFA in the first place, a certain amount of non-user fee appropriations must be spent on the process for the review of applications plus certain other costs during the same fiscal year.

There is also substantial uncertainty as to how regulatory reform measures being implemented by the Trump Administration across the government will impact the FDA and other federal agencies with jurisdiction over our activities. For example, since taking office, President Trump has issued a number of executive orders that could have a significant impact on the manner in which the FDA conducts its operations and engages in regulatory and oversight activities. If these or other orders or executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Similarly, actions by the U.S. government have significantly disrupted the operations of U.S. government agencies such as the National Institutes of Health, National Science Foundation, Centers for Disease Control and Prevention, and

FDA, which have traditionally provided funding for basic research, research and development, and clinical testing. These U.S. government actions have included, among other things, suspending, terminating and withholding of disbursements of funds owed under ongoing contracts, grants, and other financial assistance agreements; declining to continue multi-year research projects for additional annual budget periods; canceling or delaying solicitations for new contract, grant and other financial assistance awards; canceling or delaying proposal evaluation processes and issuance of such new awards; substantially reducing federal agency staff responsible for managing contract and financial assistance programs; eliminating agency information and resources for facilitating research activity; delaying or terminating federal agency procedures for authorizing international transactions; initiating aggressive enforcement actions that may disrupt the operations of major research universities that are significant contributors to life sciences research in the U.S., and threatening access to federal agency contracts and other funding awards based on companies' otherwise lawful corporate policies and choice of counsel. These U.S. government actions could, directly or indirectly, significantly disrupt, delay, prevent, or increase the costs of our research and product commercialization programs, including our ability to develop new product candidates, conduct clinical trials, implement research collaborations with other companies or institutions, and obtain approvals to market and sell new products.

In addition, government funding of government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions and could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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

Accordingly, if any of the foregoing developments and others impact the ability of the FDA to provide us with guidance regarding our clinical development programs or delay the agency's review and processing of our regulatory submissions, including INDs and NDAs/BLAs, our business would be negatively impacted. Further, any future government shutdown could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize Haduvio or any future product candidate and may affect the prices we may obtain.

In the U.S. and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of Haduvio or any future product candidate, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief and Economic Security Act, or the CARES Act.

The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with

which any such product candidate is prescribed or used. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts for Jobs Act, or TCJA, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, in June 2021, the U.S. Supreme Court dismissed a lawsuit challenging the constitutionality of the ACA after finding that the plaintiffs do not have standing to bring the litigation. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

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

In the European Union, on December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among E.U. Member States in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the European Union level for joint clinical assessments in these areas. It will permit E.U. Member States to use common HTA tools, methodologies and procedures across the European Union, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual E.U. Member States will continue to be responsible for assessing nonclinical (e.g., economic, social and ethical) aspects of health technology, and making decisions on pricing and reimbursement.

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

Current and future legislative efforts may limit the prices for our products, if and when they are licensed for marketing and that could materially impact our ability to generate revenues.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the U.S. There have been U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program to import certain prescription drugs from Canada into the U.S. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Several states have passed laws allowing for the importation of drugs from Canada. On January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. That state now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards. On May 21, 2025, the FDA announced that it would offer individual states the opportunity to submit a draft proposal for pre-review and meet with the agency to obtain initial feedback from FDA prior to formally submitting their Section 804 importation program (SIP) proposal. The intent of these meetings is to assist

states in developing their proposals by further clarifying requirements, enhancing the quality of proposals submitted to the agency and ultimately shortening the review timeline.

Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. The Inflation Reduction Act of 2022, or the IRA, further delayed implementation of this rule to January 1, 2032.

On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap and it replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). In addition, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs. The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years, but it does not apply to drugs that have been approved for a rare disease or condition. With passage of the One Big Beautiful Bill Act, or OBBBA, on July 3, 2025, which was signed into law on July 4, 2025, Congress extended this exemption to drugs and biologics with multiple orphan drug designations. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023, with the negotiated prices for ten selected drug products becoming effective on January 1, 2026. The second cycle of negotiations with participating drug companies occurred during 2025, and the negotiated prices for this second set of 15 drugs will become effective on January 1, 2027. On January 27, 2026, CMS published the list of 15 drugs selected for the third cycle of negotiations. These negotiated prices will become effective on January 1, 2028.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or “catastrophic period” of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA’s Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties also filed lawsuits in various courts with similar constitutional claims. HHS has generally won the substantive disputes in these cases or succeeded in getting claims dismissed for lack of standing or on the merits. For example, on May 8, 2025, the U.S. Court of Appeals for the Third Circuit rejected AstraZeneca L.P.’s challenge to the Medicare price negotiation program, finding that the program did not

violate the company's due process rights under the Constitution. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

On April 15, 2025, President Trump issued an Executive Order which directs the HHS to take steps to reduce the prices of pharmaceutical products. The new Executive Order repeats many of the proposals advanced during the first Trump Administration, including directing the FDA to streamline and improve its existing drug importation program so as to make it easier for states to obtain approval without sacrificing the safety or quality of drug products. Other provisions of the Executive Order relate to the 340B program. Specifically, one provision calls on the Secretary of HHS to determine the hospital acquisition cost for covered outpatient drugs at hospital outpatient departments and to consider and propose any appropriate adjustments for Medicare payment. The other provision directs HHS to condition grant funding to certain health centers on those centers passing through the 340B discounts they receive on insulin and injectable epinephrine products to patients who meet certain requirements. With respect to the IRA's Medicare drug pricing program, the Executive Order, among other things, calls for alignment in "the treatment of small molecule prescription drugs with that of biological products, ending the distortion that undermines relative investment in small molecule prescription drugs, coupled with other reforms to prevent any increase in overall costs to Medicare and its beneficiaries."

Further, on May 12, 2025, President Trump issued an additional Executive Order calling on pharmaceutical manufacturers to voluntarily reduce the prices of medicines in the United States. The Executive Order directs the Secretary of HHS to communicate most-favored-nation, or MFN, price targets to pharmaceutical manufacturers to bring prices in line with comparably developed nations. The Executive Order further provides that if such actions do not lower the costs of pharmaceuticals, the Secretary of HHS would pursue other actions, including proposing a rulemaking that imposes MFN pricing in the United States. Subsequently, on May 20, 2025, the HHS indicated that the proposed MFN pricing will apply only to brand products without generic or biosimilar competition and the reference foreign countries will include only those in which the branded product similarly does not have generic or biosimilar competition. Second, the HHS indicated that the MFN target price will be the lowest price in a country that is a member of the Organization for Economic Co-operation and Development, or OECD, with a gross domestic product, or GDP, per capita of at least 60% of the U.S. GDP per capita. Based on previous estimates, there are likely at least 22 OECD countries that would satisfy this criterion.

More recently, on July 31, 2025, President Trump issued letters to 17 pharmaceutical companies reiterating the requirements of the May 12, 2025, Executive Order and demanding that such companies extend MFN pricing to Medicaid patients, guarantee MFN pricing for newly-launched drug products, return increased revenues abroad to American patients and provide for direct purchasing at MFN pricing. The letters also urged these companies to stipulate that they will not offer other developed nations better prices for new drugs than the prices offered for such products in the U.S. The letters called for engagement with the FDA and CMS within 60 days to implement these changes and threatened to use "every tool in our arsenal" to address what the letter characterized as "abusive drug pricing practices." Virtually all of these pharmaceutical companies have entered into agreements with the administration to provide for lower prices on certain pharmaceuticals.

On December 23, 2025, CMS, through its Center for Medicare and Medicaid Innovation, or CMMI, proposed two five-year pilot programs to implement a "reference pricing" regime for drugs paid for under Medicare for 25% of covered beneficiaries. The programs are referred to as the Global Benchmark for Efficient Drug Pricing Model for Medicare Part B drugs, referred to as GLOBE, and the Guarding U.S. Medicare Against Rising Drug Costs for Medicare Part D drugs, referred to as GUARD. Under the proposed pilot programs, a manufacturer would owe rebates to Medicare if prices for their drugs exceeded the prices paid by other economically comparable reference countries, defined in the proposed regulations as OECD countries with a GDP of $400 billion and a per capita GDP that is at least 60% of the US per capita GDP (an initial list of 19 reference countries is included in the proposed rule). Comments are due on the proposed pilot program rules on or before February 23, 2026, and the pilot programs are proposed to go into effect beginning October 1, 2026.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. This is increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payors are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on

our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In the E.U., similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the U.S. and the E.U., reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the E.U., the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Any relationships we may have with customers, healthcare providers and professionals and third-party payors, among others, 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, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we are able to obtain marketing approval. Any arrangements we have with healthcare providers, third-party payors and customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws and regulations may constrain the business or financial arrangements and relationships through which we conduct clinical research, market, sell and distribute any products for which we obtain marketing approval. These include the following:

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward or in return for, either the referral of an individual for or the purchase, lease or order of a good, facility, item or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid.

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

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, executing a scheme or making materially false statements in connection with the delivery of or payment for health care benefits, items or services. Additionally, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations on covered entities and their business associates that perform certain functions or activities that involve the use or disclosure of protected health information on their behalf, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information.

Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to CMS information related to payments or transfers of value made to physicians, other healthcare providers and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members.

Analogous State and Foreign Laws. Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors and are generally broad and are enforced by many different federal and state agencies as well as through private actions. 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 require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures.

Efforts to ensure that any business arrangements we have with third parties and our business generally, 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, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the E.U. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of E.U. Member States. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain E.U. Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual E.U. Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the E.U. Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

The collection, use, disclosure, transfer or other processing of personal data, including personal health data, of individuals in the E.U. is governed by the General Data Protection Regulation, or GDPR. The GDPR became effective on May 25, 2018. It imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data; obtaining consent of individuals; providing notice to individuals regarding data processing activities; responding to data subject requests; taking certain measures when engaging third-party processors; notifying data subjects and regulators of data breaches; and implementing safeguards to protect the security and confidentiality of personal data. The GDPR imposes strict rules on the transfer of personal data to countries outside the E.U., including the U.S. Failure to comply with the requirements of the GDPR may result in fines of up to 20 million euros or four percent of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages. The GDPR increases our responsibility and potential liability in relation to personal data that we process and we may be required to change our business practices or put in place additional mechanisms ensuring compliance with the GDPR. This may be onerous and adversely affect our business, financial condition, results of operations and prospects and despite our efforts, there is a risk that we may be subject to fines, litigation and reputational harm in connection with our European activities.

In October 2022, President Biden signed an executive order to implement the E.U.-U.S. Data Privacy Framework, which would serve as a replacement to the E.U.-U.S. Privacy Shield. The E.U. initiated the process to adopt an adequacy decision for the E.U.-U.S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the E.U.-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the E.U. to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the E.U.-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the E.U.-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact any future business we may have at the international level.

Similar actions are either in place or under way in the U.S. There are a broad variety of data protection laws that are applicable to our activities and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The FTC and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being

considered at both the state and federal levels. For example, the FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the Federal Trade Commission Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security that may impact our business. We will need to account for the FTC's evolving rules and guidance for proper privacy and data security practices in order to mitigate our risk for a potential enforcement action, which may be costly. If we are subject to a potential FTC enforcement action, we may be subject to a settlement order that requires us to adhere to very specific privacy and data security practices, which may impact our business. We may also be required to pay fines as part of a settlement (depending on the nature of the alleged violations). If we violate any consent order that we reach with the FTC, we may be subject to additional fines and compliance requirements.

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

If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

New laws also are being considered at the state level. Most prominently, in California, the California Consumer Protection Act, or the CCPA, as amended by the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023, establishes a privacy framework for covered businesses by creating an expansive definition of personal information, establishing data privacy rights for consumers and employees in the State of California, imposing special rules on the collection of consumer data from minors, and creating a potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. The CPRA created a new state agency that is vested with authority to implement and enforce the CCPA and the CPRA. While clinical trial data is currently exempt from the current version of the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope.

In addition to California, a number of other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. There are also states that are considering or have already passed comprehensive privacy laws during the 2023 legislative sessions that will go into effect in 2024 and beyond. There are also states that are specifically regulating health information that may affect our business. For example, Washington state recently passed a health privacy law that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

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

Accordingly, any failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not

determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the U.S. and require us to develop and implement costly compliance programs.

If we further expand our operations outside the U.S., we will need to dedicate additional resources to comply with U.S. laws regarding international operations and the laws and regulations in each jurisdiction in which we operate and plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the company, including international subsidiaries and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry because in many countries, hospitals are operated by the government and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

On February 10, 2025, President Trump issued an Executive Order directing the Attorney General to review the guidelines and policies governing FCPA investigations and enforcement actions. Per the Executive Order, this review will result in new DOJ FCPA guidelines intended to enhance American economic competitiveness and to safeguard national security interests. During the 180-day review period, any new FCPA investigations and enforcement actions are to be suspended absent authorization from the Attorney General, and all existing FCPA investigations and enforcement actions will be reviewed. Additionally, after the Attorney General issues revised guidelines, the Executive Order directs her to assess whether "remedial measures" related to past FCPA actions are warranted. We will need to carefully navigate these developments.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the U.S., or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Further, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the E.U. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws, such as the United Kingdom Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain E.U. Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual E.U. Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the E.U. Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

If we expand our presence outside of the U.S., it will require us to dedicate additional resources to comply with these laws and these laws may preclude us from developing, manufacturing or selling certain products and product candidates outside of the U.S., which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials,

we could be held liable for any resulting damages and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from workplace and other work-related accidents, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental, health and safety laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Our business and operations would suffer in the event of system failures.

Our computer systems, as well as those of our CROs and other third-party contractors and consultants, are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, sabotage, natural disasters (including hurricanes), terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our business and development programs, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of preclinical studies or clinical trial data from completed, ongoing or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce data. To the extent any disruption or security breach 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 also incur liability, our competitive position could be harmed and the development of Haduvio or any future product candidate could be significantly delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

In the ordinary course of our business, we directly or indirectly collect and store sensitive data, including intellectual property, confidential information, preclinical and clinical trial data, proprietary business information, personal data and personally identifiable health information of our clinical trial patients and employees, in our data centers and on our networks or on those of third parties. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors or breached due to employee error, a technical vulnerability, malfeasance or other disruptions. Additionally, the risk of a security breach or disruption through cyber-attacks has generally increased as the number, intensity and sophistication of attempted attacks from around the world have increased. Although, to our knowledge, we have not experienced any such material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information and significant regulatory penalties and such an event could disrupt our operations, damage our reputation and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our future products that receive marketing approval through the NDA pathway, or such authorities do not grant such future products appropriate periods of data exclusivity before approving generic versions of our products, our sales could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of ANDAs in the U.S. In support of an ANDA, a generic manufacturer need not conduct clinical trials to assess safety and efficacy. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug is typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment

of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. Specifically, in cases where such exclusivity has been granted, an ANDA may not be submitted to the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical trials, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application.

Generic drug manufacturers may seek to launch generic products following the expiration of any applicable exclusivity period we obtain if our product candidates are approved, even if we still have patent protection for such product candidates. Competition that any such product candidates of ours may face from generic versions of such products could materially and adversely impact our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we may make in those product candidates.

Artificial intelligence presents risks and challenges that can impact our business including by posing security risks to our confidential information, proprietary information and personal data.

Issues in the use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability or other adverse consequences to our business operations. As with many technological innovations, artificial intelligence presents risks and challenges that could impact our business. Our vendors may incorporate generative artificial intelligence tools into their offerings without disclosing this use to us, and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If any of our vendors experiences an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business.

Risks Related to Employee Matters and Managing our Growth

Our future success depends on our ability to retain our executive team and to attract, retain and motivate qualified personnel.

We are highly dependent on our executive leadership and scientific teams. Except as otherwise required by law, all members of our executive team are employed "at will," meaning that they may terminate their employment with us at any time with or without notice and for any reason or no reason. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified scientific, clinical, manufacturing and sales and marketing personnel. Our industry has experienced a high rate of turnover of such personnel in recent years. If we lose one or more of our executive officers or other key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers or other 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 develop, gain marketing approval of and commercialize products successfully. Competition to hire from this limited pool is intense and we may be unable to hire, train, retain or motivate these additional key employees 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.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize Haduvio or any future product candidate will be limited.

If we expand our organization, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2025, we had 34 employees. We may experience growth in the number of our employees and the scope of our operations. For example, if any product candidate appears likely to receive marketing approval, we expect to significantly expand our sales, marketing and distribution capabilities to support the potential commercialization of the product candidate. Our management may need to devote a significant amount of its attention to managing these growth activities. Due to our limited financial resources and the limited experience of our management team in managing a company with such growth, we may not be able to effectively manage the expansion of our operations, retain key employees or identify, recruit and train additional qualified personnel. Our inability to manage the expansion of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Any significant growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of Haduvio for additional indications or the development of additional product candidates. If we are unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may be unable to implement our business strategy, including the successful commercialization of any product candidate.

Our employees, independent contractors and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors and consultants may engage in fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, to provide accurate information to the FDA or comparable non-U.S. regulatory authorities, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, to report financial information or data accurately or to disclose unauthorized activities to us. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter 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 be in compliance with such laws, standards 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 and results of operations, including the imposition of significant criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm and requirements to curtail or restructure our operations.

Risks Related to Our Common Stock

The trading price of our common stock is highly volatile, which could result in substantial losses for purchasers of our common stock.

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

- the timing and results of clinical trials of Haduvio or any future product candidates;
- the success of existing or new competitive products or technologies;
- regulatory actions with respect to Haduvio or any future product candidates or competitors' products and product candidates;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;

- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property rights;
- recruitment or departure of key personnel;
- expenses related to any of our development programs;
- results of our efforts to discover, develop, acquire or in-license additional product candidates;
- actual or anticipated changes in estimated financial results or development timelines;
- announcements or expectations of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- expiration of market stand-off or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- recommendations and changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems in the U.S. and other countries;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including recent adverse changes in the domestic and international financial markets, the impacts of inflation and the implementation of trade barriers and tariffs and government action in response thereto;
- our ability to maintain our listing on the Nasdaq Global Market;
- our ability to continue as a going concern; and
- other factors and considerations described in this "Risk Factors" section.

In addition, inflation and interest rate increases and other factors have negatively affected, and may in the future negatively affect, the stock market and investor sentiment. The price and volatility of our common stock may be disproportionately affected as investors may favor traditional profit-making industries and companies during such times of market uncertainty and instability.

Changes in and uncertainty surrounding U.S. and international trade policies may adversely impact on our business, financial condition and results of operations.

In the spring of 2025, the Trump Administration initiated a series of tariff-related actions against U.S. trading partners. On April 2, 2025, the President issued an Executive Order announcing a "baseline" reciprocal tariff of 10% on all U.S. trading partners effective April 5, 2025 and higher individualized reciprocal tariffs on 57 countries (with certain product exemptions for pharmaceutical-related products, among others). Previously, the administration had imposed a 25% tariff on Canada and Mexico for goods not covered by the United States-Mexico-Canada Agreement, or USMCA, and tariffs due to drug trafficking equaling 20% on imports from China. In response, several countries threatened retaliatory measures, including Canada and China, which then imposed retaliatory tariffs. Prior to when the country-specific reciprocal tariffs were scheduled to take effect, the administration delayed the effective date of such tariffs for all countries except China to August 1, 2025. Later, the U.S. and China reached a framework agreement that ultimately resulted in the suspension of the higher reciprocal tariffs on China until November 10, 2025. Shortly before that expiration date, the United States and China reached a one-year agreement with an expiration of November 10, 2026, that includes the continued suspension of the heightened reciprocal tariffs on China and delayed enforcement of new U.S. export rules targeting affiliates of blacklisted firms.

Since the April reciprocal tariffs announcement, several countries have also reached deals with the U.S. that include reduced tariff rates to varying levels and other measures. On July 31, 2025, President Trump issued an Executive Order detailing new reciprocal tariff rates for individual countries that took effect on August 7, 2025. The deal with the European Union, Japan, South Korea, Switzerland (and Liechtenstein), the United Kingdom and others cap pharmaceutical tariffs at 15%. In addition, an agreement with Malaysia provides a zero percent tariff exemption for pharmaceutical products that are not patented in the United States and are used in pharmaceutical applications and an agreement with Switzerland and Lichenstein caps tariffs on pharmaceuticals imported from those two countries at 15%. Finally, an agreement with Taiwan concluded on January 15, 2026, eliminates tariffs on generic pharmaceuticals and their active ingredients imported from Taiwan.

The reciprocal tariffs were imposed by Trump pursuant to the International Emergency Economic Powers Act, or the IEEPA. These tariffs were found to be unconstitutional by multiple federal courts in the spring and summer of 2025. On February 20, 2026, the U.S. Supreme Court held that the IEEPA does not authorize the President to impose tariffs, invalidating both the reciprocal tariffs and the drug trafficking tariffs. Shortly thereafter, the President issued a new Executive Order revoking the IEEPA tariffs and Customs and Border Protection ceased collecting the tariffs as of 12:01 am on February 24, 2026. At the same time, however, the Trump Administration imposed a new 10% global tariff under Section 122 of the Trade Act of 1974, effective February 24, 2026. Pursuant to the statute, absent an extension by Congress, these tariffs will expire 150 days later on July 24, 2026. For those countries that have concluded trade deals with the United States, the tariff rates agreed to – including with regard to pharmaceuticals and pharmaceutical ingredients - have now reverted to 10% until July 24, 2026.

Like the IEEPA tariffs, pharmaceuticals and pharmaceutical ingredients are exempt from the Section 122 tariffs along with a list of other products. The Trump Administration has announced that it also plans to initiate new investigations on "most major trading partners" under Section 301 of the same act, which will likely lead to additional tariffs.

Neither the U.S. Supreme Court's decision nor the Executive Order revoking the IEEPA tariffs addressed refunds, leaving the issue to renewed proceedings before the U.S. Court of International Trade, where importers may need to pursue administrative remedies and/or litigation amid continued uncertainty.

Sustained uncertainty about, or the further escalation of, trade and political tensions between the United States and China could result in a disadvantageous research and manufacturing environment in China, particularly for U.S.-based companies, including retaliatory restrictions that hinder or potentially inhibit our ability to rely on CMOs and other service providers that operate in China.

Separately, in April 2025, the U.S. Department of Commerce initiated an investigation under Section 232 of the Trade Expansion Act of 1962 into the impact on U.S. national security of the imports of pharmaceuticals and pharmaceutical ingredients, including finished drug products, medical countermeasures, critical inputs such as active pharmaceutical ingredients, and key starting materials, and derivative products of those items. On September 25, 2025, via a post on Truth Social, President Trump announced that, beginning October 1, 2025, all branded or patented drugs imported in the U.S. would face a 100% tariff. At the same time, Trump indicated that these tariffs could be avoided by building pharmaceutical manufacturing facilities in the U.S. Thereafter, Trump delayed the October 1st effective date of the tariffs on branded or patented pharmaceutical products announcing that the Administration had now "begun preparing" tariffs on manufacturers that don't build in the U.S. or enter into an MFN drug pricing agreement with the Trump administration.

As a result of changes in tariffs that have been announced and/or implemented, and the underlying uncertainty currently surrounding tariffs and international trade, we could experience a negative impact to our costs of materials and production processes, and supply chain disruptions and delays as a result of these and any new tariff policies or trade restrictions. We cannot yet predict the effect of the recently imposed U.S. tariffs on imports, or the extent to which other countries will impose quotas, duties, tariffs, taxes or other similar restrictions upon imports or exports in the future, nor can we predict future trade policy or the terms of any renegotiated trade agreements and their impact on our business.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against public companies following declines in the trading prices of their securities. This risk is especially relevant for us because companies in the life sciences space have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and our resources, which could harm our business.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, the trading price and volume of our shares could decline.

The trading market for our common stock will likely depend in part on the research and reports that securities or industry analysts publish about us and our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, the trading price of our shares would likely decline. In addition, if one or more analysts cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause the trading price and volume of our shares to decline.

Future sales of shares of our common stock, including by us, employees and significant stockholders, could negatively affect our stock price.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales or the perception in the market that the holders of a large number of shares of our common stock intend to sell their shares, could reduce the trading price of our common stock.

All of our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act, or to the extent that such shares have already been registered under the Securities Act and are held by non-affiliates of ours.

Moreover, holders of a substantial number of shares of our common stock have rights, subject to specified limitations and conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

In addition, we have registered all shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If these additional shares are sold or if it is perceived in the market that they will be sold in the public market, the trading price of our common stock could decline.

In June 2023, we filed with the SEC a universal shelf registration statement on Form S-3, or the 2023 Shelf Registration Statement, which allowed us to offer and sell up to $200.0 million of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The 2023 Shelf Registration Statement was declared effective on August 15, 2023. In June 2023, we entered into a new at-the-market sales agreement, or the ATM Sales Agreement, with Leerink Partners LLC (formerly SVB Securities LLC) and filed a prospectus under our 2023 Shelf Registration Statement for the offer and sale of shares of our common stock having an aggregate offering price of up to $75.0 million pursuant to the ATM Sales Agreement. In accordance with the terms of the ATM Sales Agreement, the sales agreement we had entered into with SVB Securities LLC in 2020 terminated upon effectiveness of the 2023 Shelf Registration Statement, at which point we were no longer able to issue and sell shares of our common stock under such prior sales agreement. From time to time, we may offer and sell under the ATM Sales Agreement common stock registered under the 2023 Shelf Registration Statement pursuant to one or more “at-the-market” offerings. The extent to which we utilize the ATM Sales Agreement as a source of funding depends on a number of factors, including the prevailing market price of our common stock, general market conditions and the extent to which we are able to secure funds from other sources.

In November 2025, we filed an automatic universal shelf registration statement on Form S-3, or the 2025 Shelf Registration Statement, with the SEC, which became effective upon filing. The 2025 Shelf Registration Statement permits us to offer and sell an indeterminate amount of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The 2025 Shelf Registration Statement was filed to replace our prior universal shelf registration statement. Concurrently with the filing of the 2025 Shelf Registration Statement, we filed a new prospectus supplement pursuant to which shares of our common stock having an aggregate offering price of up to $200.0 million may be offered and sold from time to time under the ATM Sales Agreement. No shares were sold under the ATM Sales Agreement during the twelve months ended December 31, 2025.

In October 2021, we issued to a single investor in a private placement, or the Initial Private Placement Investor, (i) 2,373,201 shares of our common stock and accompanying warrants to purchase an aggregate of 4,746,402 shares of our common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 4,926,069 shares of our common stock and accompanying warrants to purchase an aggregate of 9,852,138 shares of our common stock. All of the pre-funded warrants and accompanying common stock warrants issued to the Initial Private Placement Investor have been exercised.

Similarly, on October 18, 2021, we issued to New Enterprise Associates 16, L.P., or NEA, in a private placement, 1,851,852 shares of our common stock and accompanying warrants to purchase an aggregate of 3,703,704 shares of our common stock. As of March 12, 2026, warrants issued to NEA to purchase 1,851,852 shares of common stock remained outstanding.

Similarly, on April 11, 2022, we issued to several purchasers in a private placement, or the April 2022 Private Placement, (i) an aggregate of 4,580,526 shares of our common stock and (ii) pre-funded warrants to purchase an aggregate of 24,379,673 shares of our common stock. Under the terms of the pre-funded warrants, we may not effect the exercise of any such warrant, and a purchaser will not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of common stock beneficially owned by such purchaser (together with its affiliates, any other persons acting as a group together with such purchaser or any of such purchaser’s affiliates, and any other persons whose beneficial ownership of common stock would or could be aggregated with such purchaser's for purposes of Section 13(d) or Section 16 of the Securities Exchange Act of 1934, as amended, or the Exchange Act) would exceed 9.99% of the number of shares of common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of such warrant, which percentage may be increased or decreased at such purchaser’s election upon 61 days’ notice to us subject to the terms of such warrants, provided that such

percentage may in no event exceed 19.99%. We refer to such percentage limitations as the 2022 Private Placement Beneficial Ownership Limitations. As of March 12, 2026, pre-funded warrants that we issued and sold in the April 2022 Private Placement to purchase 12,531,332 shares of common stock remained outstanding.

Similarly, on September 27, 2022, we issued and sold an aggregate of 14,252,670 shares of our common stock, and, in lieu of common stock to certain investors, pre-funded warrants to purchase 14,247,330 shares of common stock, in a public offering, or the September 2022 Offering. Under the terms of the pre-funded warrants, we may not effect the exercise of any such warrant, and a purchaser will not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of common stock beneficially owned by such purchaser (together with its affiliates, any other persons acting as a group together with such purchaser or any of such purchaser's affiliates, and any other persons whose beneficial ownership of common stock would or could be aggregated with such purchaser's for purposes of Section 13(d) or Section 16 of the Exchange Act) would exceed 9.99% of the number of shares of common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of such warrant, which percentage may be increased or decreased at such purchaser's election upon 61 days' notice to us subject to the terms of such warrants, provided that such percentage may in no event exceed 19.99%. We refer to such percentage limitations as the September 2022 Offering Beneficial Ownership Limitations. As of March 12, 2026, pre-funded warrants that we issued and sold in the September 2022 Offering to purchase 4,717,616 shares of common stock remained outstanding.

Sales of substantial amounts of shares of our common stock or other securities by our stockholders, by us under the 2025 Shelf Registration Statement, whether pursuant to the ATM Sales Agreement or otherwise, by the private placement investors or through any other means could also lower the market price of our common stock, make it more difficult for you to sell your shares at a price that you desire and impair our ability to raise capital through the sale of equity or equity-related securities.

The number of shares of common stock underlying our outstanding warrants is significant in relation to our currently outstanding common stock, which could have a negative effect on the market price of our common stock and make it more difficult for us to raise funds through future equity offerings. In addition, in connection with any merger, consolidation or sale of all or substantially all of our assets, holders of our outstanding warrants would be entitled to receive consideration in excess of their reported beneficial ownership of our common stock and this could adversely impact the consideration our other stockholders would receive.

As part of our October 2021 private placements, we issued to NEA warrants to purchase an aggregate of 3,703,704 shares of our common stock at an exercise price of $1.37 per share. Of the common stock warrants issued to NEA, warrants to purchase an aggregate of 1,851,852 shares of our common stock would have expired on April 18, 2025 and warrants to purchase an aggregate of 1,851,852 shares of our common stock will expire on October 18, 2028. On April 17, 2025, NEA exercised all of the warrants that would have expired on April 18, 2025. None of the accompanying common stock warrants issued to NEA in the private placement that expire on October 18, 2028 have been exercised. We issued pre-funded warrants to purchase up to an aggregate of 24,379,673 shares of our common stock to the purchasers in the April 2022 Private Placement, of which pre-funded warrants to purchase 12,531,332 shares of common stock remained outstanding as of March 12, 2026. Finally, we issued pre-funded warrants to purchase up to an aggregate of 14,247,330 shares of our common stock at an exercise price of $0.001 per share to certain purchasers in the September 2022 Offering, of which pre-funded warrants to purchase 4,717,616 shares of common stock remained outstanding as of March 12, 2026.

As discussed above, the pre-funded warrants issued to the purchasers in the April 2022 Private Placement are subject to the 2022 Private Placement Beneficial Ownership Limitations and the pre-funded warrants issued to certain purchasers in the September 2022 Offering are subject to the September 2022 Offering Beneficial Ownership Limitations. Although the pre-funded warrants issued to the purchasers in the April 2022 Private Placement are subject to the 2022 Private Placement Beneficial Ownership Limitations and the pre-funded warrants issued to the purchasers in the September 2022 Offering are subject to the September 2022 Offering Beneficial Ownership Limitations, upon exercise in full of the warrants, the shares issuable upon exercise would represent a significant portion of our outstanding common stock. As a result, NEA and the other purchasers in the April 2022 Private Placement and the September 2022 Offering may be able to exert substantial influence over our business. The concentration of voting power resulting from the exercise of the warrants could delay, defer or prevent a change of control, entrench our management and our board of directors or delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire. In addition, conflicts of interest could arise in the future between us, on the one hand, and NEA, the purchasers in the April 2022 Private Placement and/or the purchasers in the September 2022 Offering on the other hand, concerning potential competitive business activities, business opportunities, the issuance of additional securities and other matters. In addition, sales of these shares could cause the market price of our common stock to decline significantly.

Furthermore, in the event of a sale of our company, whether by merger, sale of all or substantially all of our assets or otherwise, the holders of warrants would be entitled to receive, with respect to each share of common stock issuable upon

exercise of the warrants then held by them and the same amount and kind of securities, cash or property as they would have been entitled to receive if such securities had been converted into or exercised for shares of our common stock immediately prior to such sale of our company. In addition, pursuant to the terms of the common stock warrants issued to NEA in our October 2021 private placements, in specified circumstances upon a fundamental transaction by us, such warrant holders may have the right to require us to repurchase their common stock warrants at their fair value using a Black Scholes option pricing formula. As a result, in the event of a sale of our company, NEA may be entitled to receive a significantly larger portion of the total proceeds distributable to our stockholders than it would if it exercised the warrants immediately prior to the transaction, and our stockholders could receive significantly less than they otherwise would in such a transaction.

Given the amount and terms of these warrants, we may find it more difficult to raise additional equity capital on favorable terms or at all while these warrants are outstanding.

Ownership of our common stock is concentrated among our executive officers and directors and their affiliates, who have significant influence over our business, which may prevent new investors from influencing significant corporate decisions.

Our executive officers and directors and their respective affiliates, beneficially own, in the aggregate, shares representing approximately 15.3% of our common stock as of March 12, 2026. As a result, our executive officers and directors and their affiliates acting together may be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management or the board of directors; or
- impede a merger, consolidation, takeover, sale, other business combination or other significant corporate transaction involving us that other stockholders may desire.

Some of these persons or entities may have interests different than yours. For example, certain of these stockholders may have purchased their shares at prices substantially below the prices you paid for your shares or may have held their shares for a longer period, and they may be more interested in selling our company to an acquirer or they may want us to pursue strategies that deviate from your interests.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on appreciation in the price of our common stock, if any, for any return on their investment.

We have never declared or paid cash dividends on our capital stock and we do not intend to do so in the foreseeable future. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our product pipeline and business. As a result, future appreciation, if any, in the market value of our common stock will be your sole source of gain for the foreseeable future. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

We are a "smaller reporting company" and the reduced disclosure requirements applicable to us may make our common stock less attractive to investors.

We are a "smaller reporting company." We will continue to be a "smaller reporting company" so long as (i) the market value of our stock held by non-affiliates is less than $250.0 million as of the most recently completed second fiscal quarter 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 as of the most recently completed second fiscal quarter. We remain a smaller reporting company as of June 30, 2025. Smaller reporting companies are permitted to provide simplified executive compensation disclosure in their filings; and they have certain other decreased disclosure obligations in their SEC filings, including, among other things, only being required to provide two years of audited financial statements in annual reports. For as long as we continue to be a smaller reporting company, we expect that we will take advantage of the reduced disclosure obligations available to us as a result of such classification. Decreased disclosure in our SEC filings as a result of our having availed ourselves of scaled disclosure may make it harder for investors to analyze our results of operations and financial prospects.

We incur increased costs as a result of operating as a public company and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company and particularly since we ceased being an "emerging growth company", we have incurred and will continue to incur, significant legal, accounting, investor relations and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We may need to hire additional accounting, finance and other personnel in connection with our

efforts to comply with the requirements of being a public company and our management and other personnel devote a substantial amount of time in complying with these requirements, which could negatively impact our financial results. Current and changing laws, rules and regulations relating to corporate governance and public disclosure may increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, the rules and regulations applicable to us as a public company have made it and we expect that they may continue to make it, more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are evaluating these rules and regulations and cannot currently predict or estimate the additional costs we may incur or the timing of such costs. In addition, these laws, rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We have invested in and intend to continue to invest in, resources to comply with evolving laws, rules and regulations and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue generating activities to compliance activities. If, notwithstanding our efforts to comply with new laws, rules and regulations, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002, or SOX, and the rules and regulations of the Nasdaq Stock Market. The Sarbanes-Oxley Act of 2002 requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Pursuant to SOX Section 404, or SOX 404(b), we are required to furnish annual reports by our management on our internal control over financial reporting. However, until such time as we are no longer a "smaller reporting company" with less than $100 million in annual revenue and subsequently qualify as an accelerated filer or a large accelerated filer, we will continue to not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX 404(b) within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective. If we are unable to comply with the requirements of SOX 404(b) in a timely manner or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the trading price of our common stock could decline and we could be subject to sanctions or investigations by the Nasdaq Stock Market, the SEC or other regulatory authorities.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2025, we had federal and state net operating loss carryforwards of $238.3 million and federal research and development tax credit carryforwards of $8.5 million, which if not utilized generally will begin to expire in 2031 and 2032, respectively. These net operating loss and research and development tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the IRC, and corresponding provisions of state law, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three year period, is subject to limitations on its ability to utilize its pre-change net operating loss and research and development tax credit carryforwards to offset future taxable income. We previously completed a Section 382 analysis, and due to multiple historical ownership changes, all of our net operating loss carryforwards as of December 31, 2022, and research and development tax credits were subject to limitation. If a further ownership change occurs, our ability to use our tax attributes might be further limited. In addition to potential Sections 382 and 383 limitations, there are other factors that might limit the availability of our tax attributes. For example, we have not conducted a detailed research and development tax credit analysis to document whether our historical business activities qualify to support our research and development credit carryforwards. A detailed study could result in adjustment to our research and development credit carryforwards.

Under current law, the deduction for net operating losses arising in taxable years beginning after December 31, 2017 is limited to 80% of current-year taxable income (although such net operating losses may be carried forward indefinitely). There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses or other

unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our net operating losses and other tax attributes.

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

Income, sales, use or other tax laws, statutes, rules, or regulations could be enacted or amended at any time, which could affect our business or financial condition, including causing potentially adverse impacts to our effective tax rate, tax liabilities, and cash tax obligations. For example, the IRA was signed into law in August 2022, and the OBBBA was signed into law in July 2025. The IRA introduced new tax provisions, including a one percent excise tax imposed on certain stock repurchases by publicly traded companies. The one percent excise tax generally applies to any acquisition of stock by the publicly traded company (or certain of its affiliates) from a stockholder of the company in exchange for money or other property (other than stock of the company itself), subject to certain exceptions. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases. The OBBBA contains numerous tax provisions that we are currently in the process of evaluating, and which may significantly affect our business or financial condition. The recent changes under the OBBBA include tax rate extensions and changes to the business interest deduction limitation, the expensing of domestic research and development expenditures (in contrast to the continued capitalization and amortization of foreign research and development expenditures), the bonus depreciation deduction rules, and the international tax framework. Regulatory guidance under the IRA, the OBBBA, and other tax-related legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen the impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to changes to federal tax legislation.

Provisions in our organizational documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which 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 trading price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits an “interested stockholder,” which is either a person who owns at least 15% of our outstanding voting stock or an affiliate or associate who owned at least 15% of our outstanding voting stock at any time within the prior three years, from engaging in a business combination with us for a period of three years after the date of the transaction in which the person became an “interested stockholder” unless the business combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by or beneficial to, our stockholders. This could also have the effect of discouraging others from

making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders and that the federal district courts of the U.S. are the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. These choice of forum provisions could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall, to the fullest extent permitted by law, be the sole and exclusive forum for (1) any derivative action or proceeding brought on behalf of our company, (2) any action asserting a claim of breach of fiduciary duty owed by any director, officer, other employee or stockholder of our company to us or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws or governed by the internal affairs doctrine. Our certificate of incorporation further provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the U.S. shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Neither of these choice of forum provisions would affect suits brought to enforce any liability or duty created by the Exchange Act or the rules and regulations thereunder, jurisdiction over which is exclusively vested by statute in the U.S. federal courts or any other claim for which U.S. federal courts have exclusive jurisdiction.

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 our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and operating results.

If we fail to comply with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

Our common stock is currently listed for trading on Nasdaq. We must satisfy Nasdaq's continued listing requirements, including, among other things, a minimum closing bid price of $1.00 per share, or the Bid Price Requirement, or risk delisting, which would have a material adverse effect on our business. A delisting of our common stock from Nasdaq could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the potential loss of confidence by investors, suppliers, customers and employees and fewer business development opportunities.

There can be no assurance that we will be able to maintain compliance with the Bid Price Requirement or other Nasdaq continued listing requirements in the future or that we will be able to regain compliance with respect to any future deficiencies. If we fail to satisfy the Nasdaq Global Market's continued listing requirements, we may submit an application to transfer to the Nasdaq Capital Market, which generally has lower financial requirements for initial listing, in an effort to avoid delisting. However, we may not be able to satisfy the initial listing requirements for the Nasdaq Capital Market and may therefore not be able to transfer our listing to the Nasdaq Capital Market. A transfer of our listing to the Nasdaq Capital Market could adversely affect the liquidity of our common stock. Any such event could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 1C. Cybersecurity.

We have certain processes for assessing, identifying and managing cybersecurity risks, which are built into our overall risk management program and information technology function and are designed to help protect our information

assets and operations from cyber threats, protect employee and patient information from unauthorized access or attack, as well as secure our networks and systems. Such processes include physical, procedural and technical safeguards, and routine review of our operations to identify risks and enhance our practices. We engage certain external parties, including consultants and computer security firms, to enhance our cybersecurity oversight. We consider the internal risk oversight programs of third-party service providers when engaging them in order to help protect us from any related vulnerabilities.

Our board of directors does not believe that there are currently any known risks from cybersecurity threats that are reasonably likely to materially affect us or our business strategy, results of operations or financial condition.

The audit committee of our board of directors provides direct oversight over cybersecurity risk and provides updates to the board of directors regarding such oversight. The audit committee receives periodic updates from management regarding cybersecurity matters and is notified between such updates regarding significant new cybersecurity threats or incidents.

We have also established a Cybersecurity Committee that meets on a quarterly basis to review and agree on actions to address cybersecurity risks. The Cybersecurity Committee is led by our chief information officer, or CIO, who is a part-time consultant, and includes our chief executive officer and chief financial officer. Our CIO, who reports to our chief financial officer, is responsible for the strategic leadership of our cybersecurity programs, identification of cybersecurity risks and the mitigation plans that address these risks. With over 25 years of experience in information technology, the CIO works alongside individuals across other functions, such as clinical operations, legal and quality compliance, to establish and implement our cybersecurity strategy. Our CIO has a bachelor's degree in Technology and an M.B.A. along with over 10 years of experience in information technology in the life sciences industry.

In an effort to deter and detect cyber threats, we annually provide all employees, including part-time and temporary employees, with a data protection, cybersecurity training and compliance program, which covers timely and relevant topics, including social engineering, phishing, password protection, confidential data protection, use of artificial information and machine learning applications, and asset use, and educates employees on the importance of reporting all incidents immediately. We conduct frequent phishing simulations requiring employees to identify and report simulated phishing emails. We also use technology-based tools to mitigate cybersecurity risks and to bolster our employee-based cybersecurity programs.

Item 2. Properties.

Our headquarters is currently located in New Haven, Connecticut, and consists of approximately 12,500 square feet of leased office space under a lease that expires in February 2028 and under which we have an option to extend the lease by a five-year term. We believe that our existing facilities are adequate for our current needs; however, we may require additional space and facilities as our business expands.

Item 3. Legal Proceedings.

We are not subject to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock is listed on the Nasdaq Stock Market LLC under the symbol "TRVI."

Stockholders

As of March 12, 2026, there were approximately 17 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Dividend Policy

We have never declared or paid cash dividends on our common stock and we do not intend to pay any cash dividends in the foreseeable future. We currently intend to retain all available funds and any future earnings to finance the operation, development and growth of our business. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Securities Authorized for Issuance Under Equity Compensation Plan

The information concerning our equity compensation plan is incorporated by reference from the information in our Proxy Statement for our 2026 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our Consolidated Financial Statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the statements contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We have based these forward-looking statements on our current expectations and projections about future events. The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Annual Report on Form 10-K, particularly including those risks identified in Part I-Item 1A "Risk Factors" and our other filings with the SEC.

Our actual results and the timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this Annual Report on Form 10-K. Statements made herein are as of the date of the filing of this Annual Report on Form 10-K with the SEC and should not be relied upon as of any subsequent date. Even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this Annual Report on Form 10-K, they may not be predictive of results or developments in future periods. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of the investigational therapy Haduvio (oral nalbuphine ER) for the treatment of chronic cough in patients with idiopathic pulmonary fibrosis, or IPF, non-IPF interstitial lung disease, or non-IPF ILD, and refractory chronic cough, or RCC. Haduvio is an oral extended-release formulation of nalbuphine. Haduvio acts on the cough reflex arc both centrally and peripherally as a kappa receptor agonist and a mu receptor antagonist ("KAMA"), targeting opioid receptors that play a key role in controlling chronic cough. The kappa- and mu-opioid receptors are known to be critical mediators of cough. Nalbuphine has been approved and marketed as an injectable for pain indications for decades in the United States, or the U.S., and Europe. Nalbuphine's mechanism of action also mitigates the risk of abuse associated with mu-opioid agonists because it antagonizes, or blocks, the mu-opioid receptor. Parenteral nalbuphine is not scheduled as a controlled substance by the U.S. Drug Enforcement Agency and in most of Europe.

IPF-related chronic cough Program. We are developing Haduvio for the treatment of IPF-related chronic cough, which is a progressive fibrosing interstitial lung disease associated with high mortality rates.

In June 2025, we announced positive topline results from our Phase 2b CORAL trial, which was a dose-ranging study evaluating the efficacy, safety and tolerability of Haduvio for IPF-related chronic cough. The Phase 2b CORAL trial was a randomized, double-blind, placebo-controlled, parallel-arm design that evaluated three different dose groups of Haduvio (108 mg BID, 54 mg BID and 27 mg BID) as compared to placebo. The primary efficacy endpoint for the trial was the relative change in 24-hour cough frequency (coughs per hour) for the modified intent-to-treat, or mITT, population at the end of Week 6 versus Baseline for Haduvio compared to placebo, as measured via an objective cough monitor. The mITT population consists of all randomized patients who received at least one dose of study drug or placebo (n=165). The primary efficacy endpoint in the Phase 2b CORAL trial was achieved, demonstrating statistically significant reductions in 24-hour cough frequency across all dose groups at Week 6. The 108 mg BID, 54 mg BID and 27 mg BID dose groups achieved statistically significant reductions from Baseline of 60.2% ($p<0.0001$), 53.4% ($p<0.0001$), and 47.9% ($p<0.01$), respectively, compared to a placebo reduction from Baseline of 16.9%.

We have completed an End-of-Phase 2 meeting with the FDA. At the meeting, we gained overall alignment on the plan for the remaining clinical studies to potentially support an NDA submission for nalbuphine ER, including two pivotal Phase 3 clinical trials and agreement on the remaining Phase 1 clinical studies. The Phase 3 trials will run in parallel, and we remain on track to initiate the first Phase 3 trial in the second quarter of 2026 and the second Phase 3 trial in the second half of 2026. The first of the two Phase 3 trials is planned to enroll approximately 300 patients and have 52 weeks of fixed dosing with nalbuphine ER 54 mg twice-a-day (BID), with the primary endpoint at 24 weeks of fixed dosing. The second Phase 3 trial is planned to enroll approximately 130 patients and have 12 weeks of fixed dosing with nalbuphine ER 54 mg BID. The primary efficacy endpoint for both trials will be the relative change from Baseline in 24-hour cough frequency (coughs per hour), as determined by an objective cough monitor, for nalbuphine ER compared with placebo. These trial designs are subject to final review of the protocols by the FDA.

Non-IPF ILD-related Chronic Cough Program. We also plan to develop Haduvio for the treatment of non-IPF ILD-related chronic cough. We plan to initiate an adaptive design Phase 2b clinical trial for the treatment of patients with non-IPF ILD-related chronic cough in the second half of 2026, subject to review of the protocol for the trial by the FDA.

RCC Program. We are developing Haduvio for the treatment of RCC, which affects approximately 2-3 million adults in the U.S. and is related to biological changes in the central and peripheral nervous systems that lower the threshold of the cough reflex. It is highly disruptive and accompanied by a wide range of complications, ranging from urinary incontinence in females to sleep disruption and social embarrassment that causes significant social and economic burden for patients and those around them.

In March 2025, we announced positive topline data from our Phase 2a clinical trial of Haduvio for the treatment of patients with RCC, which we refer to as the Phase 2a RIVER trial. The Phase 2a RIVER trial was a randomized, double-blind, placebo-controlled, two-treatment, two-period, crossover study that was designed to evaluate the efficacy, safety, tolerability and dosing of Haduvio for the treatment of patients with RCC. The primary endpoint of the trial was the mean change in 24-hour cough frequency, as determined by an objective cough monitor, for the full analysis set population. In the trial, Haduvio met the primary endpoint at Day 21 with a statistically significant reduction in the objective 24-hour cough frequency of 67% from Baseline and 57% from Baseline on a placebo-adjusted basis ($p<0.0001$). Planned analyses of all pre-specified secondary endpoints, including patient reported endpoints, at the end of treatment were also statistically significant. The safety results of the trial were generally consistent with the known safety profile of Haduvio from previous trials in other patient populations and there were no serious adverse events reported in the trial.

We expect to initiate a Phase 2b trial of Haduvio for the treatment of patients with RCC in the second quarter of 2026, which we are planning to conduct in the United Kingdom, Canada, and possibly other European countries. The trial is subject to final review of the protocol by regulatory authorities.

Other NDA Supportive Studies. We also plan to continue to progress and advance NDA supportive studies necessary for regulatory approval, including Phase 1 clinical studies such as completing our respiratory safety study, and conducting drug-drug interaction, food effect, and hepatic and renal impairment studies.

Since commencing operations in 2011, we have devoted substantially all of our efforts and financial resources to the clinical development of Haduvio. We have not generated any revenue from product sales and, as a result, we have never been profitable and have incurred net losses in each year since commencement of our operations. As of December 31, 2025, we had an accumulated deficit of $329.8 million, primarily as a result of research and development and general and administrative expenses. We do not expect to generate product revenue unless and until we obtain marketing approval for and commercialize Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD, or RCC and we can provide no assurance that we will ever generate significant revenue or profits.

As of December 31, 2025, we had cash, cash equivalents and marketable securities of $188.3 million. We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements for at least 12 months from the date of issuance of the Consolidated Financial Statements included in this Annual Report on Form 10-K.

We expect to incur substantial expenditures in the foreseeable future as we advance Haduvio through clinical development, the regulatory approval process and, if approved, commercial launch activities. Specifically, in the near term, we expect to incur substantial expenses relating to the trials we are conducting and plan to conduct for Haduvio including our planned Phase 3 trials for the treatment of IPF-related chronic cough, our planned adaptive design Phase 2b clinical trial of Haduvio for the treatment of non-IPF ILD-related chronic cough, our planned Phase 2b clinical trial of Haduvio for the treatment of patients with RCC, and any supportive studies necessary for regulatory approval.

We will need substantial additional funding to support our continuing operations and pursue development and commercialization of Haduvio. Until such time that we can generate significant revenue from sales of Haduvio, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. Adequate funding may not be available to us on acceptable terms or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of Haduvio for one or more indications or delay our efforts to expand our product pipeline.

Components of Operating Results

Operating Expenses

Research and Development Expenses

For the periods presented, all of our research and development expenses consist of expenses incurred in connection with the development of Haduvio. These expenses include personnel-related costs, including stock-based compensation, consulting costs, fees paid to contract research organizations, or CROs, to conduct certain research and development activities on our behalf, contract manufacturing costs and fees paid to other vendors that provide goods and services related to our clinical trials. We do not allocate all of our costs by each indication for which we are developing Haduvio, as a significant amount of our development activities broadly support all indications. In addition, several of our departments support our Haduvio drug candidate development program and we do not identify internal costs for each potential indication.

We expect our research and development expenses to increase as we pursue our development program, pursue regulatory approval of Haduvio in the U.S., Europe and other jurisdictions outside the U.S. and prepare for a possible commercial launch of Haduvio. Predicting the timing or the cost to conduct our Haduvio development program and prepare for a possible commercial launch of Haduvio is difficult and delays may occur because of many factors including factors outside of our control. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on our development program. Furthermore, we are unable to predict when or if Haduvio will receive regulatory approval in the U.S. or elsewhere with any certainty.

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs, including stock-based compensation for personnel in executive, finance, commercial and other administrative functions; professional fees for legal, information technology, consulting and accounting services; as well as rent and other general operating expenses not otherwise classified as research and development expenses.

We anticipate that our general and administrative expenses will increase as a result of increased personnel costs, including stock-based compensation and expanded infrastructure. We also anticipate that our general and administrative expenses will increase as we expect to continue to incur increased costs as we continue to prepare for compliance with Section 404 of the Sarbanes-Oxley Act of 2002, or SOX 404(b).

Other Income (Expense), Net

Interest Income, Net

Interest income, net consists of interest earned primarily on our cash, cash equivalents and marketable securities as well as accretion of discounts/amortization of premiums on purchases of marketable securities.

Other Income, Net

Other income, net consists of foreign currency transaction gains and losses.

Interest Expense

Interest expense consists of the interest expense associated with our finance lease.

Results of Operations

Comparison of the Years Ended December 31, 2025 and 2024

The following table summarizes our results of operations for the periods indicated (in thousands):

	Year Ended December 31,		
	2025	2024	Change
Operating expenses:			
Research and development	$ 33,478	$ 39,377	$ (5,899)
General and administrative	15,850	12,147	3,703
Total operating expenses	49,328	51,524	(2,196)
Loss from operations	(49,328)	(51,524)	2,196
Other income (expense):			
Interest income, net	6,536	3,602	2,934
Other expense, net	(31)	(15)	(16)
Interest expense	—	(4)	4
Total other income, net	6,505	3,583	2,922
Loss before income taxes	(42,823)	(47,941)	5,118
Income tax benefit	(64)	(30)	(34)
Net loss	$ (42,759)	$ (47,911)	$ 5,152

Operating Expenses

Research and Development Expenses

The following table summarizes our research and development expenses for the periods indicated (in thousands):

	Year Ended December 31,		
	2025	2024	Change
Clinical development expenses	$ 22,940	$ 31,675	$ (8,735)
Personnel and related expenses	7,777	5,698	2,079
Stock-based compensation expenses	2,241	1,443	798
Other research and development expenses	520	561	(41)
Total research and development expenses	$ 33,478	$ 39,377	$ (5,899)

Research and development expenses for the year ended December 31, 2025 decreased to $33.5 million from $39.4 million for the corresponding period in 2024, primarily due to decreased clinical development expenses for our HAP study, our Phase 2a RIVER trial, and our Phase 2b CORAL trial, all of which were actively enrolling patients in the prior year period, partially offset by increased costs incurred associated with our recently completed Phase 1 drug-drug interaction study. This overall decrease was partially offset by an increase in personnel related expenses due to increased headcount along with a corresponding increase in stock-based compensation expense.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2025 increased to $15.9 million from $12.1 million for the corresponding period in 2024, primarily due to an increase in outside services and professional fees, personnel related expenses and stock-based compensation. The increased outside services and professional fees were primarily due to increased costs as we continue to prepare for compliance with SOX 404(b). The increased personnel related expenses and stock-based compensation were primarily due to severance costs along with increased headcount.

Other Income, Net

Other income, net for the year ended December 31, 2025 was $6.5 million compared to other income, net of $3.6 million for the corresponding period in 2024. The change was primarily due to an increase in interest income from higher invested cash equivalent and marketable securities balances.

Liquidity and Capital Resources

Since our inception, we have not generated any revenue and have incurred significant operating losses and negative cash flows from our operations.

On June 5, 2025, we issued and sold 17,400,000 shares of our common stock to the public in an underwritten offering, or the June 2025 Offering, at an offering price of $5.75 per share of common stock pursuant to an underwriting agreement with Morgan Stanley & Co. LLC, Leerink Partners LLC, Stifel, Nicolaus & Company, Incorporated and Cantor Fitzgerald & Co., as representatives of the several underwriters. In connection with the offering, we also granted the

underwriters a 30-day option to purchase up to an additional 2,610,000 shares of common stock at the price to the public, less underwriting discounts and commissions. The underwriters option was exercised in full and settled in cash, concurrent with the offering. The June 2025 Offering resulted in aggregate gross proceeds to us of approximately $115.1 million.

On December 17, 2024, we issued and sold 12,500,000 shares of our common stock to certain investors in an underwritten registered direct offering, or the December 2024 Offering, at an offering price of $4.00 per share of common stock pursuant to an underwriting agreement with Leerink Partners LLC, Stifel, Nicolaus & Company, Incorporated, and Oppenheimer & Co. Inc, as representatives of the several underwriters. The December 2024 Offering resulted in aggregate gross proceeds to us of approximately $50.0 million.

In June 2023, we filed with the SEC a universal shelf registration statement on Form S-3, or the 2023 Shelf Registration Statement, which allowed us to offer and sell up to $200.0 million of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The 2023 Shelf Registration Statement was declared effective on August 15, 2023. Further, in June 2023, we entered into a new sales agreement with Leerink Partners, LLC (formerly SVB Securities LLC), which we refer to as the ATM Sales Agreement, under which we may issue and sell shares of common stock, from time to time by any method that is deemed an "at-the-market" offering as defined in Rule 415(a)(4) under the Securities Act. We are not obligated to make any sales of our common stock under the ATM Sales Agreement. We filed a prospectus under the 2023 Shelf Registration Statement for the offer and sale of shares of our common stock having an aggregate offering price of up to $75.0 million pursuant to the ATM Sales Agreement. In accordance with the terms of the ATM Sales Agreement, the sales agreement we had entered into with SVB Securities LLC in 2020 terminated upon effectiveness of the 2023 Shelf Registration Statement, at which point we were no longer able to issue and sell shares of our common stock under such prior sales agreement.

In November 2025, we filed an automatic universal shelf registration statement on Form S-3, or the 2025 Shelf Registration Statement, with the SEC, which became effective upon filing. The 2025 Shelf Registration Statement permits us to offer and sell an indeterminate amount of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The 2025 Shelf Registration Statement was filed to replace our prior universal shelf registration statement. Concurrently with the filing of the 2025 Shelf Registration Statement, we filed a new prospectus supplement pursuant to which shares of our common stock having an aggregate offering price of up to $200.0 million may be offered and sold from time to time under the ATM Sales Agreement. No shares were sold under the ATM Sales Agreement during the twelve months ended December 31, 2025.

Cash Flows

The following table summarizes our cash flows for each of the periods presented below (in thousands):

	Twelve Months Ended December 31,		
	2025	2024	Change
Net cash used in operating activities	$ (42,089)	$ (38,256)	$ (3,833)
Net cash used in investing activities	(94,107)	(21,528)	(72,579)
Net cash provided by financing activities	121,013	61,484	59,529
Net (decrease) increase in cash and cash equivalents	$ (15,183)	$ 1,700	$ (16,883)

Operating Activities

During the year ended December 31, 2025, operating activities used $42.1 million of net cash, resulting from our net loss of $42.8 million and changes in our operating assets and liabilities of $3.5 million partially offset by net non-cash charges of $4.2 million. Changes in our operating assets and liabilities for the year ended December 31, 2025 consisted primarily of a $1.5 million increase in prepaid expenses and other current assets, a $1.4 million decrease in accrued expenses and other liabilities and a $0.6 million decrease in accounts payable. The increase in prepaid expenses and other current assets was primarily due to an increase in accrued interest and dividends receivable from our higher invested cash equivalent and marketable securities balances, as well as an increase in deposits related to our clinical trial work performed by our CROs. The decrease in accrued expenses and other liabilities was primarily due to a decrease in accruals for clinical development and clinical trial work performed by our CROs. The decrease in accounts payable was primarily due to the timing of vendor invoices. The non-cash charges consisted primarily of stock-based compensation expense of $5.2 million, and a $0.4 million change in value of our operating lease right-of-use assets and liabilities, which were partially offset by $1.6 million of accretion of our available-for-sale marketable securities.

During the year ended December 31, 2024, operating activities used $38.3 million of net cash, resulting from our net loss of $47.9 million partially offset by changes in our operating assets and liabilities of $6.8 million and net non-cash charges of $2.8 million. Changes in our operating assets and liabilities for the year ended December 31, 2024 consisted

primarily of a $2.7 million decrease in prepaid expenses and other current assets, a $2.6 million increase in accrued expenses and other liabilities and a $1.6 million increase in accounts payable. The decrease in prepaid expenses and other current assets was primarily due to a decrease in prepayments related to our clinical trial work performed by our CROs. The increase in accrued expenses and other liabilities was primarily due to an increase in accruals for clinical development and clinical trial work performed by our CROs. The increase in accounts payable was primarily due to the timing of vendor invoices. The non-cash charges consisted primarily of stock-based compensation expense of $3.6 million, a $0.5 million change in value of our operating lease right-of-use assets, which were partially offset by $1.4 million of accretion of our available-for-sale marketable securities.

Investing Activities

During the year ended December 31, 2025, net cash used in investing activities was $94.1 million, primarily related to $170.7 million of purchases of available-for-sale marketable securities partially offset by $76.6 million of proceeds from maturities of available-for-sale marketable securities.

During the year ended December 31, 2024, net cash used in investing activities was $21.5 million, consisting of $98.5 million of purchases of available-for-sale marketable securities, partially offset by $77.0 million of proceeds from maturities of available-for-sale marketable securities.

Financing Activities

During the year ended December 31, 2025, net cash provided by financing activities was $121.0 million, primarily consisting of cash proceeds of $108.2 million, net of commissions from sales of our common stock in our June 2025 Offering, $10.8 million from the exercise of warrants, $2.1 million from the exercise of stock options and $0.7 million from the disgorgement of short swing profits from a beneficial owner of our common stock, partially offset by $0.8 million in payments of offering costs related to the June 2025 and December 2024 Offerings.

During the year ended December 31, 2024, net cash provided by financing activities was $61.5 million, consisting of cash proceeds of $47.0 million, net of commissions from sales of our common stock in our December 2024 Offering, cash proceeds of $14.1 million, net of commissions from sales of our common stock under the ATM Sales Agreement, $0.4 million of cash proceeds from the exercise of stock options.

Funding Requirements

We expect to incur substantial expenditures in the foreseeable future as we advance Haduvio through clinical development, the regulatory approval process and, if approved, commercial launch activities. Specifically, in the near term, we expect to incur substantial expenses relating to:

- our planned Phase 3 trials and any additional trials of Haduvio for the treatment of IPF-related chronic cough;
- our planned adaptive design Phase 2b clinical trial and any additional trials of Haduvio for the treatment of non-IPF ILD-related chronic cough;
- our planned Phase 2b clinical trial and any additional trials of Haduvio for the treatment of patients with RCC;
- our planned Phase 1 NDA supportive studies.

In addition, we may incur additional expenses:

- if we determine to conduct additional clinical trials of Haduvio for other indications; and
- if we acquire or in-license rights to or develop other potential product candidates or technologies and seek regulatory and marketing approvals for Haduvio or any future product candidate that successfully completes clinical trials.

We expect to continue to incur costs associated with operating as a public company, including significant legal, accounting, information technology, investor relations and other expenses.

We will need substantial additional funding to support our continuing operations. Until such time as we can generate significant revenue from sales of Haduvio, if ever, we expect to finance our operations through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms or at all. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of Haduvio, including our planned Phase 3 trials of Haduvio for the treatment of IPF-related chronic cough, our planned adaptive design Phase 2b clinical trial of Haduvio for the treatment of non-IPF ILD-related chronic cough, our planned Phase 2b clinical trial for the

treatment of RCC, and our planned Phase 1 NDA supportive studies, as well as trials for any future product candidates and the costs of seeking regulatory approvals;

- the number and characteristics of indications for which we seek to develop Haduvio or any future product candidates and their respective development requirements;
- the costs to manufacture necessary quantities of Haduvio or any future product candidate for clinical development in connection with regulatory submissions;
- the costs of commercialization activities for Haduvio for the treatment of IPF-related chronic cough, non-IPF ILD and RCC or for any future product candidates that receive marketing approval, if any, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approvals, revenue, if any, received from commercial sales of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD or RCC or from any future product candidates;
- our ability to identify potential collaborators for Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD or RCC or for any future product candidates, and the terms and timing of any collaboration agreement that we may establish for the development and any commercialization of such product candidates;
- the extent to which we acquire or in-license rights to other potential product candidates or technologies and the terms and timing of any such acquisition or licensing arrangements;
- our potential obligation to make milestone payments to Keenova Therapeutics plc, or Keenova, which would become due upon the successful completion of the first Phase 3 clinical trial of a licensed product candidate and the marketing approval of a licensed product in the U.S., as well as our potential obligations to pay Keenova royalties on the net sales of the product;
- our headcount growth and associated costs as we expand our research and development activities and medical affairs activities and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining, expanding and protecting our intellectual property rights and defending against intellectual property-related claims;
- the effect of competing technologies and market developments;
- our ability to establish and maintain healthcare coverage and adequate reimbursement for our products; and
- the costs of operating as a public company.

We believe that our existing cash, cash equivalents and marketable securities, will enable us to fund our operating expenses and capital expenditure requirements into 2028. We expect these resources will enable us to fund our planned Phase 3 trials of Haduvio for the treatment of IPF-related chronic cough, our planned adaptive design Phase 2b clinical trial in non-IPF ILD-related chronic cough, our planned Phase 2b clinical trial in RCC, and our planned Phase 1 NDA supportive studies. However, these resources will not be sufficient for us to fund Haduvio for any indication or any future product candidates through regulatory approval, and we will need to raise substantial additional capital to complete the development and commercialization of Haduvio and any future product candidates.

We have based our estimates as to how long we expect we will be able to fund our operations on assumptions that may prove to be wrong and we could use our available capital resources sooner than we currently expect, in which case we would be required to obtain additional financing and financing may not be available to us on acceptable terms, on a timely basis or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We do not have any committed external source of funds. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations, licensing arrangements or other sources to complete the clinical development and commercialization of Haduvio for the treatment of chronic cough in patients with IPF, non-IPF ILD or RCC or any other indication. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any debt financing into which we enter would result in fixed payment obligations and may involve agreements that include grants of security interests on our assets and restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, granting liens over our assets, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's

ability to oversee the development of our product candidates. Any debt financing that we seek or additional equity that we raise may contain terms that could adversely affect our common stockholders.

If we are unable to raise sufficient capital as and when needed, we may be required to delay, reduce or abandon our product development programs or commercialization efforts. If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

Contractual Obligations and Commitments

A significant portion of our development activities are outsourced to third parties under agreements, including with CROs and contract manufacturers in connection with the production of clinical trial materials. The contracts are cancelable at any time by us, generally upon 45 to 60 days' prior written notice to the CRO, and therefore we believe that our non-cancelable obligations under these agreements are not material.

For information related to our future commitments relating to our lease and licensing agreements, see Note 5, “Leases” and Note 12, “Collaborative and Licensing Agreements” of our Consolidated Financial Statements.

Critical Accounting Policies and Use of Estimates

Our Consolidated Financial Statements have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these Consolidated Financial Statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the Consolidated Financial Statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We believe that the estimates and assumptions involved in the accounting policy described below may have the greatest potential impact on our Consolidated Financial Statements and, therefore, consider this to be our critical accounting policy.

Research and Development Expenses

Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized and recognized as an expense as the goods are delivered or the related services are performed.

We have entered into agreements with CROs, contract manufacturing organizations and other companies that provide services in connection with our research and development activities. Our research and development expenses as well as prepaid and accrued expenses related to these agreements, are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, timing of payments made, and contracted costs. The estimated costs of research and development provided, but not yet invoiced, are included in accrued expenses on our consolidated balance sheet. If the actual timing of the performance of services or the level of effort varies from the original estimates, we will adjust the accrual accordingly. Payments made to CROs, contract manufacturing organizations and other companies under these arrangements in advance of the performance of the related services are recorded as prepaid expenses.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Not applicable.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15 of Part IV of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Securities

Exchange Act of 1934, as amended, or the Exchange Act, as of December 31, 2025. Our disclosure controls and procedures are designed to ensure that information we are required to disclose in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosures, and is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Because of the inherent limitations in all control systems, no evaluation of controls and procedures can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected. Based on the evaluation of our disclosure controls and procedures as of December 31, 2025, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the 2013 framework in Internal Control–Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under that framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2025.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting as we are a non-accelerated filer and a "smaller reporting company", as defined in Rule 12b-2 under the Exchange Act.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2025 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

(c) Director and Officer Trading Arrangements

During the three months ended December 31, 2025, none of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K).

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) Financial Statements

The following Consolidated Financial Statements are filed as part of this Annual Report on Form 10-K.

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits.

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of Trevi Therapeutics, Inc., as amended (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38886) filed with the SEC on August 10, 2023)
3.2	Amended and Restated Bylaws of Trevi Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on April 14, 2023)
4.1	Specimen Stock Certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
4.2	Description of Registrant's Securities (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K (File No. 001-38886) filed with the SEC on March 20, 2024)
4.3	Form of 7-Year Common Stock Warrant dated October 18, 2021 (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on October 19, 2021)
4.4	Form of 3.5-Year Common Stock Warrant dated October 18, 2021 (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on October 19, 2021)
4.5	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on April 7, 2022)
4.6	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on September 23, 2022)
10.1	Second Amended and Restated Investors' Rights Agreement dated as of July 14, 2017 (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.2+	2012 Stock Incentive Plan, as amended (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.3+	Form of Nonstatutory Stock Option Agreement under the 2012 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.4+	2019 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.5+	Form of Stock Option Agreement under the 2019 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.6+	2019 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.7*+	Non-Employee Director Compensation Policy

10.8+	Trevi Therapeutics, Inc. Executive Separation Benefits and Retention Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on September 24, 2019)
10.9+	Employment Agreement, dated December 4, 2012, by and between the Registrant and Jennifer L. Good (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.10+	Offer Letter, dated as of September 27, 2024, by and between the Registrant and James Cassella, Ph.D. (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q (File No. 001 38886) filed with the SEC on November 6, 2024)
10.11+	Offer Letter, dated as of December 1, 2025, by and between the Registrant and David Hastings
10.12+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.13	Indenture of Lease, dated February 6, 2013, by and between First Niagara Bank, N.A. and the Registrant (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.14	First Amendment to Lease, dated December 5, 2017, by and between the Registrant and 195 Church Street Associates, LLC (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.15	Second Amendment to Lease, dated November 21, 2022, by and between the Registrant and 195 Church Street Associates, LLC (incorporated by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K (File No. 001-38886) filed with the SEC on March 16, 2023)
10.16†	Exclusive License Agreement, dated as of May 13, 2011, by and between the Registrant and Penwest Pharmaceuticals Co. (incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
10.17	Share Purchase Agreement, dated as of May 6, 2019, by and between the Registrant and New Enterprise Associates 16, L.P. (incorporated by reference to Exhibit 10.17 to Amendment No. 3 to Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on May 7, 2019)
10.18	Form of Securities Purchase Agreement dated September 30, 2021 (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on October 1, 2021)
10.19	Form of Registration Rights Agreement dated September 30, 2021 (incorporated by reference to Exhibit 99.2 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on October 1, 2021)
10.20	Form of Securities Purchase Agreement dated October 15, 2021 (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on October 19, 2021)
10.21	Form of Registration Rights Agreement dated October 15, 2021 (incorporated by reference to Exhibit 99.2 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on October 19, 2021)
10.22	Securities Purchase Agreement, dated April 6, 2022, by and among the Registrant and the Purchasers named therein (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on April 7, 2022)
10.23	Registration Rights Agreement, dated April 6, 2022, by and among the Registrant and the Purchasers named therein (incorporated by reference to Exhibit 99.2 to the Registrant's Current Report on Form 8-K (File No. 001-38886) filed with the SEC on April 7, 2022)
19.1*	Amended and Restated Insider Trading Policy
21.1	List of Subsidiaries (incorporated by reference to Exhibit 21.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230745) filed with the SEC on April 5, 2019)
23.1*	Consent of Ernst & Young LLP, independent registered public accounting firm
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
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
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
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
97	Dodd-Frank Compensation Recovery Policy (incorporated by reference to Exhibit 97 to the Registrant's Annual Report on Form 10-K (File No. 001-38886) filed with the SEC on March 20, 2024)
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document
104	104 Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* Filed herewith.

+ Management contract or compensatory plan or arrangement.

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

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) 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**.**

TREVI THERAPEUTICS, INC.

Date: March 17, 2026

By: /s/ Jennifer L. Good
Jennifer L. Good
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Jennifer L. Good **Jennifer L. Good**	President and Chief Executive Officer, Director (Principal Executive Officer)	March 17, 2026
/s/ David C. Hastings **David C. Hastings**	Chief Financial Officer (Principal Financial Officer)	March 17, 2026
/s/ Christopher Galletta **Christopher Galletta**	Controller (Principal Accounting Officer)	March 17, 2026
/s/ David Meeker, M.D. **David Meeker, M.D.**	Chairman of the Board	March 17, 2026
/s/ Dominick Colangelo **Dominick Colangelo**	Director	March 17, 2026
/s/ Michael Heffernan **Michael Heffernan**	Director	March 17, 2026
/s/ Edward Mathers **Edward Mathers**	Director	March 17, 2026
/s/ Anne VanLent **Anne VanLent**	Director	March 17, 2026

Trevi Therapeutics, Inc.

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Years Ended December 31, 2025 and 2024

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Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

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

Basis for Opinion

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

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

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

Critical Audit Matter

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

	Research and Development Expenses – Contract research organizations costs
Description of the Matter	As discussed in Note 2 to the consolidated financial statements, research and development costs are expensed as incurred. Research and development expenses include work performed by third party contract research organizations ("CROs"). These expenses are estimated based on the level of services performed, progress of the studies, including the phase or completion of events and contracted costs. Auditing the Company's CRO costs was especially complex because the underlying data is accumulated from multiple sources and utilized various assumptions. Such assumptions, including the determination of the work that has been completed and measurement of

	progress during the reporting period, require judgment because the timing and pattern of vendor invoicing may not correspond to the level of services provided.
How We Addressed the Matter in Our Audit	To test the CRO costs, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in the estimates and evaluating the significant assumptions made by management. To test management inputs, we inspected a sample of the Company's contracts with third-party CROs to evaluate financial and other contractual terms, corroborated the progress and timelines of a sample of clinical trials with the Company's internal personnel that oversee these activities, and obtained confirmation directly from CROs which included estimates of clinical trial costs incurred to date. We also examined, on a sample basis, invoices received from CROs through December 31, 2025 and invoices received from and cash disbursements made to CROs subsequent to December 31, 2025.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.

New York, New York

March 17, 2026

Trevi Therapeutics, Inc.

Consolidated Balance Sheets

(Amounts in thousands, except share and per share amounts)

	December 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 18,914	$ 34,097
Marketable securities	169,346	73,525
Prepaid expenses	1,263	939
Other current assets	2,133	867
Total current assets	191,656	109,428
Operating lease right-of-use assets	677	915
Property, equipment and leasehold improvements, net	178	157
Other non-current assets	928	243
Finance lease right-of-use assets	—	157
Total assets	$ 193,439	$ 110,900
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,911	$ 3,414
Accrued expenses	5,531	6,810
Operating lease liabilities	307	254
Finance lease liabilities	—	31
Total current liabilities	9,749	10,509
Operating lease liabilities	446	747
Total liabilities	10,195	11,256
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock: $0.001 par value; 5,000,000 shares authorized at December 31, 2025 and December 31, 2024; no shares issued or outstanding at December 31, 2025 and December 31, 2024.	—	—
Common stock: $0.001 par value; 200,000,000 shares authorized at December 31, 2025 and December 31, 2024; and 128,306,056 and 93,602,631 shares issued and outstanding at December 31, 2025 and December 31, 2024, respectively.	128	94
Additional paid-in capital	512,772	386,534
Accumulated other comprehensive income	148	61
Accumulated deficit	(329,804)	(287,045)
Total stockholders' equity	183,244	99,644
Total liabilities and stockholders' equity	$ 193,439	$ 110,900

See accompanying notes.

Trevi Therapeutics, Inc.

Consolidated Statements of Comprehensive Loss

(Amounts in thousands, except share and per share amounts)

	Year Ended December 31,	
	2025	2024
Operating expenses:		
Research and development	$ 33,478	$ 39,377
General and administrative	15,850	12,147
Total operating expenses	49,328	51,524
Loss from operations	(49,328)	(51,524)
Other income (expense):		
Interest income, net	6,536	3,602
Other expense, net	(31)	(15)
Interest expense	—	(4)
Total other income, net	6,505	3,583
Loss before income taxes	(42,823)	(47,941)
Income tax benefit	(64)	(30)
Net loss	$ (42,759)	$ (47,911)
Basic and diluted net loss per common share outstanding	$ (0.32)	$ (0.47)
Weighted average common shares used in net loss per share attributable to common stockholders, basic and diluted	134,747,198	101,971,873
Net loss	$ (42,759)	$ (47,911)
Other comprehensive income:		
Net unrealized gains on available-for-sale marketable securities	87	90
Comprehensive loss	$ (42,672)	$ (47,821)

See accompanying notes.

Trevi Therapeutics, Inc.

Consolidated Statements of Stockholders' Equity

(Amounts in thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2023	68,283,699	$ 68	$ 321,642	$ (29)	$ (239,134)	82,547
Stock-based compensation	—	—	3,588	—	—	3,588
Issuance of common stock from exercise of stock options	262,009	—	394	—	—	394
Issuance of common stock from Employee Stock Purchase Plan	45,483	—	70	—	—	70
Issuance of common stock under the at-the-market sales agreement, net of commissions and allocated fees	4,498,065	5	14,094	—	—	14,099
Issuance of common stock from pre-funded warrant exercise	8,013,375	8	(8)	—	—	—
Issuance of common stock under offering, less issuance costs	12,500,000	13	46,754	—	—	46,767
Unrealized gains on available-for-sale marketable securities	—	—	—	90	—	90
Net loss	—	—	—	—	(47,911)	(47,911)
Balance at December 31, 2024	93,602,631	$ 94	$ 386,534	$ 61	$ (287,045)	$ 99,644
Stock-based compensation	—	—	5,185	—	—	5,185
Issuance of common stock from exercise of stock options	851,567	—	2,079	—	—	2,079
Issuance of common stock from Employee Stock Purchase Plan	28,131	—	118	—	—	118
Issuance of common stock from warrant exercise	7,851,852	8	10,749	—	—	10,757
Issuance of common stock from pre-funded warrant exercise	5,961,875	6	(6)	—	—	—
Issuance of common stock under offering, less issuance costs	20,010,000	20	107,388	—	—	107,408
Unrealized gains on available-for-sale marketable securities	—	—	—	87	—	87
Proceeds from disgorgement of beneficial owner's short-swing profits	—	—	725	—	—	725
Net loss	—	—	—	—	(42,759)	(42,759)
Balance at December 31, 2025	128,306,056	$ 128	$ 512,772	$ 148	$ (329,804)	$ 183,244

See accompanying notes.

Trevi Therapeutics, Inc.

Consolidated Statements of Cash Flows

(Amounts in thousands)

	Year Ended December 31,	
	2025	**2024**
Operating activities:		
Net loss	$ (42,759)	$ (47,911)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	5,185	3,588
Operating lease right-of-use assets	437	460
Depreciation and amortization	144	147
Accretion of available-for-sale marketable securities, net	(1,638)	(1,367)
Write off of deferred offering costs	26	—
Loss on disposal of property, equipment and leasehold improvements	7	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,478)	2,659
Accrued expenses and other liabilities	(1,415)	2,563
Accounts payable	(598)	1,605
Net cash used in operating activities	(42,089)	(38,256)
Investing activities:		
Proceeds from maturities of available-for-sale marketable securities	76,567	76,970
Purchases of available-for-sale marketable securities	(170,662)	(98,463)
Purchases of property, equipment and leasehold improvements	(12)	(35)
Net cash used in investing activities	(94,107)	(21,528)
Financing activities:		
Proceeds from offering, net of commissions	108,154	47,000
Proceeds from exercises of warrants	10,757	—
Proceeds from exercises of stock options	2,079	394
Proceeds from disgorgement of beneficial owner's short-swing profits	725	—
Proceeds from employee stock purchase plan	118	70
Payments of offering costs	(809)	—
Payments of finance lease	(11)	(126)
Proceeds from at-the-market sales, net of commissions	—	14,146
Net cash provided by financing activities	121,013	61,484
Net (decrease) increase in cash and cash equivalents	(15,183)	1,700
Cash and cash equivalents at beginning of period	34,097	32,397
Cash and cash equivalents at end of period	$ 18,914	$ 34,097
Supplemental disclosure of cash flow information:		
Interest paid	$ —	$ (4)
State research tax credits exchanged for cash	$ 33	$ 32
Supplemental disclosure of non-cash financing activities:		
Offering costs included in accrued expenses	$ —	$ 233

See accompanying notes.

Trevi Therapeutics, Inc.

Notes to Consolidated Financial Statements

(Amounts in thousands, except share and per share data)

1. Nature of the Business

Trevi Therapeutics, Inc. ("Trevi" or the "Company") is a clinical-stage biopharmaceutical company focused on the development and commercialization of the investigational therapy Haduvio (oral nalbuphine ER) for the treatment of chronic cough in patients with idiopathic pulmonary fibrosis ("IPF"), non-IPF interstitial lung disease ("non-IPF ILD"), and refractory chronic cough ("RCC").

Haduvio is an oral extended-release formulation of nalbuphine. Haduvio acts on the cough reflex arc both centrally and peripherally as a kappa receptor agonist and a mu receptor antagonist ("KAMA"), targeting opioid receptors that play a key role in controlling chronic cough. Nalbuphine has been approved and marketed as an injectable for pain indications for decades in the United States ("U.S.") and Europe. Nalbuphine's mechanism of action also mitigates the risk of abuse associated with mu-opioid agonists because it antagonizes or blocks, the mu-opioid receptor. Parenteral nalbuphine is not scheduled as a controlled substance by the U.S. Drug Enforcement Agency and in most of Europe.

The Company's Consolidated Financial Statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. The Company financed its operations prior to its initial public offering ("IPO") primarily through private placements of its redeemable convertible preferred stock and convertible notes, and has financed its operations since becoming a public company primarily through borrowings under its prior term loan facilities, proceeds from its IPO and concurrent private placement completed in May 2019, sales of its common stock pursuant to the at-the-market Sales Agreements (Note 8) with SVB Securities LLC (formerly SVB Leerink LLC) ("SVB Securities") and Leerink Partners LLC, proceeds from private placements completed in October 2021 and April 2022 (Note 8), proceeds from the exercise of warrants, and proceeds from registered offerings completed in October 2022, December 2024 and June 2025 (Note 8). The Company has incurred recurring losses since inception, including net losses of $42.8 million and $47.9 million for the years ended December 31, 2025 and 2024, respectively. As of December 31, 2025, the Company had cash, cash equivalents and marketable securities of $188.3 million compared to $107.6 million of cash, cash equivalents and marketable securities as of December 31, 2024. The Company had incurred losses and negative cash flows from operations and had an accumulated deficit of $329.8 million as of December 31, 2025. The Company expects to continue to incur losses for the foreseeable future. As of March 17, 2026, the date of issuance of these Consolidated Financial Statements, the Company believes that its cash, cash equivalents and marketable securities as of December 31, 2025, will be sufficient to fund its operating expenses and capital expenditure requirements for 12 months from the date of issuance of these Consolidated Financial Statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying Consolidated Financial Statements include the accounts of Trevi Therapeutics, Inc. and its wholly-owned subsidiary Trevi Therapeutics Limited. Intercompany balances and transactions have been eliminated.

All amounts presented are in thousands of dollars, except share and per share amounts, unless noted otherwise. The Company has evaluated events occurring subsequent to December 31, 2025 for potential recognition or disclosure in the Consolidated Financial Statements and concluded there were no subsequent events that required recognition or disclosure.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the U.S. ("GAAP") requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of the expenses during the reporting periods. Significant estimates and assumptions reflected in these Consolidated Financial Statements include but are not limited to the recognition of prepaid expenses, accrued expenses and research and development ("R&D") expenses, the valuation of stock-based awards and the valuation allowance of deferred tax assets. In addition, management's assessment of the Company's ability to continue as a going concern involves the estimation of the amount and timing of future cash inflows and outflows. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

Cash Equivalents

The Company classifies short-term, highly liquid investments with an original term of three months or less at the date of purchase as cash equivalents.

Marketable Securities

The Company generally invests its excess cash in money market funds and investment grade short- to intermediate-term fixed income securities. Such investments are included in cash and cash equivalents or marketable securities on the Consolidated Balance Sheets. Marketable securities with an original maturity date greater than 90 days at each balance sheet date are classified as short-term. Marketable securities are classified as current assets as these investments are intended to be available to the Company for use in funding current operations. All of the Company's marketable securities are considered available-for-sale and are reported at fair value. For securities with unrealized gains and losses, when the Company expects to receive cash flows sufficient to recover the amortized cost basis of a security, such gains and losses are included in accumulated other comprehensive income as a component of stockholders' equity. Credit losses are identified when the Company does not expect to receive cash flows sufficient to recover the amortized cost basis of a security. In the event of a credit loss, only the amount associated with the credit loss is recognized in interest income, net on the Consolidated Statements of Comprehensive Loss. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income, net on the Consolidated Statements of Comprehensive Loss. Realized gains and losses, if any, on marketable securities are included in interest income, net on the Consolidated Statements of Comprehensive Loss. The cost of securities sold is determined using specific identification.

The Company evaluates whether declines in the fair values of its marketable securities below their amortized cost are credit losses on a quarterly basis. This evaluation consists of several qualitative and quantitative factors such as the extent to which the fair value is less than the amortized cost basis and the issuer's financial condition. Additionally, declines in value are evaluated in order to assess whether the decline is other than temporary. In order to perform this evaluation, the Company assesses whether it has plans to sell the marketable security or whether it is more likely than not that it will be required to sell any marketable securities before recovery of its amortized cost basis. Factors considered include quoted market prices, recent financial results and operating trends, implied values from any recent transactions or offers of investee securities, credit quality of debt instrument issuers, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and the Company's strategy and intentions for holding the marketable security.

Fair Value Measurements

The Company's financial instruments have consisted of cash and cash equivalents, available-for-sale marketable securities, other current assets, accounts payable, accrued expenses, term loans and warrants to acquire the Company's common stock. Fair value estimates of these instruments are made at a specific point in time, based on relevant market information. The carrying amounts of cash and cash equivalents, other current assets, accounts payable and accrued expenses are generally considered to be representative of their respective fair values because of the short-term nature of those instruments. Available-for-sale marketable securities are reported at their fair values, based upon pricing of securities with the same or similar investment characteristics as provided by third-party pricing services, as described below. The warrants to acquire the Company's common stock are not required to be accounted for at fair value.

Current accounting guidance defines fair value, establishes a framework for measuring fair value in accordance with Accounting Standards Codification ("ASC") 820, *Fair Value Measurements and Disclosures*, and requires certain disclosures about fair value measurements. The valuation techniques included in the guidance are based on observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, while unobservable inputs reflect market assumptions and are classified into the following fair value hierarchy:

Level 1—Observable inputs—quoted prices in active markets for identical assets and liabilities.

Level 2—Observable inputs other than the quoted prices in active markets for identical assets and liabilities—such as quoted prices for similar instruments, quoted prices for identical or similar instruments in inactive markets, or other inputs that are observable or can be corroborated by observable market data.

Level 3—Unobservable inputs—includes amounts derived from valuation models where one or more significant inputs are unobservable and require the company to develop relevant assumptions.

Valuation Techniques - Level 2 Inputs

The Company estimates the fair values of its financial instruments categorized as level 2 in the fair value hierarchy, including U.S. treasury securities, U.S. government agency obligations, corporate bonds, commercial paper, asset-backed securities and municipal bonds, by taking into consideration valuations obtained from third-party pricing services. The pricing services use industry standard valuation models, including both income- and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities, benchmark yields, issuer credit spreads, benchmark securities,

and other observable inputs. The Company obtains a single price for each financial instrument and does not adjust the prices obtained from the pricing service.

Property, Equipment and Leasehold Improvements

Property, equipment and leasehold improvements (consisting of furniture, computer and office equipment and leasehold improvements) are stated at cost, net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the respective assets (three years for computer equipment, five years for furniture and office equipment, and the shorter of the term of the lease or useful life for leasehold improvements).

Impairment of Long-Lived Assets

The Company continually evaluates whether events or circumstances have occurred that indicate that the estimated remaining useful life of its long-lived assets may warrant revision or that the carrying value of these assets may be impaired. The Company has not recognized any significant impairment charges from inception through December 31, 2025.

Foreign Currency Transactions

The Company, at times, contracts with vendors and consultants outside of the U.S., resulting in liabilities denominated in foreign currency. The transactions are recorded in U.S. dollars on the transaction dates and any currency fluctuation through the payment date is recorded as currency gains or losses in other income, net in the Consolidated Statements of Comprehensive Loss.

Deferred Offering Costs

The Company capitalizes certain legal, professional, accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of an equity financing, these costs are recorded in stockholders' equity as a reduction of additional paid-in capital generated as a result of the financings. Should the planned equity financing no longer be considered probable of being consummated, the deferred offering costs are expensed immediately as a charge to general and administrative expenses. The deferred offering costs are included in Other current assets and Other non-current assets on the Consolidated Balance Sheets.

Research and Development ("R&D") Expenses

All of the Company's R&D expenses consist of expenses incurred in connection with the development of Haduvio. These expenses include certain payroll and personnel expenses, including stock-based compensation, consulting costs, contract manufacturing costs and fees paid to contract research organizations ("CROs") to conduct certain R&D activities on the Company's behalf. The Company expenses both internal and external R&D expenses as they are incurred.

The Company has entered into agreements with CROs, contract manufacturing organizations ("CMOs") and other companies that provide services in connection with the Company's R&D activities. The value of goods and services received from CROs and CMOs in the reporting period are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, timing of payments made and contracted costs. The estimated costs of R&D provided, but not yet invoiced, are included in accrued expenses on the Consolidated Balance Sheets. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly. Payments made to CROs, CMOs and other companies under these arrangements in advance of the performance of the related services are recorded as prepaid expenses or as other current assets on the Consolidated Balance Sheets, as applicable, and are recognized as expenses as the goods are delivered or the related services are performed.

Patent Costs

All patent-related costs in connection with filing and prosecuting patent applications are expensed to general and administrative expense as incurred, as recoverability of such expenditures is uncertain.

Warrants

The Company determines the accounting classification of warrants that are issued, as either liability or equity, by first assessing whether the warrants meet liability classification in accordance with ASC 480, *Distinguishing Liabilities from Equity* ("ASC 480"), and then in accordance with ASC 815, *Derivatives and Hedging* ("ASC 815"), depending on the specific terms of the warrant. Under ASC 480, warrants are considered liability classified if the warrants are mandatorily redeemable, obligate the issuer to settle the warrants or the underlying shares by paying cash or other assets, or must or may require settlement by issuing variable number of shares.

If the warrants do not meet liability classification under ASC 480, the Company assesses the requirements under ASC 815, which states that contracts that require or may require the issuer to settle the contract for cash are liabilities recorded at fair value, irrespective of the likelihood of the transaction occurring that triggers the net cash settlement feature. If the

warrants do not require liability classification under ASC 815, in order to conclude equity classification, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815 or other applicable GAAP. After all relevant assessments are made, the Company concludes whether the warrants are classified as liability or equity. Liability classified warrants are required to be accounted for at fair value both on the date of issuance and on subsequent accounting period ending dates, with all changes in fair value after the issuance date recorded in the statements of comprehensive loss as a gain or loss. For equity classified warrants, no changes in fair value are recognized after the issuance date.

Stock-Based Compensation

The Company accounts for stock-based compensation arrangements with employees and non-employees for consultancy services in accordance with ASC 718, *Stock Compensation* ("ASC 718"). ASC 718 requires the recognition of compensation expense, using a fair-value based method, for costs related to all stock-based awards including stock options. The Company's determination of the fair value of stock-based awards on the date of grant utilizes the Black-Scholes valuation model for stock options with time-based and performance-based vesting and is impacted by the price of its common stock as well as changes in assumptions regarding a number of subjective variables. These variables include the expected term that stock options will remain outstanding, expected common stock price volatility over the term of the stock options, risk-free interest rates and expected dividends.

Changes in the variables can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require analysis and judgment to develop.

Expected Term—The expected term assumption represents the weighted average period that the stock-based awards are expected to be outstanding. The Company has elected to use the "simplified method" for estimating the expected term of its stock options, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the stock option.

Expected Volatility—For all stock options granted to date, the volatility data was estimated based on a study of publicly traded industry peer companies. For purposes of identifying these peer companies, the Company considered the industry, stage of development, size and financial leverage of potential comparable companies.

Expected Dividend—The Black-Scholes valuation model calls for a single expected dividend yield as an input. The Company currently has no history or expectation of paying cash dividends on its common stock.

Risk-Free Interest Rate—The risk-free interest rate is based on the yield available on U.S. Treasury zero-coupon issues similar in duration to the expected term of the stock-based award.

The fair value is recognized over the period during which an optionee is required to provide services in exchange for the stock option, known as the requisite service period (usually the vesting period) on a straight-line basis. For performance-based vesting, the fair value is recognized when it is probable the performance conditions will be achieved. The Company reassesses the probability of achieving the performance conditions at each reporting date. Forfeitures are accounted for as they occur.

Income Taxes

The Company accounts for income taxes using the asset and liability method. Under this method, deferred tax assets and liabilities are determined based on differences between the financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized.

The Company applies the provisions of ASC 740, *Income Taxes*("ASC 740"), which prescribes a comprehensive model for how a company should recognize, measure, present and disclose in its financial statements uncertain tax positions that the company has taken or expects to take on a tax return. These Consolidated Financial Statements reflect expected future tax consequences of such positions presuming the taxing authorities possess full knowledge of the position and all relevant facts. There are no material uncertainties regarding the tax positions that the Company has taken through December 31, 2025 and December 31, 2024. The Company does not have any interest or penalties accrued related to tax positions as it does not have any unrecognized tax benefits.

Leases

Under ASC 842, *Leases*, the Company determines if an arrangement is a lease at its inception. Leases are classified as either operating or finance, based on the Company's evaluation of certain criteria. If a lease has a term greater than one year, the lease is recognized in the balance sheet as a right-of-use asset and a lease liability at lease commencement. The Company elected the short-term lease practical expedient, therefore, if a lease has a term less than one year, the Company will not recognize the lease on its balance sheet. The right-of-use asset represents the Company's right of use to an underlying asset for the term of the lease and the lease liability represents the Company's obligation to make lease payments arising from the lease.

If the Company's leases do not provide an implicit rate within the lease, the Company uses its incremental borrowing rate, based on information available at the commencement date of the lease to determine the present value of the lease payments.

Operating lease right-of-use assets and operating lease liabilities are determined and recognized on the commencement date of the lease based on the present value of lease payments over the term of the lease. For operating leases, rent expense is recognized on a straight-line basis over the term of the lease, and right-of-use assets are subsequently re-measured to reflect the effect of uneven lease payments.

For finance leases, right-of-use assets are amortized on a straight-line basis over the shorter of the lease term or the useful life of the underlying asset. Expenses for finance leases include the amortization of right-of-use assets, which is recorded as depreciation and amortization expense, and interest expense, which reflects interest accrued on the lease liability.

Basic and Diluted Net Loss per Common Share

Basic and diluted net loss per common share outstanding is determined by dividing net loss by the weighted average common shares outstanding during the period. Basic shares outstanding includes the weighted average effect of the Company's outstanding pre-funded warrants, the exercise of which requires little or no consideration for the delivery of shares of common stock.

For all periods presented, shares issuable upon exercise of stock options and warrants to purchase shares of common stock (other than pre-funded warrants) have been excluded from the calculation because their effects would be anti-dilutive. Therefore, the weighted average common shares used to calculate both basic and diluted net loss per share are the same for each of the periods presented.

Segments

The Company has one reportable segment, which is also the Company's only operating segment. Management uses one measurement of profitability and does not segregate its business for internal reporting.

Comprehensive Loss

Comprehensive loss represents the net change in stockholders' equity during a period from sources other than transactions with stockholders. As reflected in the accompanying Condensed Consolidated Statements of Comprehensive Loss, our comprehensive loss is comprised of net losses and unrealized gains and losses on marketable securities.

Recently Adopted Accounting Pronouncements

In November 2023, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2023-07, Segment Reporting (Topic 280): *Improvements to Reportable Segment Disclosures*, which requires quarterly disclosure of segment expenses if they are (i) significant to the segment, (ii) regularly provided to the chief operating decision maker ("CODM") and (iii) included in each reported measure of a segment's profit or loss. In addition, this ASU requires an annual disclosure of the CODM's title and a description of how the CODM uses the segment's profit/loss measure to assess segment performance and to allocate resources. The Company adopted this accounting standard for the fiscal year beginning on January 1, 2024 and it has resulted in incremental disclosures within the footnotes to the Company's consolidated financial statements.

In December 2023, the FASB issued ASU 2023-09, *Improvements to Income Tax Disclosures*, which requires entities to disclose disaggregated information about their effective tax rate reconciliation as well as expanded information on income taxes paid by jurisdiction. The Company adopted this accounting standard, on a prospective basis, for the fiscal year beginning on January 1, 2025 and it has resulted in incremental disclosures within the footnotes to the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements

In November 2024, the FASB issued ASU 2024-03, *Disaggregation of Income Statement Expenses*, which requires disaggregation and disclosure of specified information about certain costs and expenses in the notes to the financial statements. The standard is effective for fiscal years beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027, with early adoption permitted. The Company is currently evaluating the impact of adopting ASU 2024-03.

3. Marketable Securities

The fair value and amortized cost of available-for-sale marketable securities by major security type are presented in the following tables as of the periods presented:

Type of Security	December 31, 2025 Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. treasury securities	$ 62,572	$ 100	—	$ 62,672
Commercial paper	46,773	14	(4)	46,783
Corporate bonds	41,991	17	(3)	42,005
Asset backed securities	13,558	17	—	13,575
U.S. government agency securities	4,304	7	—	4,311
Total marketable securities	$ 169,198	$ 155	$ (7)	$ 169,346

Type of Security	December 31, 2024 Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. treasury securities	$ 22,838	$ 25	$ (12)	$ 22,851
Corporate bonds	18,921	20	—	18,941
Commercial paper	12,999	3	(2)	13,000
U.S. government agency securities	11,402	21	—	11,423
Asset backed securities	7,304	6	—	7,310
Total marketable securities	$ 73,464	$ 75	$ (14)	$ 73,525

The net amortized cost and fair value of available-for-sale marketable securities are presented in the following table as of the periods presented by contractual maturity. Actual maturities may differ from contractual maturities because securities may be restructured, called or prepaid, or the Company may intend to sell a security prior to maturity.

	December 31, 2025 Amortized Cost	Fair Value
Due to mature:		
Less than one year	$ 110,769	$ 110,863
One year through three years	58,429	58,483
Total	$ 169,198	$ 169,346

	December 31, 2024 Amortized Cost	Fair Value
Due to mature:		
Less than one year	$ 55,323	$ 55,386
One year through two years	18,141	18,139
Total	$ 73,464	$ 73,525

During the years ended December 31, 2025 and 2024, there were no realized gains or losses on available-for-sale marketable securities.

As of the years ended December 31, 2025 and 2024, no marketable securities had been in a continuous unrealized loss position for more than 12 months and the Company considered any such losses to be temporary in nature. The Company reviewed the securities in the tables above and considered the decline in market value for these securities to be primarily attributable to economic and market conditions. As of the periods noted in the tables above, the Company did not intend to sell these securities and did not believe it was more likely than not that it would be required to sell these securities before recovery of their amortized cost basis. Additionally, the Company did not recognize any credit losses related to its marketable securities in an unrealized loss position during any of the periods noted in the table above.

As of December 31, 2025 and 2024, accrued interest receivables on the Company's available-for-sale marketable securities were $986 and $532, respectively, and were included within Other current assets as presented on its Consolidated Balance Sheets.

4. Fair Value Measurements

The following table summarizes the Company's financial assets and financial liabilities measured at fair value on a recurring basis and the basis for that measurement, by level within the fair value hierarchy as follows:

Balance Sheet Classification	Type of Instrument	Fair Value Measurement Using: Level 1	Level 2	Level 3	Total
December 31, 2025					
Financial assets:					
Cash equivalents	Money market funds	$ 17,926	$ —	$ —	$ 17,926
Marketable securities	U.S. treasury securities	—	62,672	—	62,672
Marketable securities	Commercial paper	—	46,783	—	46,783
Marketable securities	Corporate bonds	—	42,005	—	42,005
Marketable securities	Asset backed securities	—	13,575	—	13,575
Marketable securities	U.S. government agency securities	—	4,311	—	4,311
Total assets		$ 17,926	$ 169,346	$ —	$ 187,272

Balance Sheet Classification	Type of Instrument	Fair Value Measurement Using: Level 1	Level 2	Level 3	Total
December 31, 2024					
Financial assets:					
Cash equivalents	Money market funds	$ 28,605	$ —	$ —	$ 28,605
Marketable securities	U.S. treasury securities	—	22,851	—	22,851
Marketable securities	Corporate bonds	—	18,941	—	18,941
Marketable securities	Commercial paper	—	13,000	—	13,000
Marketable securities	U.S. government agency securities	—	11,423	—	11,423
Marketable securities	Asset backed securities	—	7,310	—	7,310
Cash equivalents	Commercial paper	—	4,479	—	4,479
Total assets		$ 28,605	$ 78,004	$ —	$ 106,609

5. Leases

The Company entered into a lease for office space in New Haven, Connecticut, effective March 1, 2013, and entered into a First Amendment (the "First Amendment") to such lease on December 5, 2017 and a Second Amendment (the "Second Amendment") to such lease on November 21, 2022 (collectively, the "Office Space Lease"). The leased space approximated 5,600 square feet and, prior to the Second Amendment, the Office Space Lease had a term of 60 months expiring on February 28, 2023. Under the First Amendment, the Company was required to make monthly payments ranging from approximately $10 to $12 through February 1, 2023 and received two designated months of free rent. As a result of the Company entering into the Second Amendment, the leased space increased to 12,500 square feet effective in March 2023 and the term for the Office Space Lease was extended for an additional 60 months from its prior termination date, until February 28, 2028. The Second Amendment requires monthly payments ranging from approximately $23 to $32 effective in March 2023 through February 2028. The first year of payments are based on 10,500 square feet of occupied space, the second year of payments are based on 11,500 square feet of occupied space and the remaining lease payments are based on 12,500 square feet of occupied space.

In December 2022, the Company entered into a 24-month lease for the financing of the furniture installed in the Company's new office space. The furniture lease requires monthly payments of approximately $11 starting in March 2023.

The following table presents the Company's lease-related assets and liabilities as presented on its Consolidated Balance Sheets:

	Classification on the Consolidated Balance Sheet	December 31, 2025	December 31, 2024
Assets:			
Operating lease assets	Operating lease right-of-use assets	$ 677	$ 915
Finance lease assets	Finance lease right-of-use assets	—	157
Total lease assets		$ 677	$ 1,072
Liabilities:			
Current			
Operating lease liabilities	Operating lease liabilities, current portion	$ 307	$ 254
Finance lease liabilities	Finance lease liabilities, current portion	—	31
Non-current			
Operating lease liabilities	Operating lease liabilities, non-current portion	446	747
Total lease liabilities		$ 753	$ 1,032

The following table presents information related to the Company's lease expense for the periods shown:

	Year Ended December 31, 2025	Year Ended December 31, 2024
Operating lease expense	$ 342	$ 341
Finance lease expense	12	48
Total lease expense	$ 354	$ 389

Future minimum lease payments from December 31, 2025 until the expiration of the leases are as follows:

	Operating Leases
2026	$ 371
2027	380
2028	95
2029	—
Total minimum lease payments	846
Less: Amount of lease payments representing interest	(93)
Present value of future minimum lease payments	$ 753

The following table presents certain information related to the lease terms and discount rates for the Company's leases:

	December 31, 2025	December 31, 2024
Weighted average remaining lease term:		
Operating leases	2.2 years	3.3 years
Finance leases	—	0.3 years
Weighted average discount rate:		
Operating leases	10.92%	11.00%
Finance leases	—	4.37%

The following table presents supplemental cash flow information related to the Company's leases for the periods shown:

	Year Ended December 31,	
	2025	2024
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash outflows relating to operating leases	$ 351	$ 303
Finance lease payments	$ 11	$ 126
Supplemental non-cash information:		
Right-of-use assets obtained in exchange for new operating lease liabilities	$ 9	$ —

6. Property, Equipment and Leasehold Improvements, Net

Property, equipment and leasehold improvements, net consist of the following:

	December 31,	
	2025	2024
Computer, website development and office equipment	$ 309	$ 308
Furniture and fixtures	198	41
Leasehold improvements	29	29
Construction in progress	1	7
	537	385
Less: Accumulated depreciation and amortization	(359)	(228)
Total property, equipment and leasehold improvements, net	$ 178	$ 157

Depreciation was $132 and $94 for the years ended December 31, 2025 and 2024, respectively.

7. Accrued Expenses

Accrued expenses consisted of the following:

	December 31,	
	2025	2024
Accrued compensation and benefits	$ 2,746	$ 2,538
Accrued R&D projects	2,043	3,482
Accrued consulting and professional fees	558	747
Accrued other	184	43
Total accrued expenses	$ 5,531	$ 6,810

8. Stockholders' Equity

Preferred Stock

As of December 31, 2025 and 2024, the Company's restated certificate of incorporation authorized the Company to issue 5,000,000 shares of preferred stock, with a par value of $0.001 per share.

Common Stock

As of December 31, 2025 and 2024, the Company's restated certificate of incorporation authorized the Company to issue 200,000,000 shares of common stock, with a par value of $0.001 per share.

The Company had reserved shares of common stock for future issuance as shown in the table below:

	December 31,	
	2025	2024
Shares of common stock reserved for future issuance upon exercise of outstanding warrants and pre-funded warrants	19,100,800	32,915,346
Shares of common stock reserved for future issuance under the 2019 Stock Incentive Plan	9,023,200	7,555,310
Shares of common stock reserved for future issuance under the 2019 Employee Stock Purchase Plan	1,103,842	1,131,973
Shares of common stock reserved for future issuance under the 2012 Stock Incentive Plan	278,418	288,944
	29,506,260	41,891,573

At-the-Market Offering

In June 2020, the Company entered into the ATM Sales Agreement with SVB Securities, under which the Company was able to issue and sell shares of its common stock, from time to time, having an aggregate offering price of up to $12.0 million. In May 2022, the Company and SVB Securities amended the ATM Sales Agreement to increase the maximum aggregate offering price of common stock that it was able to issue and sell from time to time under the ATM Sales Agreement by $50.0 million, from $12.0 million to up to $62.0 million.

Sales of common stock under the ATM Sales Agreement were able to be made by any method that was deemed an "at-the-market" offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended (the "Securities Act"). The Company was not obligated to make any sales of its common stock under the ATM Sales Agreement. The Company began making sales pursuant to the ATM Sales Agreement in July 2020. As of August 15, 2023, the date of termination of the ATM Sales Agreement, the Company had issued and sold an aggregate of 4,333,394 shares of common stock for gross proceeds of $12.7 million pursuant to the ATM Sales Agreement, before deducting estimated commissions and allocated fees of $1.0 million.

In June 2023, the Company filed with the SEC a universal shelf registration statement on Form S-3 (the "2023 Shelf Registration Statement"), which allowed the Company to offer and sell up to $200.0 million of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The 2023 Shelf Registration Statement was declared effective on August 15, 2023. Further, in June 2023, the Company entered into a new at-the-market sales agreement with Leerink Partners LLC (formerly SVB Securities LLC) (the "ATM Sales Agreement"), under which the Company may issue and sell shares of common stock, from time to time by any method that is deemed an "at-the-market" offering as defined in Rule 415(a)(4) under the Securities Act. The Company is not obligated to make any sales of its common stock under the ATM Sales Agreement. The Company filed a prospectus under the 2023 Shelf Registration Statement for the offer and sale of shares of the Company's common stock having an aggregate offering price of up to $75.0 million pursuant to the ATM Sales Agreement. In accordance with the terms of the ATM Sales Agreement, the sales agreement we had entered into with SVB Securities LLC in 2020 terminated upon effectiveness of the 2023 Shelf Registration Statement, at which point the Company was no longer able to issue and sell shares of its common stock under such prior sales agreement. As of December 31, 2024, the Company had issued and sold 4,498,065 shares of common stock under the ATM Sales Agreement for gross proceeds of $14.6 million, before deducting estimated commissions and allocated fees of $0.5 million.

In November 2025, the Company filed an automatic universal shelf registration statement on Form S-3 (the "2025 Shelf Registration Statement") with the SEC, which became effective upon filing. The 2025 Shelf Registration Statement permits the Company to offer and sell an indeterminate amount of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The 2025 Shelf Registration Statement was filed to replace the Company's prior universal shelf registration statement. Concurrently with the filing of the 2025 Shelf Registration Statement, the Company filed a new prospectus supplement pursuant to which shares of the Company's common stock having an aggregate offering price of up to $200.0 million may be offered and sold from time to time under the ATM Sales Agreement. No shares were sold under the ATM Sales Agreement during the year ended December 31, 2025.

Private Placements

On October 5, 2021, the Company issued and sold to an initial investor, in a private placement priced at-the-market under Nasdaq rules, (i) 2,373,201 shares of the Company's common stock and accompanying warrants to purchase an aggregate of 4,746,402 shares of the Company's common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 4,926,069 shares of the Company's common stock and accompanying warrants to purchase an aggregate of 9,852,138

shares of the Company's common stock. All of the pre-funded warrants and accompanying common stock warrants have been exercised.

On October 18, 2021, the Company issued and sold to New Enterprise Associates 16, L.P., an existing stockholder of the Company ("NEA") and related party, in a private placement, 1,851,852 shares of the Company's common stock and accompanying warrants to purchase an aggregate of 3,703,704 shares of the Company's common stock. Each share of the Company's common stock and accompanying common stock warrants were sold together at a combined price of $1.62 for gross proceeds of approximately $3.0 million. The accompanying common stock warrants have an exercise price of $1.37 per share and became exercisable immediately upon issuance. Of the accompanying common stock warrants, warrants to purchase an aggregate of 1,851,852 shares of the Company's common stock were scheduled to expire on April 18, 2025, and warrants to purchase an aggregate of 1,851,852 shares of the Company's common stock will expire on October 18, 2028. On April 17, 2025, NEA exercised all of the warrants that would have expired on April 18, 2025. None of the accompanying common stock warrants issued to NEA in the private placement that expire on October 18, 2028 have been exercised.

On April 6, 2022, the Company entered into a securities purchase agreement with certain purchasers, pursuant to which the Company agreed to issue and sell to the purchasers, in a private placement priced at-the-market under Nasdaq rules, (i) 4,580,526 shares of the Company's common stock at a purchase price of $1.90 per share, and (ii) pre-funded warrants to purchase up to an aggregate of 24,379,673 shares of common stock at a purchase price of $1.899 per warrant (the "April 2022 Private Placement"). Each pre-funded warrant has an exercise price of $0.001 per share, became exercisable immediately upon issuance and will be exercisable until the pre-funded warrant is exercised in full. The April 2022 Private Placement, which closed on April 11, 2022, resulted in gross proceeds to the Company of approximately $55.0 million. NEA, an existing stockholder of the Company and a related party, as well as an affiliate of NEA, participated in the offering. As of December 31, 2025, pre-funded warrants that were issued and sold in the April 2022 Private Placement to purchase 12,531,332 shares of common stock remain outstanding.

Registered Offerings

On September 27, 2022, the Company issued and sold 14,252,670 shares of the Company's common stock and, in lieu of common stock to certain investors, pre-funded warrants to purchase 14,247,330 shares of common stock in a public offering (the "September 2022 Offering"), at a public offering price of $1.93 per share of common stock and $1.929 per pre-funded warrant pursuant to an underwriting agreement (the "Underwriting Agreement") with SVB Securities, Stifel, Nicolaus & Company, Incorporated and Oppenheimer & Co. Inc., as representatives of the several underwriters (the "Underwriters"). Each pre-funded warrant has an exercise price of $0.001 per share, became exercisable immediately upon issuance and will be exercisable until the pre-funded warrant is exercised in full. Under the terms of the Underwriting Agreement, the Company granted the Underwriters an option (the "Option"), exercisable for 30 days, to purchase up to an additional 4,275,000 shares of common stock (the "Additional Shares"), at the public offering price of $1.93 per share. The Underwriters partially exercised the Option to purchase 1,600,428 Additional Shares, which shares were issued and sold on October 25, 2022. The September 2022 Offering, including the initial closing on September 27, 2022 and the Option closing on October 25, 2022, resulted in aggregate gross proceeds to the Company of approximately $58.1 million. As of December 31, 2025, pre-funded warrants that were issued and sold in the September 2022 Offering to purchase 4,717,616 shares of common stock remain outstanding.

On December 17, 2024, the Company issued and sold 12,500,000 shares of the Company's common stock to certain investors in an underwritten registered direct offering (the "December 2024 Offering"), at an offering price of $4.00 per share of common stock pursuant to an underwriting agreement (the "Underwriting Agreement") with Leerink Partners LLC, Stifel, Nicolaus & Company, Incorporated and Oppenheimer & Co. Inc, as representatives of the several underwriters. The December 2024 Offering resulted in aggregate gross proceeds to the Company of $50.0 million.

On June 5, 2025, the Company issued and sold 17,400,000 shares of the Company's common stock to the public in an underwritten offering, or (the "June 2025 Offering"), at an offering price of $5.75 per share of common stock pursuant to an underwriting agreement with Morgan Stanley & Co. LLC, Leerink Partners LLC, Stifel, Nicolaus & Company, Incorporated and Cantor Fitzgerald & Co., as representatives of the several underwriters. In connection with the offering, the Company also granted the underwriters a 30-day option to purchase up to an additional 2,610,000 shares of common stock at the price to the public, less underwriting discounts and commissions. The underwriters exercised the option in full and settled in cash, concurrent with the offering. The June 2025 Offering resulted in aggregate gross proceeds to the Company of approximately $115.1 million.

Warrants

Warrant activity, including activity related to pre-funded warrants, is shown in the table below:

	Number of Pre-funded Warrant Shares	Number of Common Stock Warrant Shares	Total Number of Warrant Shares	Weighted Average Exercise Price	Weighted Average Contractual Term
Outstanding as of December 31, 2024	23,211,642	9,703,704	32,915,346	$ 0.40	3.1
Exercised	(5,962,694)	(7,851,852)	(13,814,546)	$ 1.37	
Outstanding as of December 31, 2025	17,248,948	1,851,852	19,100,800	$ 0.13	2.8

The pre-funded and common stock warrants are classified as equity in accordance with ASC 815 given that the pre-funded and common stock warrants are indexed to the Company's own shares of common stock and meet the requirements to be classified in permanent equity.

Stock-Based Awards

The 2012 Stock Incentive Plan (the "2012 Plan") was adopted by the Company's board of directors and stockholders. The 2012 Plan provides for the issuance of stock-based awards to the Company's employees, officers, directors, consultants and advisors. The Company's board of directors administers the 2012 Plan. In April 2019, the Company's board of directors adopted a resolution effective May 7, 2019, that no further equity-based awards may be granted under the 2012 Plan.

In April 2019, the Company's board of directors adopted the 2019 Stock Incentive Plan (the "2019 Plan"), which became effective on May 7, 2019. The 2019 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The Company's employees, officers, directors, consultants and advisors are eligible to receive awards under the 2019 Plan. The 2019 Plan is administered by the Company's board of directors.

In April 2025, the Company's board of directors approved, and the Company's stockholders subsequently approved, an amendment to the 2019 Plan (the "Plan Amendment"), which (i) increased the number of shares authorized for issuance under the 2019 Plan by 6,000,000 shares to 16,490,422 shares and (ii) eliminated the evergreen provision of the 2019 Plan. Accordingly, the total number of shares of common stock that may be issued under both the 2019 Plan and the 2012 Plan was 16,212,645 as of December 31, 2025, of which 6,911,027 shares remained available for grant under the 2019 Plan.

Options granted under the 2019 Plan and the 2012 Plan have a maximum term of ten years. Options granted to employees, officers and non-employees generally vest over four years based on varying vesting schedules that primarily include: 25% vesting on the first anniversary date of grant and the balance ratably over the next 36 months or vesting in equal monthly or quarterly installments over four years. Options granted to directors generally vest over one to two years. The Company generally settles stock option exercises with newly issued shares of common stock. As of December 31, 2025 and 2024, respectively, options to purchase 9,023,200 and 7,555,310 shares of common stock were granted and outstanding, net of cancellations, under the 2019 Plan. As of December 31, 2025 and 2024, respectively, options to purchase 278,418 and 288,944 shares of common stock were granted and outstanding, net of cancellations, under the 2012 Plan.

In February 2024, the Company granted options to purchase 832,250 shares of common stock subject to performance-based vesting ("PSOs") to employees of the Company. The PSOs were subject to vesting based on performance criteria related to the timing and results of two of the Company's clinical trials. By May 2025, the timing and results of both clinical trials had been determined, and the compensation committee of the Company's board of directors had certified to the satisfaction of the related performance metrics, resulting in PSOs to purchase 642,160 shares vesting and the remaining PSOs being cancelled.

A summary of the Company's combined stock option activity for the 2019 Plan and the 2012 Plan is as follows:

	Number of Option Shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2024	7,844,254	$ 3.08	7.5	$ 11,669
Granted	2,999,800	$ 4.67		
Forfeited	(690,869)	$ 3.38		
Exercised	(851,567)	$ 2.44		
Expired	—	$ —		
Outstanding as of December 31, 2025	9,301,618	$ 3.63	7.2	$ 82,723
Options exercisable as of December 31, 2025	5,179,850	$ 3.34	5.9	$ 47,568
Options unvested as of December 31, 2025	4,121,768	$ 3.99	8.8	$ 35,155

The weighted average grant-date fair value per share of stock options granted was $4.01 and $2.17 for the years ended December 31, 2025 and 2024, respectively.

The aggregate fair value of stock options that vested during the years ended December 31, 2025 and 2024 was $4.5 million and $2.4 million, respectively.

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2025 and 2024 was $4,337 and $305, respectively.

The range of assumptions that the Company used to determine the fair value of the stock options granted were as follows:

	Year Ended December 31,	
	2025	2024
Risk-free interest rate	3.8% - 4.4%	3.5% - 4.3%
Expected volatility	98.0% - 110.1%	97.3% - 114.6%
Expected dividend yield	—	—
Expected term (in years)	5.5 - 7.0	5.5 - 7.0

In April 2019, the Company's board of directors adopted the 2019 Employee Stock Purchase Plan (the "2019 ESPP"), which became effective on May 7, 2019. The 2019 ESPP is administered by the Company's board of directors.

The total number of shares of common stock that may be issued under the 2019 ESPP was 1,103,842 as of December 31, 2025. The number of shares of the Company's common stock that have been approved to be issued under the 2019 ESPP is equal to the sum of i) 155,106 shares plus ii) an annual increase to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2020 and continuing for each fiscal year until and including, the fiscal year ending December 31, 2029, equal to the least of (a) 526,315 shares of common stock, (b) 1% of the number of outstanding shares of the Company's common stock on such date and (c) an amount determined by the Company's board of directors. No annual increase was made on January 1, 2024 and 2025, respectively.

The following table summarizes the classifications of stock-based compensation expenses for the 2012 Plan, the 2019 Plan and the 2019 ESPP recognized in the Consolidated Statements of Comprehensive Loss:

	Year Ended December 31,	
	2025	2024
General and administrative expense	$ 2,944	$ 2,145
Research and development expense	2,241	1,443
Total stock-based compensation expenses	$ 5,185	$ 3,588

As of December 31, 2025, total unrecognized compensation cost related to the unvested share-based awards was $11.5 million, which is expected to be recognized over a weighted average period of 2.7 years. As of December 31, 2024, total unrecognized compensation cost related to the unvested share-based awards was $6.8 million, which was expected to be recognized over a weighted average period of 2.7 years.

9. Income Taxes

The Company recorded an income tax benefit related to state research and development tax credits. The components of the income tax benefit for the periods shown are as follows:

	Year Ended December 31,	
	2025	2024
Current:		
Federal	$ —	$ —
State	(64)	(30)
	(64)	(30)
Deferred:		
Federal	—	—
State	—	—
	—	—
Income tax benefit	$ (64)	$ (30)

The following table provides a reconciliation between income tax benefit and the expected tax benefit at the statutory rate:

	Year Ended December 31,			
	2025		2024	
U.S. Federal statutory tax rate	$ (8,993)	21.0%	$ (10,068)	21.0%
State and local income taxes, net of federal income tax effect	(69)	0.1	(82)	0.2
Tax credits				
Federal R&D tax credit	(1,181)	2.7	(1,116)	2.3
Changes in valuation allowance	8,961	(20.9)	10,356	(21.6)
Nontaxable or nondeductible items				
Stock based compensation	1,204	(2.8)	895	(1.8)
Other	14	0.0	(15)	0.0
Income tax benefit and effective income tax rate	$ (64)	0.1%	$ (30)	0.1%

The following table summarizes income taxes paid, net of refunds received:

	Year Ended December 31,	
	2025	2024
U.S. Federal	$ —	$ —
U.S. State and Local		
Connecticut	(33)	(32)
Total income taxes paid, net of (refunds) received	$ (33)	$ (32)

Significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31,	
	2025	2024
Net operating loss carryforwards	$ 64,173	$ 53,797
Capitalized R&D	17,598	17,239
Federal and state tax credits	8,798	7,532
Other	3,300	4,232
Deferred tax assets	93,869	82,800
Other	(183)	(351)
Deferred tax liabilities	(183)	(351)
Valuation allowance	(93,686)	(82,449)
Net deferred tax asset	$ —	$ —

For the years ended December 31, 2025 and 2024, the Company generated federal and state net operating losses ("NOLs") of approximately $38.5 million and $13.1 million, respectively. At December 31, 2025 and 2024, the federal and state net operating loss balances were approximately $238.3 million and $199.8 million, respectively. The federal operating losses generated prior to 2018 will expire in years 2031 through 2037, unless previously utilized. The federal operating losses generated in 2018 or later can be carried forward indefinitely, however will only offset 80% of taxable income in a carryforward year. The state operating losses generated will expire in years 2031 through 2044, unless previously utilized. The Company also generated federal R&D tax credits for the years ended December 31, 2025 and 2024 of approximately $1.2 million and $1.1 million, respectively. At December 31, 2025 and 2024, the federal R&D tax credit carryforwards were approximately $8.5 million and $7.3 million, respectively. These credits will expire in years 2032 through 2055, unless previously utilized. The Company completed a detailed Section 382 analysis, and due to multiple historical ownership changes, the Company's NOLs as of December 31, 2022, in the amount of $178.4 million and R&D tax credits in the amount of $5.4 million are subject to limitation. If a further ownership change occurs, the Company's ability to use its tax attributes might be further limited.

The Company also generated state research tax credits for the years ended December 31, 2025 and 2024 of approximately $372 and $296, respectively. At December 31, 2025 and 2024, the state R&D tax credit carryforwards were approximately $351 and $244, respectively. The Company applied to exchange a portion of these credits for cash under a state-run program. These amounts, $64 and $30 for the years ended December 31, 2025 and 2024, respectively, were recognized as current income tax benefits in the Company's Consolidated Statements of Comprehensive Loss. At each of December 31, 2025 and 2024, the Company's Consolidated Balance Sheets reflect income tax receivables of $72 and $130 respectively, related to these credits. Because of the net operating loss and research credit carryforwards, tax years 2011 through 2024 remain open to U.S. federal and state tax examinations.

On July 4, 2025, the One Big Beautiful Bill Act ("OBBBA") was enacted in the U.S. The OBBBA includes significant provisions, such as the permanent extension of certain expiring provisions of the Tax Cuts and Jobs Act and restoration of favorable tax treatment for certain business provisions including the expensing of domestic research and development expenditures. The OBBBA did not have a material impact on our Consolidated Financial Statements.

Income taxes are provided using the asset/liability method, in which deferred taxes are recognized for the tax consequences of temporary differences between the financial statement carrying amounts and tax bases of existing assets and liabilities. The Company reviews deferred tax assets for recoverability on a regular basis. In assessing the need for a valuation allowance, the Company considers both positive and negative evidence related to the likelihood of realization of the deferred tax assets. The weight given to the positive and negative evidence is commensurate with the extent to which the evidence may be objectively verified. Accounting guidance states that a cumulative loss in recent years is a significant piece of negative evidence that is difficult to overcome in determining that a valuation allowance is not needed against deferred tax assets. As such, it is generally difficult for positive evidence regarding projected future taxable income exclusive of reversing taxable temporary differences to outweigh objective negative evidence of recent financial reporting losses.

The Company determined that operating losses it incurred since its inception on March 17, 2011, represented negative evidence sufficient to conclude a valuation allowance was necessary. As such, the Company has recorded a valuation allowance of $93.7 million and $82.4 million at December 31, 2025 and 2024, respectively, as a reserve against its net deferred tax assets. These balances reflect increases in the valuation allowance of $11.2 million and $12.9 million in 2025 and 2024, respectively, both representing an increase in net deferred tax assets.

The Company applies the provisions of ASC 740, which prescribes a comprehensive model for how a company should recognize, measure, present, and disclose in its financial statements uncertain tax positions that the Company has taken or expects to take on a tax return. The financial statements reflect expected future tax consequences of such positions presuming the taxing authorities possess full knowledge of the position and all relevant facts. As a result of the implementation of ASC 740, the Company recognized no adjustment for unrecognized income tax benefits. The Company has not, as of yet, conducted a study of R&D tax credit carryforwards. Such a study could result in an adjustment to the Company's R&D tax credit carryforwards; however, until a study is completed and any potential adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's R&D tax credits and, if an adjustment is required in the future, this adjustment would be offset by a corresponding adjustment to the valuation allowance. For the years ended December 31, 2025 and 2024, the Company had no unrecognized tax benefits or related interest and penalties accrued. In the event the Company determines that accrual of interest or penalties are necessary in the future, the amount will be presented as a component of interest expense.

10. Net Loss per Share

The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company:

	Year Ended December 31,	
	2025	2024
Net loss	$ (42,759)	$ (47,911)
Weighted average common shares used in net loss per share attributable to common stockholders, basic and diluted	134,747,198	101,971,873
Basic and diluted net loss per common share outstanding	$ (0.32)	$ (0.47)

Basic shares outstanding includes the weighted average effect of the Company's pre-funded warrants from the date of issuance, the exercise of which requires little or no consideration for the delivery of shares of common stock. As of December 31, 2025 and 2024, the Company had pre-funded warrants to purchase 17,248,948 and 23,211,642 shares of common stock outstanding, respectively, which were issued in the April 2022 Private Placement and the September 2022 Offering, which warrants are included in the weighted average common shares used in calculating the net loss per share attributable to common stockholders, basic and diluted, for the years ended December 31, 2025 and 2024.

The Company's potential dilutive securities, which include stock options and warrants that are not pre-funded, have been excluded from the computation of diluted net loss per share attributable to common stockholders whenever the effect of including them would be to reduce the net loss per share. In periods where there is a net loss, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The following potential common shares, presented based on shares outstanding as of December 31, 2025 and 2024, respectively, were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Shares as of December 31,	
	2025	2024
Stock Options	9,301,618	5,312,300
Warrants	1,851,852	9,703,704
Total potential common shares	11,153,470	15,016,004

11. Segments

The Company operates and manages its business as one reportable segment, which is also the Company's only operating segment. Such segment is the business of developing and commercializing the investigational therapy Haduvio (oral nalbuphine ER) for the treatment of chronic cough in patients with IPF, non-IPF ILD, and RCC. The Company's chief operating decision maker ("CODM") is the President and Chief Executive Officer. The CODM assesses performance for the segment and decides how to allocate resources based on consolidated net loss that is also reported on the Company's consolidated statements of comprehensive loss.

The measure of segment assets is reported on the consolidated balance sheets as total consolidated assets.

The CODM uses consolidated net loss to evaluate the Company's spend and monitor budget versus actual results. The monitoring of budgeted versus actual results is used in assessing performance of the segment and in establishing resource allocation across the organization.

The accounting policies of the segment are the same as those described in Note 2 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K.

The following table presents reportable segment loss, including significant expense categories, attributable to the Company's reportable segment for the periods presented:

	Year Ended December 31,	
	2025	2024
Chronic cough in IPF clinical trial expense	$ 7,992	$ 14,615
Refractory chronic cough clinical trial expense	1,457	6,042
Other clinical trials and studies [1]	6,219	4,313
Clinical trial material	1,827	3,235
Other clinical development expenses [2]	5,942	4,008
Employee compensation (excluding stock compensation expense)	11,820	9,265
Stock compensation expense	5,185	3,588
Other segment items [3]	8,853	6,447
Interest income, net	(6,536)	(3,602)
Net loss	$ 42,759	$ 47,911

(1) Includes expense related to the Company's drug-drug interaction study, human abuse potential study, Phase 2 CANAL trial of Haduvio for the treatment of IPF-related chronic cough.
(2) Includes expense related to general research and development activities, regulatory, medical affairs, and quality assurance.
(3) Includes general administrative expense, interest expense, net, other (expense) income, net and income tax benefit.

12. Collaborative and Licensing Agreements

The Company enters into collaborative and licensing agreements with pharmaceutical companies to in-license, develop, manufacture and/or market products that fit within its business strategy.

Keenova Therapeutics plc

In May 2011, the Company entered into an agreement with Penwest Pharmaceuticals Co., which subsequently merged into Endo, Inc. and which has since been merged into Mallinckrodt plc which was then renamed Keenova Therapeutics plc ("Keenova"), for an exclusive worldwide sublicensable license under certain patent rights and know-how controlled by Keenova to develop and commercialize products incorporating nalbuphine hydrochloride in any formulation, including an extended-release formulation such as Haduvio, in all fields and for any use.

Under the license agreement, the Company paid Keenova a non-creditable, non-refundable upfront license fee. The Company may also become obligated to make milestone payments to Keenova of $0.3 million, which would become due upon the successful completion of the first Phase 3 clinical trial of a licensed product candidate, and $0.8 million, which would become due upon the marketing approval of a licensed product in the U.S., and to pay royalties based on net sales of the licensed products by the Company, its affiliates and sublicensees. In addition, the Company is obligated to pay Keenova a low-to-mid double-digit percentage of certain income it receives from sublicensees, based on the date of the definitive agreement under which the sublicense was granted.

The Company's royalty obligation with respect to each licensed product in each country commences upon the first commercial sale of the product in that country and extends until the later of the expiration, unenforceability or invalidation of the last valid claim of any licensed patent or application covering the licensed product in the country or the expiration of 10 years after the first commercial sale of the licensed product in the country, which period is referred to as the royalty term. Upon the expiration of the royalty term for a product in a country, the Company is thereafter obligated to pay a low single-digit know-how and trademark royalty.

Under the agreement, the Company has granted Keenova a non-exclusive, royalty-free (except for pass-through payments to third parties), sublicensable license under its relevant patent rights to use any improvement the Company makes to Endo's controlled release technology for any product other than the products under which it is licensed by Endo.

Both the Company and Keenova have the right to terminate the agreement if the other party materially breaches the agreement and fails to cure the breach within specified cure periods. Keenova also has the right to terminate in the event the Company undergoes specified bankruptcy, insolvency or liquidation events. The Company has the right to terminate the agreement at its convenience at any time on 180 days' notice to Endo. Additionally, if the Company or any of the Company's sublicensees challenge the validity or enforceability of any licensed patent rights covering a licensed product and that challenge is not terminated within a specified period, the agreement will immediately terminate and all licenses granted under the agreement shall be revoked.

Upon termination of the agreement, the Company must transfer to Keenova all regulatory filings and approvals relating to the development, manufacture or commercialization of the licensed products and all trademarks, other than the Company's corporate trademarks, then being used in connection with the licensed products. If the agreement is terminated under certain specified circumstances, the Company will be deemed to have granted Keenova a perpetual, royalty-free

(except for pass-through payments to third parties), worldwide, exclusive, sublicensable license, under any improvements the Company made to the licensed know-how and any related patent rights the Company has, to manufacture and commercialize the licensed products.

13. Commitments and Contingencies

A significant portion of the Company's development activities are outsourced to third parties under agreements, including with CROs and contract manufacturers in connection with the production of clinical trial materials. These arrangements may require the Company to pay termination costs to the third parties for reimbursement of costs and expenses incurred in the event of the orderly termination of contractual services.

The Company also has commitments under lease and licensing agreements (Note 5 and Note 12).

Exhibit 10.7

Non-Employee Director Compensation Program

(a) ***Initial Stock Option Grant***. Each non-employee director will receive an option under the 2019 Stock Incentive Plan (the "2019 Plan") to purchase 70,000 shares of Common Stock upon his or her initial election or appointment to the Board. Subject to the non-employee director's continued service as a director, employee or consultant, the option will vest with respect to (i) 50% of the underlying shares on the earlier of (A) the first anniversary of the date of grant and (B) the date of the first annual meeting of stockholders of the Company held following the date of grant and (ii) the remaining 50% of the underlying shares on the earlier of (A) the second anniversary of the date of grant and (B) the date of the second annual meeting of stockholders of the Company held following the date of grant, and, in the event of a change in control of the Company, the vesting of the option will accelerate in full. The exercise price of the option will be equal to the fair market value of the Common Stock on the date of grant.

(b) ***Annual Stock Option Grant***. Each non-employee director who has served on the Board for at least six months will receive a grant of an option under the 2019 Plan to purchase 35,000 shares of Common Stock on the date of each of the Company's annual meetings of stockholders. Unless otherwise provided at the time of grant, subject to the non employee director's continued service as a director, employee or consultant, the option will vest in full on the earlier of the first anniversary of the date of grant or the date of the next annual meeting of stockholders held following the date of grant, and, in the event of a change in control of the Company, the vesting of the option will accelerate in full. The exercise price of the option will be equal to the fair market value of the Common Stock on the date of grant.

(c) ***Annual Fee; Reimbursement of Travel and Other Expenses***. Each non-employee director will receive an annual fee of $40,000 relating to such director's service on the Board. Each non-employee director will also receive an annual fee of $10,000 for serving on the Audit Committee, $10,000 for serving on the Compensation Committee and $5,000 for serving on the Nominating and Corporate Governance Committee of the Board. The chair of the Audit Committee will receive an additional annual fee of $10,000, the chair of the Compensation Committee will receive an additional annual fee of $10,000 and the chair of the Nominating and Corporate Governance Committee will receive an additional annual fee of $5,000. The chair of the Board will receive an additional annual fee of $30,000. If there is a lead director, the lead director will receive an additional annual fee of $15,000 if further approved by the Board. Each annual fee shall be payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment shall be prorated for any portion of such quarter that the director was not serving on the Board, on such committee or in such position. Each non-employee director will also be reimbursed for reasonable travel and other expenses in connection with attending meetings of the Board and any committee on which he or she serves.

November 24, 2025

David Hastings
[**]

Dear Dave:

We are pleased to offer you employment with Trevi Therapeutics, Inc. (the "Company" or "Trevi") under the terms and conditions described in this letter. If you accept this offer, please sign, date, and return one copy of the signed letter by Monday, December 1, 2025.

Position. You will hold the position of **Chief Financial Officer** and will assume the responsibilities of that position (and other duties as assigned or delegated to you by your supervisor). Your supervisor will be the Chief Executive Officer and President of the Company.

Term. Your employment will begin approximately **Tuesday, January 6, 2026**, "Start Date", and your employment will be at will. This means that both you and the Company have the right to terminate the employment relationship at any time and for any reason. Like all other employees, your employment is subject in all respects to the Company's employment policies, which may change from time to time. This letter shall not be construed as an agreement, either expressed or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at will.

Compensation. As a Full-Time Exempt employee, your compensation will be:

- Base Salary: Your base salary will be at the rate of **$20,076.92** per bi-weekly pay period (which if annualized equals **$522,000**), payable in accordance with the regular payroll practices of the Company and subject to all applicable deductions and withholdings.

- Annual Incentive Bonus: Following the end of each fiscal year and subject to the approval by the Company's Board of Directors in its sole discretion, you will be eligible to earn an annual incentive bonus, based on your performance and the Company's performance, as determined by the Company in its sole discretion, during the applicable fiscal year. Your target annual incentive bonus opportunity shall be up to **40%** of your annualized base salary. To be eligible for the bonus, you must be employed and in good standing on the date of payment, as such bonus also serves as an incentive to remain employed by the Company.

- Trevi Equity Grants: Upon your Start Date, you will be granted a stock option (the "Option") to purchase **375,000** shares of the Company's common stock under the Company's 2019 Equity Incentive Plan ("Plan"). The exercise price of the Option will be equal to the fair market value of the Common Stock as determined by the Board of Directors of the Company on the date of the grant of the Option (the "Grant Date"). You will also be eligible for the grant of any performance shares granted in 2026.

  Promptly after the Grant Date, the Company and you shall execute and deliver to each other the Company's then standard form of stock option agreement, evidencing the Option and the terms thereof. The Option shall be subject to, and governed by, the terms, provisions, and restrictions on transfer of the Plan, your stock option agreement, and any other agreement to which you shall become, or are required to become, a party pursuant to the terms of the Plan.

  You may be awarded additional equity grants from time to time in accordance with normal business practice and at the sole discretion of the Board of Directors. The terms of any future equity grant(s) will be consistent with any plan under which they are granted and the terms of the applicable agreement under which the award(s) are granted.

Severance. You are eligible for severance benefits pursuant to the terms and conditions of the Company's Executive Separation Benefits and Retention Plan, as may be amended from time to time.

Schedule. You will be primarily working remotely and will be expected to visit the office in New Haven, CT as agreed upon with your manager. The Company may modify your work schedule at the sole discretion of the Company. The Company will reimburse all reasonable commuting costs including transportation, meals, and lodging while visiting the office in New Haven, CT. Further, you agree to travel as may be required for the performance of your duties and responsibilities.

Benefits. You may participate in all benefits and conditions of employment available generally to employees of the same level and responsibility under the benefit policies and programs offered by the Company, provided you are eligible under (and subject to all provisions of) the plan documents governing those programs, e.g.: group health, dental, vision, short and long-term disability coverage, and life insurance, etc. The Company also offers a 401(k) Plan. Employees are eligible to receive a fixed match equal to 50% of their Eligible Contributions up to the first 6% of their annual income based on their actual salary deferrals, subject to IRS limits. The benefit plans and programs made available by the Company, and the rules, terms and conditions for participation in such benefit plans, may be changed by the Company at any time without advance notice at the sole discretion of the Company. Please contact the Human Resources Department for a description of these benefits.

Vacation. You will accrue vacation days at a rate of 6.153 hours per pay period, with a maximum accrual of up to 20 days per year.

Sick Time and Holiday Pay. You will receive five (5) Sick Days each year and will also be eligible for all Company designated Holidays.

Contingencies.

- This offer is contingent on your successful completion of a background check/investigation prior to your agreed upon starting date. The Company may obtain background reports both pre-employment and from time to time during your employment with the Company, as necessary.

- You agree that, during the term of your employment with Trevi, you will neither engage in any other employment, occupation, consulting or other business activity directly related to the business in which Trevi is now involved (or becomes involved during the term of your employment), nor engage in any other activities that conflict with your obligations to Trevi.

- You agree to devote your full business time, best efforts, skill, knowledge, attention and energies to the advancement of the Company's business and interest and to the performance of your duties and responsibilities as an employee of the Company and shall not engage in any other employment, consulting or other business activity without prior written consent by the CEO.

- You will be subject to, and required to comply with, all Company policies and procedures and all applicable laws and regulations during your employment with the Company.

- You will be required to execute and deliver at or prior to the Start Date for the benefit of the Company the Invention and Non-Disclosure Agreement and Non-Competition and Non-Solicitation Agreement which is an express condition of your employment with the Company.

- Your offer of employment is contingent upon your disclosure to Trevi of any and all agreements relating to your prior employment that may affect your eligibility to be employed by Trevi or limit the manner in which you may be employed. You hereby represent and warrant to the Company that the execution, delivery and performance of this offer letter by you does not and shall not conflict with, breach, violate or cause a default under any contract, agreement, instrument, order, judgment or decree to which you are a party or by which you are bound.

Cooperation. During your employment with the Company and thereafter, you shall cooperate with the Company and be reasonably available to the Company with respect to continuing and /or future matters relating to your employment period with the Company and/or its affiliates, whether such matters are business-related, legal, regulatory or otherwise (including, without limitation, your appearing at the Company's request to give testimony without requiring service of a subpoena or other legal process, volunteering to the Company all pertinent information and turning over to the Company all relevant documents which are or may come into your possession). Following your employment with the Company, the Company shall reimburse you for all reasonable out-of-pocket travel expenses incurred by you in rendering such services that are approved by the Company.

I have enclosed several documents for your review prior to your first day. They are:

- A copy of the Invention & Non-Disclosure Agreement and the Non-Competition and Non-Solicitation Agreement.
- INS Work Authorization Form: You are required to present documentation verifying your right to work in the United States on your first day.

Entire Agreement. This letter sets forth the entire agreement between you and the Company and supersedes all written and oral agreements relating to the subject matter of this offer letter or your employment with the Company. The provisions of this letter may be amended or waived only by a written instrument executed by both you and the Company, and no course of conduct or course of

dealing or failure or delay by you or the Company in enforcing or exercising any of the provisions of this letter shall affect the validity, binding effect or enforceability of the letter or be deemed to be an implied waiver of any similar or dissimilar requirement, provision or condition of this letter at the same or any prior subsequent time.

Dave, we look forward to having you join the Trevi leadership team during this important time of growth.

Sincerely,

/s/ Jennifer Good
President & CEO

I accept employment with Trevi under the terms and conditions set forth in this letter.

/s/ David Hastings **Date:** December 1, 2025

Exhibit 19.1

Trevi Therapeutics, Inc.

Insider Trading Policy

1. BACKGROUND AND PURPOSE

1.1. Why Have We Adopted This Policy?

The federal securities laws prohibit any member of the Board of Directors (a "Director"), officer (as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934 (the "Exchange Act"), an "executive officer") or employee of Trevi Therapeutics, Inc. (together with its subsidiaries, the "Company") from purchasing or selling Company securities on the basis of material nonpublic information concerning the Company, or from tipping material nonpublic information to others. These laws impose severe sanctions on individuals who violate them. In addition, the Securities and Exchange Commission (the "SEC") has the authority to impose large fines on the Company and on the Company's Directors, executive officers and controlling stockholders if the Company's employees engage in insider trading and the Company has failed to take appropriate steps to prevent it (so-called "controlling person" liability).

This insider trading policy is being adopted in light of these legal requirements, and with the goal of helping:

- prevent inadvertent violations of the insider trading laws;
- avoid embarrassing proxy disclosure of reporting violations by persons subject to Section 16 of the Exchange Act;
- promote compliance with the Company's obligation to publicly disclose information related to its insider trading policies and practices and the use of certain trading arrangements by Company insiders;
- avoid even the appearance of impropriety on the part of those employed by, or associated with, the Company;
- protect the Company from controlling person liability; and
- protect the reputation of the Company, its Directors and its employees.

As detailed below, this policy applies to family members and certain other persons and entities with whom Directors and employees have relationships. However, nothing in this policy is applicable to transactions by the Company itself.

1.2. What Type of Information is "Material"?

Information concerning the Company is considered material if there is a substantial likelihood that a reasonable stockholder would consider the information important in making an investment decision with respect to the Company's securities. Stated another way, there must be a substantial likelihood that a reasonable shareholder would view the information as having significantly altered the "total mix" of

information available about the Company. Material information can include positive or negative information about the Company. Information concerning any of the following subjects, or the Company's plans with respect to any of these subjects, would often be considered material:

- the Company's liquidity, cash burn rate, revenues, earnings or losses (including the Company's forecasts of the same);
- a significant merger or acquisition involving the Company;
- a significant change in the management or the Board of Directors of the Company;
- information concerning upcoming U.S. Food and Drug Administration actions or other significant regulatory developments, including significant new clinical trial results;
- the Company's decision to commence or terminate the payment of cash dividends;
- the public or private sale of a significant amount of securities of the Company;
- the establishment of a program to repurchase securities of the Company;
- a stock split;
- a default on outstanding debt of the Company or a bankruptcy filing;
- a new product release or a significant development, invention or discovery;
- information concerning significant clinical trials or non-clinical studies, including the timing of and findings and data from such trials and studies;
- a significant licensing or collaboration agreement, or serious discussions regarding such an agreement;
- the loss, delay or gain of a significant contract, sale or order or other important development regarding customers, collaborators or suppliers;
- a significant operational issue or investigation of a potential such issue, including cybersecurity incidents and product defects;
- a conclusion by the Company or a notification from its independent auditor that any of the Company's previously issued financial statements should no longer be relied upon; or
- a change in or dispute with the Company's independent auditor.

This list is illustrative only and is not intended to provide a comprehensive list of circumstances that

could give rise to material information.

1.3. When is Information "Nonpublic"?

Information concerning the Company is considered nonpublic if it has not been disseminated in a manner making it available to investors generally.

Information will generally be considered nonpublic unless (1) the information has been disclosed in a press release, in a public filing made with the SEC (such as a Report on Form 10- K, Form 10-Q or Form 8-K), or through a news wire service or daily newspaper of wide circulation, and (2) a sufficient amount of time has passed so that the information has had an opportunity to be digested by the marketplace.

2. PROHIBITIONS RELATING TO TRANSACTIONS IN THE COMPANY'S SECURITIES

2.1. Covered Persons. This Section 2 applies to:

- all Directors;
- all employees;
- all family members of Directors and employees who share the same address as, or are financially dependent on, the Director or employee and any other person who shares the same address as the Director or employee (other than (x) an employee or tenant of the Director or employee or (y) another unrelated person whom the Chief Executive Officer or Chief Financial Officer determines should not be covered by this policy); and
- all corporations, limited liability companies, partnerships, trusts or other entities controlled by any of the above persons, unless the entity has implemented policies or procedures designed to ensure that such person cannot influence transactions by the entity involving Company securities or the entity is a professional investment organization (e.g. venture capital fund, investment fund, registered investment company or registered investment advisor) and has established policies and procedures designed to ensure its compliance with federal securities laws and regulations prohibiting trading in the securities of a company on the basis of material, non-public information.

2.2. Prohibition on Trading While Aware of Material Nonpublic Information.

(a) Prohibited Activities. Except as provided in Section 2.2(b), no person or entity covered by Section 2 may:

- purchase, sell or donate any securities of the Company while he or she is aware of any material nonpublic information concerning the Company or recommend to another person that they do so;
- tip or otherwise disclose to any other person in violation of the insider trading laws any material nonpublic information concerning the Company;

- purchase, sell or donate any securities of another company while he or she is aware of any material nonpublic information concerning such other company which he or she learned in the course of his or her service as a Director or employee of the Company or recommend to another person that they do so; or

- tip or otherwise disclose to any other person in violation of the insider trading laws any material nonpublic information concerning another company which he or she learned in the course of his or her service as a Director or employee of the Company.

(b) Exceptions. The prohibitions in Sections 2.2(a) and 2.3 on purchases, sales and donations of Company securities do not apply to:

- exercises of stock options or other equity awards or the surrender of shares to the Company in payment of the exercise price or in satisfaction of any tax withholding obligations, in each case in a manner permitted by the applicable equity award agreement; provided, however, that the securities so acquired may not be sold (either outright or in connection with a "cashless" exercise transaction through a broker) while the employee or Director is aware of material nonpublic information or during an applicable blackout period (as defined in Section 2.3(b));

- acquisitions or dispositions of Company common stock under the Company's 401(k) or other individual account plan that are made pursuant to standing instructions, in a form approved by the Company, that are not entered into or modified while the employee or Director is aware of material nonpublic information or during an applicable blackout period;

- other purchases of securities from the Company (including purchases under the Company's employee stock purchase plan pursuant to standing instructions, in a form approved by the Company) or sales of securities to the Company; provided, however, that if the transaction involves the exercise of stock options or other equity awards, the transaction must be permitted by the first bullet above;

- bona fide gifts that are approved in advance by the Company;

- purchases, sales or donations made pursuant to a binding contract, written plan or specific instruction which satisfies the applicable affirmative defense conditions of Rule 10b5-1(c), including as applicable the requirements applicable to an eligible sell-to-cover transaction as defined in Rule 10b5-1(c)(1)(ii)(D)(3), or for which the affirmative defense is available under Rule 10b5-1(c) because such plan was adopted prior to February 27, 2023, met the affirmative defense conditions in effect at the time of adoption, and was not modified or changed on or after February 27, 2023 (a "trading plan"); provided such trading plan: (1) is in writing and (2) was submitted to the Company for review prior to its adoption; and

- purchases, sales or donations made pursuant to a binding contract, written plan or specific instruction which satisfies the definition of a "non-Rule 10b5-1 trading arrangement" as such term is defined in Item 408(c) of Regulation S-K, provided such non-Rule 10b5-1

trading arrangement: (1) is in writing and (2) was submitted to the Company for review prior to its adoption.

(c) Application of Policy After Cessation of Service. If a person ceases to be a Director or employee of the Company at a time when he or she is aware of material nonpublic information concerning the Company, the prohibition on purchases, sales or donations of Company securities in Section 2.2(a) shall continue to apply to such person until that information has become public or is no longer material.

2.3. Blackout Periods.

(a) Regular Blackout Periods. Except as provided in Section 2.2(b), no person or entity covered by this Section 2 may purchase, sell or donate any securities of the Company (i) in the case of the first fiscal quarter, during the period beginning on the 15th calendar day of the second month of such fiscal quarter and (ii) in the case of each other fiscal quarter, during the period beginning on the 15th calendar day following the most recently ended fiscal quarter and, in each case, ending upon the completion of the second full trading day after the public announcement of earnings for such quarter (a "regular blackout period").

(b) Corporate News Blackout Periods. The Company may from time to time notify Directors, executive officers and other specified employees that an additional blackout period (a "corporate news blackout period") is in effect in view of significant events or developments involving the Company. In such event, except as provided in Section 2.2(b), no such individual may purchase, sell or donate any securities of the Company during such corporate news blackout period or inform anyone else that a corporate news blackout period is in effect. (In this policy, regular blackout periods and corporate news blackout periods are each referred to as a "blackout period.")

(c) Awareness of Material Non-Public Information when a Blackout Period is Not in Effect. Even if no blackout period is then in effect, if a person is aware of material nonpublic information the prohibitions contained in Section 2.2(a)apply.

2.4. Prohibition on Pledges. No person or entity covered by this Section 2 may purchase Company securities on margin, borrow against Company securities held in a margin account, or pledge Company securities as collateral for a loan. However, an exception may be granted in extraordinary situations where a person wishes to pledge Company securities as collateral for a loan (other than a margin loan) and clearly demonstrates the financial capacity to repay the loan without resort to the pledged securities. Any person who wishes to pledge Company securities as collateral for a loan must submit a request for approval to the Chief Financial Officer. In addition, any such request by a Director or executive officer must also be reviewed and approved by the Audit Committee.

2.5. Prohibition on Short Sales and Derivative Transactions. No person or entity covered by this Section 2 may engage in any of the following types of transactions:

- short sales of Company securities, including short sales "against the box"; or

- purchases or sales of puts, calls or other derivative securities based on the Company's securities; or

- purchases of financial instruments (including prepaid variable forward contracts, equity swaps, collars and exchange funds) or other transactions that hedge or offset or are designed to hedge or offset any decrease in the market value of Company securities.

2.6. Partnership Distributions. Nothing in this policy is intended to limit the ability of a venture capital partnership or other similar entity with which a Director is affiliated to distribute Company securities to its partners, members or other similar persons. It is the responsibility of each affected Director and the affiliated entity, in consultation with their own counsel (as appropriate), to determine the timing of any distributions, based on all relevant facts and circumstances and applicable securities laws.

2.7. Underwritten Public Offering. Nothing in this policy is intended to limit the ability of any person to sell Company securities as a selling stockholder in an underwritten public offering pursuant to an effective registration statement in accordance with applicable securities law.

3. ADDITIONAL PROHIBITIONS APPLICABLE TO DIRECTORS, EXECUTIVE OFFICERS AND DESIGNATED EMPLOYEES

3.1. Covered Persons. This Section 3 applies to:

- all Directors;

- all executive officers;

- such other employees as are designated from time to time by the Board of Directors, the Chief Executive Officer or the Chief Financial Officer as being subject to this Section 3 (the "Designated Employees");

- all family members of Directors, executive officers and Designated Employees who share the same address as, or are financially dependent on, the Director, executive officer or Designated Employee and any other person who shares the same address as the Director, executive officer or Designated Employee (other than (x) an employee or tenant of the Director, executive officer or Designated Employee or (y) another unrelated person whom the Chief Executive Officer or the Chief Financial Officer determines should not be covered by this policy); and

- all corporations, limited liability companies, partnerships, trusts or other entities controlled by any of the above persons, unless (x) the entity has implemented policies or procedures designed to ensure that such person cannot influence transactions by the entity involving Company securities or (y) the entity is a professional investment organization (e.g. venture capital fund, investment fund, registered investment company or registered investment advisor) and has established policies and procedures designed to ensure its compliance with

federal securities laws and regulations prohibiting trading in the securities of a company on the basis of material, non-public information.

3.2. Notice and Pre-Clearance of Transactions.

(a) Pre-Transaction Clearance. No person or entity covered by this Section 3 (a "Pre-Clearance Person") may purchase, sell, donate, transfer or otherwise acquire or dispose of securities of the Company, either directly or indirectly, other than in a transaction permitted under Section 2.2(b), unless such person pre-clears the transaction with either the Chief Executive Officer or Chief Financial Officer. A request for pre-clearance may be oral or in writing (including by e-mail), should be made at least two business days in advance of the proposed transaction and should include the identity of the Pre-Clearance Person, the type of proposed transaction (for example, an open market purchase, a privately negotiated sale, an option exercise, etc.), the proposed date of the transaction and the number of shares or options to be involved. In addition, the Pre-Clearance Person must execute a certification (in the form approved by the Chief Executive Officer and Chief Financial Officer) that he, she or it is not aware of material nonpublic information about the Company. The Chief Executive Officer or Chief Financial Officer shall have sole discretion to decide whether to clear any contemplated transaction. The Chief Executive Officer shall have sole discretion to decide whether to clear transactions by the Chief Financial Officer or persons or entities subject to this policy as a result of their relationship with the Chief Financial Officer, and the Chief Financial Officer shall have sole discretion to decide whether to clear transactions by the Chief Executive Officer or persons or entities subject to this policy as a result of their relationship with the Chief Executive Officer. All trades that are pre-cleared must be effected within three business days of receipt of the pre-clearance unless a longer or shorter period has been specified by the Chief Executive Officer or the Chief Financial Officer. A pre-cleared trade (or any portion of a pre- cleared trade) that has not been effected during the three business day period must be pre-cleared again prior to execution. **Notwithstanding receipt of pre-clearance, if the Pre-Clearance Person becomes aware of material non-public information or becomes subject to a blackout period before the transaction is effected, the transaction may not be completed.**

(b) Post-Transaction Notice. Each person or entity covered by this Section 3 who is subject to reporting obligations under Section 16 of the Exchange Act shall also notify the Chief Executive Officer or the Chief Financial Officer (or his or her designee) of the occurrence of any purchase, sale, donation, transfer or other acquisition or disposition of securities of the Company as soon as possible following the transaction, but in any event within one business day after the transaction. Such notification may be oral or in writing (including by e-mail) and should include the identity of the covered person, the type of transaction, the date of the transaction, the number of shares involved, the purchase or sale price, and whether the transaction was effected pursuant to a contract, instruction or written plan that is intended either to satisfy the affirmative defense conditions of Rule 10b5-1(c) or to constitute a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K).

(c) Deemed Time of a Transaction. For purposes of this Section 3.2, a purchase, sale, donation, transfer or other acquisition or disposition shall be deemed to occur at the time the person becomes irrevocably committed to it (for example, in the case of an open market purchase or sale, this occurs when the trade is executed, not when it settles).

4. REGULATION BTR

If the Company is required to impose a "pension fund blackout period" under Regulation BTR,

each Director and executive officer shall not, directly or indirectly sell, purchase or otherwise transfer during such blackout period any equity securities of the Company acquired in connection with his or her service as a Director or officer of the Company, except as permitted by Regulation BTR.

5. PENALTIES FOR VIOLATION

Violation of any of the foregoing rules is grounds for disciplinary action by the Company, including termination of employment. In addition to any disciplinary actions the Company may take, insider trading can also result in administrative, civil or criminal proceedings which can result in significant fines and civil penalties, being barred from service as an officer or director of a public company, or imprisonment.

6. COMPANY ASSISTANCE AND EDUCATION

6.1. Education. The Company shall take reasonable steps designed to ensure that all Directors and employees of the Company are educated about, and periodically reminded of, the federal securities law restrictions and Company policies regarding insider trading.

6.2. Assistance. The Company shall provide reasonable assistance to all Directors and executive officers, as requested by such Directors and executive officers, in connection with the filing of Forms 3, 4 and 5 under Section 16 of the Exchange Act. However, the ultimate responsibility, and liability, for timely filing remains with the Directors and executive officers.

6.3. Limitation on Liability. None of the Company, the Chief Executive Officer, the Chief Financial Officer or the Company's other employees will have any liability for any delay in reviewing, or refusal of, a trading plan submitted pursuant to Section 2.2(b), a request for pre- clearance submitted pursuant to Section 3.2(a) or a request to allow a pledge submitted pursuant to Section 2.4. Notwithstanding any review of a trading plan pursuant to Section 2.2(b) or pre- clearance of a transaction pursuant to Section 3.2(a), none of the Company, the Chief Executive Officer, Chief Financial Officer or the Company's other employees assumes any liability for the legality or consequences of such trading plan or transaction to the person engaging in or adopting such trading plan or transaction.

7. DISSEMINATION

This policy shall be distributed to each new employee, officer and Director of the Company upon commencement of his or her employment or other relationship with the Company and annually thereafter, and each employee, officer and Director shall annually certify that he or she has received, read and understood the policy and has complied with its terms.

Adopted as of December 9, 2025

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-3 Nos. 333-260279, 333-260820, 333-264614, and 333-291517) of Trevi Therapeutics, Inc.,

(2) Registration Statement (Form S-8 No. 333-231260) pertaining to the 2012 Stock Incentive Plan, as amended, the 2019 Stock Incentive Plan and the 2019 Employee Stock Purchase Plan of Trevi Therapeutics, Inc.,

(3) Registration Statements (Form S-8 Nos. 333-237193, 333-257729, 333-264615, and 333-271839) pertaining to the 2019 Stock Incentive Plan and the 2019 Employee Stock Purchase Plan of Trevi Therapeutics, Inc., and

(4) Registration Statement (Form S-8 No. 333-278101, 333-285879, and 333-289362) pertaining to the 2019 Stock Incentive Plan of Trevi Therapeutics, Inc.;

of our report dated March 17, 2026, with respect to the consolidated financial statements of Trevi Therapeutics, Inc. included in this Annual Report (Form 10-K) of Trevi Therapeutics, Inc. for the year ended December 31, 2025.

/s/ Ernst & Young LLP

New York, New York
March 17, 2026

Exhibit 31.1

CERTIFICATION 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

I, Jennifer L. Good, certify that:

1. I have reviewed this Annual Report on Form 10-K of Trevi Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2026

By: /s/ Jennifer L. Good
Jennifer L. Good
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION 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

I, David C. Hastings, certify that:

1. I have reviewed this Annual Report on Form 10-K of Trevi Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2026

By: /s/ David C. Hastings
David C. Hastings
Chief Financial Officer
(Principal Financial 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

In connection with the Annual Report on Form 10-K of Trevi Therapeutics, Inc. (the "Company") for the period ended December 31, 2025, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Jennifer L. Good, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to her knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: March 17, 2026

By: /s/ Jennifer L. Good
Jennifer L. Good
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

In connection with the Annual Report on Form 10-K of Trevi Therapeutics, Inc. (the "Company") for the period ended December 31, 2025, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, David C. Hastings, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: March 17, 2026

By: /s/ David C. Hastings
David C. Hastings
Chief Financial Officer
(Principal Financial Officer)