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, 2024

OR

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

Commission File Number 001-39594

Spruce Biosciences, Inc.
(Exact name of Registrant as specified in its Charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**81-2154263** **(I.R.S. Employer Identification No.)**
611 Gateway Boulevard, Suite 740 **South San Francisco, California** **(Address of principal executive offices)**	**94080** **(Zip Code)**

Registrant's telephone number, including area code: (415) 655-4168

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, par value $0.0001 per share	SPRB	Nasdaq Capital Market

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

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

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

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

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

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

The aggregate market value of the Registrant's common stock held by non-affiliates of the Registrant as of June 28, 2024, the last business day of the Registrant's most recently completed second fiscal quarter, was approximately $18.8 million, based on the closing price of the Registrant's common stock on the Nasdaq Capital Market of $0.52 per share.

The number of shares of Registrant's Common Stock outstanding as of April 11, 2025 was 42,231,285.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive Proxy Statement for its 2025 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K are incorporated by reference into Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

		Page
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS		1
SUMMARY OF RISKS ASSOCIATED WITH OUR BUSINESS		2
PART I		
Item 1.	Business	4
Item 1A.	Risk Factors	28
Item 1B.	Unresolved Staff Comments	86
Item 1C.	Cybersecurity	86
Item 2.	Properties	87
Item 3.	Legal Proceedings	87
Item 4.	Mine Safety Disclosures	87
PART II		
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	88
Item 6.	[Reserved]	88
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	89
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	98
Item 8.	Financial Statements and Supplementary Data	99
Item 9.	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	125
Item 9A.	Controls and Procedures	125
Item 9B.	Other Information	126
Item 9C.	Disclosure Regarding Foreign Jurisdictions that Prevent Inspections	126
PART III		
Item 10.	Directors, Executive Officers and Corporate Governance	127
Item 11.	Executive Compensation	127
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	127
Item 13.	Certain Relationships and Related Transactions, and Director Independence	127
Item 14.	Principal Accountant Fees and Services	128
PART IV		
Item 15.	Exhibit and Financial Statement Schedules	129
Item 16	Form 10-K Summary	132

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (the "Annual Report") contains forward-looking statements within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, research and development costs; the ability to seek accelerated approval of TA-ERT for MPS IIIB based on existing clinical data; the anticipated timing, costs and conduct of our clinical trials for our product candidates, such as a confirmatory Phase 3 trial of TA-ERT for MPS IIIB; the timing and likelihood of regulatory filings and approvals for our product candidates; our ability to commercialize our product candidates, including TA-ERT, if approved, in the United Sates and in international markets; the anticipated market opportunity and level of sales for our product candidates, including TA-ERT for MPS IIIB, if approved; our ability to establish a commercial organization in the United States and leverage regional partnerships and a network of third-party distributors in international markets; the coverage, pricing and reimbursement of our product candidates, if approved; the potential benefits of strategic alliances and our ability to enter into strategic alliances; our ability to identify and benefit from strategic collaborations with other biopharmaceutical companies; the ability to in-license or acquire development and commercial stage product candidates in disorders that have the potential to complement our existing portfolio; the timing and likelihood of success, plans and objectives of management for future operations; future results of anticipated product development efforts; our ability to continue as a going concern; and our expected future financing needs, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this Annual Report are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of risks, uncertainties and assumptions described under the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Annual Report. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we undertake no obligation to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. You should, however, review the factors and risks we describe in the reports we will file from time to time with the Securities and Exchange Commission ("SEC") after the date of this Annual Report.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this Annual Report, and while we believe such information provides a reasonable basis for these statements, such information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to unduly rely on these statements.

SUMMARY OF RISKS ASSOCIATED WITH OUR BUSINESS

We face risks and uncertainties associated with our business, many of which are beyond our control. Some of the material risks associated with our business include the following:

- We have a limited operating history, have incurred significant net losses since our inception, and anticipate that we will continue to incur significant net losses for the foreseeable future, and such net losses are expected to increase as we continue our clinical development of, and seek regulatory approvals for, our product candidates, tralesinidase alfa, tildacerfont, SPR202, SPR204 and any future product candidates.
- We will need substantial additional financing to develop our product candidates and implement our operating plan. If we fail to obtain additional financing, we may be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- We do not currently have sufficient working capital to fund our planned operations for the next twelve months and substantial doubt exists as to our ability to continue as a going concern.
- If we are unable to advance our product candidates in clinical development, obtain regulatory approval, and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- Our clinical trials may fail to adequately demonstrate the safety and efficacy of our product candidates, which could prevent or delay regulatory approval and commercialization.
- We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.
- Preclinical and clinical drug development involves a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of tralesinidase alfa, tildacerfont and our other current and future product candidates.
- If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- Any delays in the commencement or completion, or termination or suspension, of our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue, and adversely affect our commercial prospects.
- Tralesinidase alfa and tildacerfont are, and our other current and future product candidates will be, subject to extensive regulation and compliance obligations, which are costly and time-consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize tralesinidase alfa, tildacerfont and our other current and future product candidates.
- Interim, topline, and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- If the market opportunities for tralesinidase alfa, tildacerfont and our other current and future product candidates are smaller than we believe they are, our future revenue may be adversely affected and our business may suffer.
- We currently have no marketing and sales organization and have yet to commercialize a product. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell tralesinidase alfa, tildacerfont and our other current and future product candidates, we may not be able to generate product revenues.
- Unfavorable U.S. and global economic and geopolitical conditions could adversely affect our business, financial condition or results of operations.

- We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.
- Coverage and reimbursement may be limited or unavailable in certain market segments for tralesinidase alfa, tildacerfont and our other current and future product candidates, which could make it difficult for us to sell tralesinidase alfa, tildacerfont and our other current and future product candidates profitably.
- If we fail to develop and commercialize additional product candidates, we may be unable to grow our business.
- We depend on intellectual property licensed from others, the termination of which could result in the loss of significant rights, which would harm our business.
- We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize tralesinidase alfa, tildacerfont, and our other product candidates.
- We rely completely on third parties to manufacture our preclinical and clinical drug supplies and we intend to rely on third parties to produce commercial supplies of tralesinidase alfa, tildacerfont and any future product candidates, if approved, and these third parties may fail to obtain and maintain regulatory approval for their facilities, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.
- If we are unable to obtain and maintain sufficient intellectual property protection for TA-ERT, SPR202, tildacerfont, any future product candidates, and other proprietary technologies we develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize TA-ERT, SPR202, and tildacerfont, if approved, any future product candidates, and other proprietary technologies if approved, may be adversely affected.
- If we fail to meet all applicable requirements of the Nasdaq Capital Market ("Nasdaq") and Nasdaq determines to delist our common stock, the delisting could adversely affect the market liquidity of our common stock and the market price of our common stock could decrease.

PART I

Item 1. Business.

Overview

We are a biopharmaceutical company focused on developing and commercializing novel therapies for neurological disorders with significant unmet medical need. We have a diverse portfolio of product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are either no approved therapies treating the underlying disease or suboptimal treatment options. We were founded in April 2016 and are led by a management team experienced in the development and commercialization of groundbreaking therapeutics.

Our Strategy

- **Seek regulatory approval and maximize the U.S. commercial potential of TA-ERT for the treatment of MPS IIIB.** We intend to seek U.S. accelerated approval of TA-ERT for MPS IIIB based on existing non-clinical and clinical data. As a condition of seeking such approval of a BLA from the FDA, we will initiate a confirmatory trial. If the BLA is approved, we intend to build a highly specialized commercial and medical affairs organization to support the commercialization of TA-ERT. Given that a relatively small number of clinicians and specialists treat most of the patients with MPS IIIB, we believe this market can be effectively addressed with a modest-sized and targeted patient-centric field team, alongside various high-touch patient initiatives.
- **Commercialize globally through a patient-focused organization.** We seek to commercialize TA-ERT and its other investigational products throughout the developed world, including North America, the European Union (EU), the United Kingdom, Latin America, Turkey, Asia, and other international markets. We intend to establish our own commercial organization in the United States, EU, and the United Kingdom, and seek regional strategic collaborations and a network of third-party distributors in other international markets.
- **Focus on serious diseases with significant unmet medical need and clear biology.** We focus on diseases that have biology that is well understood. We believe that developing drugs that directly impact known disease pathways will increase the probability of success of our development programs.

Our Pipeline and Anticipated Milestones

We have a diverse portfolio of biologics and small molecule product candidates aimed at addressing diseases with significant unmet medical need and clear biology for treatment, for which there are suboptimal treatment options or no approved therapies treating the underlying disease.

TA-ERT for the Treatment of Mucopolysaccharidosis Type IIIB (MPS IIIB)

TA-ERT is a fusion protein comprised of recombinant human alpha-N-acetylglucosaminidase ("rhNAGLU") with modified human insulin-like growth factor 2 via an amino acid linker. TA-ERT is intended as an enzyme replacement therapy for the treatment of patients with MPS IIIB (Sanfilippo Syndrome Type B) who lack rhNAGLU enzyme activity. TA-ERT is expected to restore rhNAGLU enzyme activity in the central nervous system ("CNS") following intracerebroventricular ("ICV") injection.

MPS IIIB is a rare, inherited, autosomal recessive disease caused by severe deficiency in the activity of NAGLU, a lysosomal enzyme required for the degradation of the glycosaminoglycan, heparan sulfate ("HS"), and the MPS IIIB-specific non-reducing end of heparan sulfate ("HS-NRE"). In the absence of NAGLU enzyme activity, HS accumulates in many tissues and organs, particularly the CNS, and is excreted in the urine.

Since MPS IIIB results in severe neurodegeneration, successful treatment is likely dependent on replacement of NAGLU enzyme activity throughout the CNS. In addition, enzyme replacement must be broadly disseminated and chronically active in order to be therapeutic. TA-ERT is not expected to cross the blood-brain barrier in appreciable amounts, so systemic administration is unlikely to deliver therapeutic concentrations at the site of disease pathology in the CNS. To circumvent the blood-brain barrier, TA-ERT is to be administered directly to

the CNS by ICV infusion into the cerebrospinal fluid ("CSF"). It is expected that TA-ERT will distribute to the target tissues in the CNS via the CSF flow and be trafficked to lysosomes, where it will catabolize accumulated HS. We expect TA-ERT to restore NAGLU enzyme activity, reduce HS storage in the CNS, and improve signs and symptoms of MPS IIIB disease.

Human exposure to TA-ERT has occurred in 3 clinical studies (201, 202, and 401) sponsored by Allievex. Study 201 was a completed Phase 1/2, first-in-human, multicenter, multinational, open-label, dose-escalation study. Study 250-202 was an extension study for patients who completed Study 201, and Study 401 was an extension study for patients who completed Study 202. Patients entered Study 201 by either completing Study 201's Part 1 dose-escalation study, or completing Study 901, an observational study of progressive MPS IIIB symptomatology.

In Studies 201 and 202, TA-ERT was administered weekly by ICV infusion, and patients were evaluated in terms of neurocognitive function, behavior, sleep, quality of life (both of the patient and of the family/caregiver), MRI imaging characteristics, biochemical markers of disease burden and, in some cases, hearing. The primary objectives of these studies were to evaluate the safety and tolerability of TA-ERT administered to patients with MPS IIIB via an ICV reservoir and catheter, and to evaluate the impact of TA-ERT on cognitive function defined as communication skills in patients with MPS IIIB as assessed by the raw score and age-equivalent quotient ("AEq"). Patients in Study 202 were eligible for weekly or every other week dosing after Week 96. 22 patients enrolled in Study 201 and a total of 21 patients completed the study. 20 of these patients transitioned to Study 202. Study 401 was a Phase 3B/4 study to allow patients that completed Study 202 to continue receiving TA-ERT for up to 3 additional years. The study was discontinued in October 2023 due to financial constraints of the product's prior sponsor.

Study 901 was a prospective, non-treatment study of MPS IIIB open to 1 – 10 year-old patients with cognitive developmental quotients ≥ 50 (determined by the BSID-III or KABC-II (each as defined below)) upon study entry. This study aimed to quantify MPS IIIB disease progression over time; to correlate changes in clinical features of the disease, in particular cognitive decline, with MRI characteristics and biochemical markers of disease burden; and to serve as a comparator for Studies 201 and 202. Following a screening period, patients were assessed every 12 weeks for up to 96 weeks. 22 patients enrolled and 20 patients matriculated into Study 201.

Study 902 was a prospective, non-treatment study of MPS IIIB that aimed to quantify the progression of cognitive decline in pediatric patients with MPS IIIB over time. The study enrolled patients regardless of age or baseline DQ. To this end, data collected from Study 902 will augment and extend data from Study 901. Data was prospectively collected from 44 patients for up to 192 weeks, with study visits occurring every 24 weeks.

In Studies 201 and 202, TA-ERT was shown to significantly and durably normalize HS and HS-NRE levels over a five-year period. In Study 201, TA-ERT was shown to normalize liver and spleen volume, while stabilizing cortical grey matter volume, reflecting removal of HS deposits from these target organs. We also believe that early intervention with TA-ERT stabilizes cognitive decline in patients with MPSIIIB. In Study 201, patients with early disease, as defined by baseline cognition Bayley Scales of Infant and Toddler Development, Third Edition ("BSID-III") or the Kaufman Assessment Battery for Children, Second Edition ("KABC-II") Cognition AEq>40 months or Cognitive Disease Quotient>75, seven of ten patients (70%) demonstrated disease stability, or no meaningful loss of cognitive function at endpoint evaluation, as defined by BSID-III/KABC-11 cognition AEq ≥6 change from baseline. Three of twelve patients (25%) with more progressed disease demonstrated disease stability at endpoint evaluation.

In March 2024, in a type C meeting with the FDA, the FDA confirmed to Allievex that HS-NRE is deemed to be a biomarker reasonably likely to predict clinical benefit and could serve as a basis for accelerated approval. The FDA also confirmed that the completed clinical and nonclinical studies of TA-ERT were sufficient for a BLA submission and provided guidance around key design elements of a confirmatory Phase 3 trial (placebo-controlled 5-year study with a 2-year interim analysis in 14 patients), which must be initiated prior to potential accelerated approval of TA-ERT. We intend to submit the BLA for TA-ERT for the treatment of MPSIIIB in the first half of 2026.

Tildacerfont and Cortibon for the Treatment of Major Depressive Disorder

Major depressive disorder ("MDD") is a highly debilitating mental disorder characterized by the presence of depressed mood and typically accompanied by cognitive-affective and somatic changes including anhedonia, weight alterations, and altered sleeping patterns.

Current antidepressants therapies, including selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, and tricyclic antidepressants have several limitations: they work in too few patients, need too much time until they work, and have too many side effects. All current antidepressants share one mechanistic feature, as they enhance neurotransmission conveyed by biogenic amines, including serotonin, norepinephrine, and dopamine. In recent years, antidepressants with alternative modes of action, such as the N-methyl-D-aspartate antagonist esketamine (Spravato) and the gamma-aminobutyric acid positive allosteric modulators, brexanolone (Zulresso) and zuranolone (Zurzuvae), have been approved by the FDA for the treatment of treatment-resistant depression and post-partum depression, respectively.

Abnormal CRF neurotransmission and CRF_1 receptor signal transduction has been proposed to be a critical mechanism for stress pathophysiology that leads to MDD. One of the most robust findings in depressed patients is aberrant stress regulation, mostly hyperreactivity of a hormonal system termed the hypothalamus-pituitary-adrenal ("HPA") axis. The master molecule in the brain coordinating behavioral response and adaptation to a stressor is the neuropeptide corticotropin releasing hormone ("CRH", also referred to as corticotropin-releasing factor "CRF"). CRF signaling through one of its receptors, CRF receptor 1 ("CRF_1"), is highly relevant in the context of depression therapy. The CRF_1 receptor is abundantly expressed in the brain and pituitary gland, where it is the primary regulator of the HPA axis. Preclinical research revealed that CRF_1 signaling affects anxiety, sleep disturbance, loss of appetite, anhedonia, and cognitive impairment. Clinical research on (postmortem tissue from) MDD patients revealed increased numbers of CRF-expressing neurons and decreased CRH binding. Clinical research further revealed that, on average, the CRF level in the CSF is elevated in MDD patients as compared to normal subjects. Of note, between 30% and 50% of MDD patients, considered individually, have CRF concentrations higher than the average values of healthy controls, suggesting that CRF_1 might be directly related to MDD etiology in a subset of MDD patients.

Due to the inability of most peptides to cross the blood-brain barrier, several pharmaceutical companies developed small, CRF_1 receptor antagonists. These compounds were hypothesized to alleviate symptoms of psychiatric disorders including MDD and generalized anxiety disorder. However, except for the first explorative open-label trial in inpatients conducted by the Max Planck Institute of Psychiatry, all randomized controlled trials in MDD outpatients did not meaningfully separate from placebo. As a result, most pharmaceutical companies abandoned their CRF_1 development programs. We believe that these clinical trials did not separate from placebo due to the fact that CRF_1signaling is only altered in a subgroup of patients. Therefore, only in those patients would a CRF_1 receptor antagonist have the potential for clinical benefit. By blocking the CRF_1 receptor, tildacerfont has the potential to address hyperactive brain CRF neurotransmission and aberrant functioning of the HPA axis in patients with MDD. Additionally, by utilizing genetic markers, Cortibon aims to identify MDD patients who are more likely to respond to CRF_1receptor antagonism, thereby enhancing treatment outcomes and reducing the trial-and-error period typical in depression treatment.

In May 2024, we formed a strategic partnership with HMNC Holding GmbH ("HMNC") to investigate the potential of tildacerfont, a potent and highly selective, oral, small-molecule antagonist of the CRF_1 receptor, and the Cortibon Genetic Selection Tool ("Cortibon"), a companion diagnostic developed to identify MDD patients most likely to benefit from CRF_1receptor antagonism. Cortibon was developed using DNA samples from patients that were enrolled in a large-scale randomized controlled trial where a CRF_1receptor antagonist was compared with the standard of care (escitalopram) and placebo. Cortibon stratifies the patient sample with a sensitivity and specificity above 80% and post-hoc analysis suggests treatment benefit of a CRF_1receptor antagonist in the Cortibon-positive population.

HMNC and Spruce will collaborate in a Phase 2 proof-of-concept clinical trial called Tildacerfont as Antidepressant Medication and Relief in Depression ("TAMARIND"). TAMARIND's primary objective will be to explore efficacy of 400mg twice-daily tildacerfont versus placebo in improving depressive symptoms in MDD patients that are Cortibon-positive. Topline results from TAMARIND are anticipated in the first half of 2026.

Under the terms of the study and collaboration agreement, HMNC will fund and conduct TAMARIND. We have an option to in-license exclusive worldwide rights to Cortibon after completion of the study, if results are positive. If Spruce exercises its option, it will be responsible for the future worldwide development and commercialization of tildacerfont and Cortibon for the treatment of MDD under a collaboration framework that leverages HMNC's ongoing expertise in precision psychiatry and companion diagnostics. Pursuant to the license terms, HMNC would be entitled to receive certain milestone payments and tiered royalties on net sales of tildacerfont in MDD.

SPR202 for the Treatment of Congenital Adrenal Hyperplasia

Congenital Adrenal Hyperplasia ("CAH") is a chronic and potentially life-threatening rare disease with no cure. The most common cause of classic CAH, accounting for an estimated 95% of cases, is a genetic mutation leading to the production of dysfunctional 21-hydroxylase, an enzyme necessary for the biosynthesis of both corticosteroids and mineralocorticoids. Patients with classic CAH present with dysregulation across the HPA axis due to this enzymatic deficiency that shuts down the production of corticosteroids and, in approximately 75% of cases, the production of mineralocorticoids.

The immediate goal of treatment is the prevention of adrenal crises by replacing the missing physiological levels of corticosteroids. However, cortisol levels in the body vary daily, and normally increase during periods of high stress, making adequate control very difficult to achieve for most patients. In response to chronically absent or inadequate cortisol levels, the pituitary gland secretes higher levels of adrenocorticotropic hormone ("ACTH") to further stimulate steroid synthesis in the adrenal gland. This results in hyperplasia of the gland and the shunting of the steroid precursors to androgen synthesis, resulting in excess levels of androgens such as testosterone and A4 with overt symptoms of virilization. Therefore, the long-term symptomatic control in these patients is to reduce ACTH through supraphysiological doses of exogenous glucocorticoids via a negative feedback response.

The consequences of being born with CAH are severe. All patients born with classic CAH have cortisol deficiency, which makes these patients susceptible to adrenal crises in as early as one to four weeks of age. Due to the life-threatening adrenal crisis, screening for classic CAH is a standard part of routine neonatal screening in the United States and many other major geographies around the world. The most common cause of an adrenal crisis is an infection. Adrenal crisis can also be precipitated by other inducers of stress including surgery, dehydration, or trauma, and is characterized by extreme weakness, nausea, and vomiting. To prevent adrenal crises, physiological replacement of glucocorticoids is initiated in the neonatal period. Data from approximately 6.5 million newborn infants screened worldwide show an estimated incidence of approximately one in 14,000 – 18,000 live births.

Even when patients are diagnosed early and treated with steroids, the associated, continued exposure to high levels of androgens results in premature or precocious puberty, with onset sometimes occurring as early as five years of age. Early puberty drives early maturation of the body's bones, resulting in an adult height that is typically significantly below the height expected based on the parents' heights. In females, the presence of excess androgens in the body causes virilization, often leading to ambiguous genitalia and masculinizing features apparent at birth. Female adolescents and adults may develop male-pattern alopecia, acne, hirsutism, menstrual irregularities, and impaired fertility. Often commencing in early adolescence, a substantial proportion of males can develop testicular adrenal rest tumors, benign tumors that can lead to pain and impaired fertility.

In January 2025, we entered into a Collaboration and License Agreement (the "HBM License Agreement") with HBM Alpha Therapeutics, Inc ("HBM"). Pursuant to the HBM License Agreement, we obtained an exclusive license to a specified anti-CRH monoclonal antibody targeting CRF, now known as SPR202, for the treatment of Congenital Adrenal Hyperplasia ("CAH") and other indications.

SPR204 for the Treatment of Post-Bariatric Hypoglycemia

Bariatric surgery, such as Roux-en-Y gastric bypass, gastric banding, or sleeve gastrectomy, carries significant metabolic benefits, including weight loss, diabetes remission, and reduction of macrovascular and microvascular events. As a result of this clinical evidence, bariatric surgery is more often considered as an option for the treatment of obesity and diabetes, as well as for other metabolic complications such as non-alcoholic fatty liver disease. Given the increasing prevalence of bariatric surgery, clinicians are increasingly encountering complications of surgery. One such complication is post-bariatric hypoglycemia ("PBH"). PBH is usually defined as post-prandial hyperinsulinemic hypoglycemia, occurring typically 2–4 hours after ingestion of food, and presenting with documented low glucose values and hypoglycemic symptomatology, which subsides once euglycemia is restored.

PBH is associated with a lower quality of life, which improves after treatment. Hypoglycemia leads to psychological consequences, prolonged disruption of work and leisure activities, the possibility of road traffic accidents and limitations to the types of work that can be taken up. Moreover, recurrent hypoglycemia can lead to impaired awareness of hypoglycemia, impaired cognitive function, cardiac arrhythmia and mortality. As a result, it is important to identify, diagnose, and adequately treat PBH in people who have undergone bariatric surgery. PBH is believed to result from an excessive Glucagon-Like Peptide 1 ("GLP-1") response. There are no approved therapies for PBH, which affects approximately 160,000 people in the U.S.

In December 2024, we entered into the Antibody License Agreement (the "Antibody License Agreement") with Twist Bioscience Corporation ("Twist"). Pursuant to the Antibody License Agreement, we obtained a license to certain intellectual property rights related to SPR204, a monoclonal antibody antagonist. We plan to investigate SPR204 for the treatment of PBH.

License and Collaboration Agreements

License Agreement with Eli Lilly and Company

In May 2016, we entered into a license agreement (the "Lilly License Agreement") with Eli Lilly and Company ("Lilly"). Pursuant to the terms of the Lilly License Agreement, Lilly granted us an exclusive, worldwide, royalty bearing, sublicensable license under certain technology, patent rights, know-how, and proprietary materials (collectively, the "Lilly IP", and such patents, the "Lilly Licensed Patents"), relating to the CRF1 receptor antagonist compounds either listed in the Lilly License Agreement or covered by patent rights controlled by Lilly (collectively, the "Lilly Compounds"), to research, develop, commercialize, make, have made, use, sell, offer to sell, and import the Lilly Compounds and any products containing a Lilly Compound, including any products containing a Lilly Compound and one or more additional active pharmaceutical ingredients other than a Lilly Compound (collectively, the "Lilly Licensed Products"), for all pharmaceutical uses, including all diagnostic, therapeutic, and prophylactic uses, for human or animal administration (the "Field"). Lilly retained rights under the Lilly IP and the Lilly Licensed Patents for internal research purposes.

Under the Lilly License Agreement, we are required to use commercially reasonable efforts to develop and commercialize a Lilly Licensed Product in the Field. In addition, we are responsible to oversee, monitor, and manage all regulatory interactions, communications, and filings with, and submissions to regulatory authorities, with respect to the Lilly Licensed Products, and shall have final decision-making authority regarding all such regulatory activities, including the regulatory and labeling strategy and the content of submissions.

As partial consideration for the rights granted to us under the Lilly License Agreement, we made a one-time upfront payment to Lilly of approximately $0.8 million. We are also required to pay Lilly up to an aggregate of $23.0 million upon the achievement, during the time the Lilly License Agreement remains in effect, of certain milestones relating to the clinical development and commercial sales of the Lilly Licensed Products. Such payments are for predetermined fixed amounts, are paid only upon the first occurrence of each event, and are due shortly after achieving the applicable milestone. In addition, we are required to pay Lilly tiered royalties on annual worldwide net sales of Lilly Licensed Products in the Field, with rates ranging from mid-single-digits to low double-digits (the "Lilly Royalties"). The Lilly Royalties shall commence on a country-by-country basis on the date of the first commercial sale of Lilly Licensed Product in such country, and shall expire on a country-by-country basis on the latest of the following dates: (i) the tenth anniversary of the date of first commercial sale in such country, (ii) the expiration in such country of the last-to-expire Lilly Licensed Patent having a valid claim covering the manufacture, use, or sale of the Lilly Licensed Product as commercialized in such country, and (iii) the expiration of any data or regulatory exclusivity period for the Lilly Licensed Product in such country. Upon such expiration, the license granted to us with respect to such country shall be come fully paid-up, royalty-free, perpetual and irrevocable. In addition, the Lilly Royalties may be reduced upon the occurrence of certain events.

The Lilly License Agreement shall remain in effect until the expiration of all payment obligations thereunder, unless terminated earlier as follows, (i) termination upon mutual agreement, (ii) unilateral termination by us, on a worldwide basis or with respect to any country or countries, in our sole discretion, upon 60 days' advance written notice, (iii) unilateral termination by either party upon written notice of the other party's material breach of its obligations under the Lilly License Agreement and failure to cure such breach within 90 days after receiving written notice of such breach, and (iv) unilateral termination by either party in the event of a general assignment for the benefit of creditors of the other party or if proceedings are commenced against such other party relating to bankruptcy, insolvency, liquidation, reorganization, winding up, or composition or adjustment of debt, and such proceedings continue undismissed, or an order with respect to the foregoing shall be entered and continue unabated, for a period of more than 60 days.

Collaboration and License Agreement with Kaken Pharmaceutical Co. Ltd

In January 2023, we entered into a Collaboration and License Agreement (the "Kaken License Agreement") with Kaken Pharmaceutical Co. Ltd ("Kaken"). Under the terms of the Kaken License Agreement, we granted to Kaken the exclusive right to develop, manufacture and commercialize our product candidate, tildacerfont, for the

treatment of CAH in Japan. Pursuant to the Kaken License Agreement, Kaken will be responsible for securing and maintaining regulatory approvals necessary to commercialize tildacerfont in Japan. We will retain all rights to tildacerfont in all other geographies.

We have also granted to Kaken a right of first negotiation with respect to the development, manufacturing and commercialization of tildacerfont for CAH in China (including Hong Kong, Taiwan and Macau), South Korea and certain other specified southeastern Asian countries, and for indications other than CAH.

Pursuant to the Kaken License Agreement, Kaken made an upfront payment to us of $15.0 million. In addition to the upfront payment, we are entitled to receive up to an aggregate of approximately $65.0 million (at exchange rates in effect on the date of the Kaken License Agreement) upon the achievement of specified milestones related to the development, regulatory approval and commercialization of tildacerfont in Japan, including the achievement of specified net sales thresholds, if approved. Kaken has agreed to pay us a non-creditable, non-refundable specified purchase price for each unit of Company-manufactured product supplied to Kaken for commercial sale. In addition, we will also be entitled to receive a royalty for each unit of non-Company manufactured product sold equal to a range of double-digit percentages up to the mid-twenties based on annual net sales of tildacerfont in Japan. Both the purchase price for each unit and the royalty rate are subject to reduction in certain circumstances as specified in the Kaken License Agreement. Kaken's obligation to pay royalties will continue for ten years after the first commercial sale in Japan or, if later, until the expiration of regulatory exclusivity of tildacerfont or the expiration of the last valid claim of a Company-licensed patent covering tildacerfont in Japan (the "Royalty Term").

We have agreed to supply Kaken's clinical drug supply requirements of tildacerfont pursuant to a clinical supply agreement that the parties plan to consummate. During the Royalty Term, we have agreed to supply Kaken's requirements of tildacerfont pursuant to the Kaken License Agreement and a commercial supply agreement to be entered into by the parties, though Kaken may procure alternate suppliers. Following the Royalty Term, Kaken at its option may continue to purchase Company-manufactured tildacerfont at a purchase price equal to our manufacturing cost plus a low double-digit administrative fee.

Either party may terminate the Kaken License Agreement (i) in the event the other party shall have materially breached its obligations thereunder and such default shall have continued for a specified period after written notice thereof or (ii) upon the bankruptcy or insolvency of the other party. In addition, we may terminate the Kaken License Agreement upon prior written notice if (i) Kaken ceases all development or commercialization activities for a specified period of time, subject to certain exceptions, or (ii) challenges the validity, enforceability or scope of any of the patents licensed by us to Kaken under the Kaken License Agreement, subject to certain conditions. Kaken may terminate the Kaken License Agreement at any time for convenience upon prior written notice provided within a specified period of time to us.

Strategic Partnership with HMNC Brain Health

In May 2024, we entered into a license, development and option agreement (the "HMNC Agreement") with HMNC. Under the terms of the HMNC Agreement, HMNC will fund and conduct a Phase 2 proof-of-concept study of tildacerfont, a potent and highly selective, oral, small-molecule antagonist of the CRF1 receptor, in patients with MDD, who will be screened using Cortibon, HMNC's proprietary genetic selection tool. We have an option to in-license exclusive worldwide rights to Cortibon after completion of the study, if results are positive. If we exercise our option, we will be responsible for the future worldwide development and commercialization of tildacerfont and Cortibon for the treatment of MDD.

License Agreement with BioMarin Pharmaceutical, Inc.

In October 2024, we entered into that certain Asset Purchase Agreement (the "Purchase Agreement") with AVX (ABC), LLC, a Delaware limited liability company, in its sole and limited capacity as the assignee for the benefit of creditors of Allievex Corporation ("Allievex"). Pursuant to the Purchase Agreement, we acquired, among other things, that certain Exclusive License Agreement, by and between BioMarin Pharmaceutical Inc. ("BioMarin") and Allievex, dated October 22, 2019 (the "BioMarin License Agreement"). Pursuant to the terms of the BioMarin License Agreement, we obtained a worldwide exclusive, royalty-bearing, license under certain intellectual property to develop and commercialize enzyme replacement therapy products for the prevention or treatment of Sanfilippo Type A Syndrome, MPS IIIB, GM1 Gangliosidosis and GM2 Gangliosidosis, and we obtained a worldwide exclusive, royalty-bearing, license under certain other intellectual property to develop and commercialize products for the prevention or treatment of any indication. We also assumed the obligations of Allievex to pay BioMarin up to an aggregate of $88.0 million upon the achievement of certain development and regulatory milestones (up to

$22.5 million for the first MPSIIIB product) and up to an aggregate of $100.0 million per licensed product upon the achievement of certain sales milestones. In addition, we are required to pay to BioMarin certain (i) high-single digit to low double-digit tiered royalties on aggregate annual net sales of licensed MPS IIIB products and (i) mid-to-high single digit tiered royalties on aggregate annual net sales of licensed products other than MPS IIIB products, in each case during the applicable royalty term, subject to certain customary reductions and floors.

We may terminate the BioMarin License Agreement at any time for convenience upon prior written notice provided within a specified period of time. BioMarin may terminate the BioMarin License Agreement upon written notice if we (i) challenge the validity, enforceability or scope of any of the patents licensed by us under the BioMarin License Agreement, subject to certain conditions, or (ii) cease all material research and development activity for any licensed product for a specified period of time, subject to certain exceptions. Either we or BioMarin may also terminate the BioMarin License Agreement (i) in the event the other party shall have materially breached its obligations thereunder and such default shall have continued for a specified period after written notice thereof or (ii) upon the bankruptcy or insolvency of the other party.

License Agreement with Twist Bioscience Corporation

In December 2024, we entered into the Antibody License Agreement with Twist. Pursuant to the Antibody License Agreement, we obtained a license to certain intellectual property rights related to SPR204, a monoclonal antibody antagonist, controlled by Twist. At our election, we can pay an additional fee to extend the initial term of the research license. In addition, we have the exclusive option, upon payment of a one-time, non-refundable license fee, to acquire from Twist a license, with the right to sublicense, to (a) research and develop the antibody, (b) incorporate the antibody into products ("Products") and (c) commercialize such Products. We are also obligated to pay Twist up to $5 million upon the achievement of a certain regulatory milestone and up to $125.0 million per Product upon the achievement of certain sales milestones by each such Product. In addition, we are required to pay to Twist certain mid to high-single digit tiered royalties on aggregate annual net sales of Products during the applicable royalty term, subject to a certain customary reduction.

The Antibody License Agreement expires upon the expiration of the research license unless we exercise our option to receive a commercial license, after which the Antibody License Agreement will expire upon the expiration of the last remaining royalty term. Either we or Twist may terminate the Antibody License Agreement (i) in the event the other party shall have materially breached its obligations thereunder and such default shall have continued for a specified period after written notice thereof or (ii) upon the bankruptcy or insolvency of the other party. Twist may terminate the Antibody License Agreement upon prior written notice if we challenge the validity, scope, enforceability or patentability of any of the patents licensed by us to Twist under the Antibody License Agreement, subject to certain conditions.

Collaboration and License Agreement with HBM Alpha Therapeutics, Inc.

In January 2025, we entered into a Collaboration and License Agreement with HBM. Pursuant to the HBM License Agreement, we obtained an exclusive license to a specified product candidate developed by HBM in all countries outside of mainland China, Taiwan, Hong Kong, and Macau, for upfront consideration of $5.0 million and the issuance to HBM of a pre-funded warrant equal to 4.99% of our outstanding common stock as of the date of issuance of such warrant. Furthermore, we are obligated to pay HBM up to an aggregate of $390.0 million upon the achievement of certain development, regulatory, and sales milestones. In addition, we are required to pay to HBM certain mid to high-single digit tiered royalties on aggregate annual net sales of licensed products during the applicable royalty term, subject to certain customary reductions.

We may terminate the HBM License Agreement on a licensed product-by-licensed product basis or in its entirety at any time for convenience upon prior written notice provided within a specified period of time. Either we or HBM may also terminate the HBM License Agreement (i) in the event the other party shall have materially breached its obligations thereunder and such default shall have continued for a specified period after written notice thereof or (ii) upon the bankruptcy or insolvency of the other party. HBM may terminate the HBM License Agreement upon prior written notice if we (i) cease all development or commercialization activities for a specified period of time, subject to certain exceptions, or (ii) challenge the validity, enforceability or scope of any of the patents licensed by us to HBM under the HBM License Agreement, subject to certain conditions.

Sales and Marketing

We currently do not have a commercial organization for the marketing, sales, and distribution of

pharmaceutical products. We intend to build a highly specialized commercial organization to support the commercialization of TA-ERT, if approved, in the United States. Given a relatively small number of specialists treat a large proportion of patients with MPSIIIB, we believe this market can be effectively addressed with a modest-sized commercial sales force, alongside various high-touch patient initiatives. We also plan to seek strategic collaborations to benefit from the resources of biopharmaceutical companies specialized in either relevant disease areas or geographies in markets outside the United States.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including obtaining, maintaining and defending our patent rights. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications and obtaining issued patents, or in-licensing issued patents and patent applications, in the United States and in markets outside of the United States directed to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates and continuing innovation to develop, strengthen and maintain our proprietary position in the field of oncology. We also plan to rely on data exclusivity, market exclusivity and patent term extensions when available. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions, improvements and product candidates; to preserve the confidentiality of our trade secrets; to defend and enforce our proprietary rights, including any patents that we may own or license in the future; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

We have developed and continue to expand our patent portfolio for tildacerfont. Our patent portfolio consists of issued patents and pending applications that we own or in-licensed related to tildacerfont. As of December 31, 2024, the in-licensed portfolio from Lilly includes 4 issued U.S. patents, 32 granted patents in various markets outside of the United States, and one pending patent application in Venezuela.

As of December 31, 2024, the patent portfolio covering tildacerfont exclusively in-licensed from Lilly includes issued patents in Argentina, Azerbaijan, Brazil, Canada, Chile, China, the Czech Republic, Eurasia, France, Germany, Great Britain, Israel, India, Italy, Japan, Korea, Mexico, Pakistan, Portugal, Russia, Spain, Switzerland, Tajikistan, Taiwan, and the United States, along with a pending application in Venezuela. The issued United States patent covering tildacerfont is expected to expire in 2027, absent any patent term adjustments or extensions. Additionally, the in-licensed portfolio includes issued patents in the United States and granted patents in various markets outside of the United States covering methods of making tildacerfont. The issued United States patent is expected to expire in 2029, absent any patent term adjustments or extensions.

We have filed our own patent applications in the United States and other countries throughout the world directed to various methods of use and formulations. As of December 31, 2024, the company-owned portfolio includes at least 10 issued U.S. patents, 9 pending U.S. patent applications, 14 granted patents in various markets outside of the United States, 48 pending patent applications in various markets outside of the United States, and 2 pending international patent applications filed under the Patent Cooperation Treaty (PCT). The issued United States patents covering methods of treating CAH are expected to expire in 2038, absent any patent term adjustments or extensions. The remaining patent applications, if issued, would be expected to expire between 2038 and 2045, absent any patent term adjustments or extensions.

We have acquired Allievex's rights to 19 patent families, which Allievex in-licensed from BioMarin Pharmaceuticals. The in-licensed patent portfolio includes issued patents and pending patent applications related to TA-ERT and other programs. As of December 31, 2024, the portfolio includes 26 issued U.S. patents, 4 pending U.S. patent applications, 214 granted patents in various markets outside of the United States, and 22 pending patent applications in various markets outside of the United States.

As of January 15, 2025, we have licensed 2 patent families from HBM Alpha Therapeutics, Inc. The in-licensed portfolio includes pending patent applications related to SPR202. The in-licensed portfolio includes 1 pending U.S. patent application and 7 pending patent applications in various markets outside of the United States.

As of December 31, 2024, the patent portfolio covering TA-ERT exclusively in-licensed from BioMarin includes issued patents in Australia, Brazil, Canada, China, Europe, Hong Kong, Israel, India, Japan, Korea, Mexico, Russia, Taiwan, the United States, and South Africa, along with patent applications pending in the United

States and other markets outside of the United States. The issued United States patent covering TA-ERT as composition of matter is expected to expire in 2040, absent any patent term adjustments or extensions. We also in-licensed issued patents in Australia, Europe, Israel, Japan, Russia, and the United States along with pending patent applications in Brazil, Canada, China, Korea, Mexico, and New Zealand related to formulations of TA-ERT and methods of use. Patents related to tildacerfont may be eligible for patent term extensions in certain jurisdictions, including up to five years in both the United States and the EU, upon approval of a commercial use of the corresponding product by a regulatory agency in the jurisdiction where the patent was granted.

If approved in the United States, as TA-ERT, SPR202, and tildacerfont have not previously been approved in the United States for any indication, TA-ERT, SPR202, and tildacerfont may be eligible for new chemical entity regulatory exclusivity, which would run concurrently with their seven years of orphan drug exclusivity, respectively, if we obtain orphan drug exclusivity for their approved uses.

In addition to patent protection, we rely on trade secret protection and know-how to expand our proprietary position around our chemistry, technology, and other discoveries and inventions that we consider important to our business. Under the License Agreements with Lilly, BioMarin, and HBM, Lilly, BioMarin, and HBM granted intellectual property rights to know-how that are important to our business. The License Agreements impose various development, regulatory, and commercial diligence obligations, payment of milestones and/or royalties, and other obligations.

We also seek to protect our intellectual property in part by entering into confidentiality agreements with companies with whom we share proprietary and confidential information in the course of business discussions, and by having confidentiality terms in our agreements with our employees, consultants, scientific advisors, clinical investigators, and other contractors and also by requiring our employees, commercial contractors, and certain consultants and investigators, to enter into invention assignment agreements that grant us ownership of any discoveries or inventions made by them while in our employ.

Manufacturing

We rely on contract manufacturing organizations ("CMOs") to produce TA-ERT, tildacerfont, and our other investigational product candidates in accordance with the FDA's and comparable foreign regulatory authorities' current Good Manufacturing Practices ("cGMP"), regulations for use in our clinical trials. The manufacture of pharmaceuticals for human use is subject to extensive cGMP regulations, which impose various procedural and documentation requirements and govern all areas of record keeping, production processes and controls, personnel training, and quality control. TA-ERT, tildacerfont, and our other investigational product candidates are manufactured using common chemical engineering and synthetic processes from readily available raw materials. We have entered into manufacturing, development, and supply agreements with our CMOs that provide for the procurement of active pharmaceutical ingredient ("API") and drug product in connection with our planned and future clinical trials of TA-ERT and tildacerfont. These agreements contain no minimum purchase commitments or other purchase obligations. To date, the CMOs have met our manufacturing requirements, and we currently expect them to be capable of providing sufficient quantities of API and drug product to meet estimated full-scale commercial needs. Our relationships with CMOs are managed by internal personnel with extensive experience in pharmaceutical development and manufacturing.

Our contract manufacturing agreements give us visibility into the expected future cost of producing TA-ERT and tildacerfont at commercial scale. Based upon a range of prices of currently marketed therapies indicated for orphan diseases and MDD, we believe that our cost of goods for TA-ERT and tildacerfont, respectively, will be highly competitive.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid technological advancement, significant competition and an emphasis on proprietary products. We face potential competition from many different sources, including major and specialty pharmaceutical and biotechnology companies, academic research institutions, governmental agencies, compounding pharmacies and public and private research institutions. Any product candidates that we successfully develop and commercialize may compete with current therapies and new therapies that may become available in the future. We believe that the key competitive factors affecting the success of any of our product candidates will include efficacy, safety profile, dosing, cost, effectiveness of promotional support and intellectual property protection.

Many of our competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, preclinical testing, clinical trials, manufacturing, and marketing than we do. Future collaborations and mergers and acquisitions may result in further resource concentration among a smaller number of competitors. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated. These competitors may also vie for a similar pool of qualified scientific and management talent, sites and patient populations for clinical trials, as well as for technologies complementary to, or necessary for, our programs.

Government Regulation and Product Approval

As a pharmaceutical company that operates in the United States, we are subject to extensive regulation. Government authorities in the United States (at the federal, state, and local level) and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of drug products such as those we are developing. Any drug candidates that we develop must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in the EU are addressed in a centralized way, but country-specific regulation remains essential in many respects.

U.S. Biopharmaceutical Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act ("FDCA") and biologics additionally under the Public Health Service Act, and their implementing regulations. These biopharmaceutical products are also subject to other federal, state, and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. FDA sanctions could include, among other actions, refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. The process required by the FDA before a biopharmaceutical may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies in accordance *with* applicable regulations, including the FDA's Good Laboratory Practices ("GLP"), regulations, and other applicable regulations;
- *submission* to the FDA of an IND, which must become effective before human clinical trials may begin;
- *approval* by an institutional review board ("IRB") at each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable regulations, *including* the FDA's current good clinical practices ("GCP"), regulations to establish the safety and efficacy of the proposed drug for its proposed indication;
- submission to the FDA of a new drug application ("NDA") or BLA;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file it for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the biopharmaceutical is produced to assess compliance with the FDA's current cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality, and purity;

- potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the application;
- satisfactory completion of an FDA advisory committee review, if applicable; and
- FDA review and approval of the NDA or BLA prior to any commercial marketing or sale of the product in the United States.

Before testing any compounds with potential therapeutic value in humans, the candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity, and formulation, as well as animal studies, to assess the potential safety and activity of the candidate. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLPs. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a candidate at any time before or during clinical trials due to safety concerns or non-compliance.

Clinical trials involve the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an IRB or ethics committee, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1*. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution, and excretion, the side effects associated with increasing doses and if *possible*, to gain early evidence of effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2*. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, *to* preliminarily evaluate the efficacy of the product for specific targeted diseases or conditions and to determine dosage tolerance, optimal dosage, and dosing schedule.
- *Phase 3*. *Clinical* trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall benefit/risk ratio of the product and provide an adequate basis for product approval. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA or BLA.

In some cases, FDA may require, or sponsors may voluntarily pursue, post-approval studies, or Phase 4 clinical trials, that are conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, such as with accelerated approval drugs, FDA may mandate the performance of Phase 4 trials. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial.

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

U.S. Review and Approval Processes

If we successfully complete all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product. Data may come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product to the satisfaction of the FDA. The submission of an NDA or BLA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, the Pediatric Research Equity Act ("PREA") requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation. Unless otherwise required by regulation, the Pediatric Research Equity Act does not apply to any drug for an indication for which orphan designation has been granted. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s).

The FDA reviews all NDAs and BLAs submitted before it accepts them for filing and may request additional information rather than accepting them for filing. The FDA must make a decision on accepting an NDA or BLA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review. Under the Prescription Drug User Fee Act ("PDUFA"), guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA or BLA to review and act on the submission. This review typically takes 12 months from the date the application is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted. The FDA does not always meet its PDUFA goal dates for standard and priority applications, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the submission is accepted for filing, the FDA reviews it to determine, among other things, whether the proposed product is safe and effective for its intended use and whether the product is being manufactured in

accordance with cGMP to assure and preserve the product's identity, strength, quality, and purity. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions and typically follows the advisory committee's recommendations.

Before approving an NDA or BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA may inspect one or more clinical sites to assure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process, and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA or BLA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies, or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the application, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is submitted, the FDA may ultimately decide that the application does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, or precautions be included in the product labeling or may condition the approval on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. For example, the FDA may require Phase 4 testing, which involves clinical trials designed to further assess a drug safety and effectiveness, and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also determine that a risk evaluation and mitigation strategy ("REMS") is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor must submit a proposed REMS; the FDA will not approve the application without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools.

Accelerated Approval

Accelerated approval may be granted for products that are intended to treat a serious or life-threatening condition and that generally provide a meaningful therapeutic advantage to patients over existing treatments. A product eligible for accelerated approval may be approved on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. The accelerated approval pathway is contingent on a sponsor's agreement to conduct additional post-approval confirmatory studies to verify and describe the product's clinical benefit. These confirmatory trials must be completed with due diligence and, in some cases, the FDA may require that the trial be designed, initiated and/or fully enrolled prior to approval. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of

developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA or BLA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Orphan drug status in the EU has similar but not identical benefits in that jurisdiction.

Post-Approval Requirements

Any drug products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, manufacturing, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, and complying with FDA promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval to ensure the long-term stability of the drug product. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP requirements. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs 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 cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards 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 new safety risks; or imposition of distribution restrictions 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 untitled letters;
- clinical *holds* on 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;
- *consent* decrees, corporate integrity agreements, debarment, or exclusion from federal healthcare programs;
- *mandated* modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases, and other communications containing warnings or other safety information about the product; or injunctions or the imposition of civil or criminal penalties.

The FDA also may require post-marketing testing, known as Phase 4 testing, and surveillance to monitor the effects of an approved product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures.

The FDA closely regulates the marketing, labeling, advertising, and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity, and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

Both the Drug Supply Chain Security Act and state laws impose requirements to ensure accountability in distribution.

Marketing Exclusivity

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA ofor a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application ("ANDA"), or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety , where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the NDA holder.

The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from accepting ANDAs or 505(b)(2) NDAs for drugs referencing the approved application for review. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled

clinical trials necessary to demonstrate safety and effectiveness.

For biologics, the Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic without such alteration or switch. Upon licensure by the FDA, an interchangeable biosimilar may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

A reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product. In addition, the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product.

Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of non-patent market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Other U.S. Healthcare Laws and Compliance Requirements

Although we currently do not have any products on the market, we are and, upon approval and commercialization, will be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. In the United States, such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, price reporting, and physician sunshine laws and regulations.

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

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

The federal False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Several

pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-covered, uses.

The Health Insurance Portability and Accountability Act ("HIPAA") also created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items, or services. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Additionally, the federal Physician Payments Sunshine Act within the Affordable Care Act, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) annually report information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, certain ownership and investment interests held by physicians and their immediate family members.

We may also be subject to health data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH") and its implementing regulations, impose requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity, and their covered subcontractors. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

In order to distribute products commercially, we must also comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers, and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, track, and report gifts, compensation and other remuneration made to physicians and other healthcare providers, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we or our collaborators obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we or our collaborators receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such drug products.

In the United States, third-party payors include federal and state healthcare programs, government authorities, private managed care providers, private health insurers, and other organizations. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Such payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We or our collaborators may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Nonetheless, our product candidates may not be considered medically necessary or cost-effective. Moreover, the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

If we elect to participate in certain governmental programs, we may be required to participate in discount and rebate programs, which may result in prices for our future products that will likely be lower than the prices we might otherwise obtain. For example, drug manufacturers participating under the Medicaid Drug Rebate Program must pay rebates on prescription drugs to state Medicaid programs. Under the Veterans Health Care Act ("VHCA"), drug companies are required to offer certain drugs at a reduced price to a number of federal agencies, including the U.S. Department of Veterans Affairs and the U.S. Department of Defense, the Public Health Service and certain private Public Health Service designated entities in order to participate in other federal funding programs, including Medicare and Medicaid. Recent legislative changes require that discounted prices be offered for certain U.S. Department of Defense purchases for its TRICARE program via a rebate system. Participation under the VHCA also requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations. If our products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply.

Different pricing and reimbursement schemes exist in other countries. In Europe, governments may influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. Other countries may approve a specific price for a product, or they may instead adopt a system of director or indirect controls on the profitability of the company placing the product on the market. In addition, to obtain reimbursement or pricing approval, some countries of the European Economic Area ("EEA") may require the completion of clinical studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies. This Health Technology Assessment ("HTA") process is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. Other Member States allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates for which we or our collaborators receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates

may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other healthcare funding and applying new payment methodologies. For example, in March 2010, the Affordable Care Act was enacted, which affected existing government healthcare programs and resulted in the development of new programs.

Among the provisions of the Affordable Care Act are that it established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; expands eligibility criteria for Medicaid programs; increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program; created a new Medicare Part D coverage gap discount program; established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services ("CMS") to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

There have been executive, judicial and Congressional challenges and amendments to certain aspects of the Affordable Care Act. For example, the Inflation Reduction Act of 2022 ("IRA") was signed into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges and amendments in the future. It is unclear how such challenges and the healthcare reform measures of the second Trump administration will impact the Affordable Care Act and our business.

Other legislative changes have also been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect until 2032, unless additional Congressional action is taken.

There has also been heightened governmental scrutiny recently over the manner in which pharmaceutical companies set prices for their marketed products, which has resulted in several Presidential executive orders, Congressional inquiries and proposed federal legislation, as well as state efforts, designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, the IRA, among other things (i) directs the department of Health and Human Services ("HHS") to negotiate the price of certain high-expenditure, single-source drugs and biologics that have been on the market for at least 7 years covered under Medicare (the "Medicare Drug Price Negotiation Program") and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions took effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon prices of the first ten drugs that were subject to price negotiations, which take effect in January 2026. HHS will select up to fifteen additional products covered under Part D for negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program. In response to an October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency

measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Additional health reform measures may continue and affect our business in unknown ways, particularly given the recent change in administration. The current Trump administration is pursuing policies to reduce regulations and expenditures across government including at HHS, the FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. These actions may include, for example, directives to reduce agency workforce, rescinding a Biden administration executive order tasking the Center for Medicare and Medicaid Innovation to consider new payment and healthcare models to limit drug spending and eliminating the Biden administration's executive order that directed HHS to establishing an AI task force and developing a strategic plan, and directing certain federal agencies to enforce existing law regarding hospital and price plan transparency and by standardizing prices across hospitals and health plans. Additionally, in its June 2024 decision in Loper Bright Enterprises v. Raimondo, the U.S. Supreme Court overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper Bright decision could result in additional legal challenges to current regulations and guidance issued by federal agencies applicable to our operations, including those issued by the FDA. Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program created under the IRA.

In December 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA Regulation, was adopted in the EU. The HTA Regulation is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at EU level for joint clinical assessments in these areas. The HTA Regulation has applied from January 12, 2025 although it will enter into force iteratively and initially apply to new active substances to treat cancer and to all advanced therapy medicinal products, it will then be expanded to orphan medicinal products in January 2028, and to all centrally authorized medicinal products as of 2030. Selected high-risk medical devices will also be assessed under the HTA Regulation as of 2026.

We anticipate that these new laws and executive orders will result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business, especially given recent U.S. Presidential and Congressional elections. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition, and results of operations.

Data Privacy and Security

We and the third parties with whom we work are also subject to federal, state, local, and foreign data privacy and security laws, regulations, guidance, industry standards and other obligations related to personal data. Such obligations include, as applicable, U.S. state data breach notification laws, U.S. state health information privacy laws, federal and state consumer protection laws and regulations (e.g., Section 5 of the FTC Act), HIPAA, as amended by HITECH, and its implementing regulations, U.S. state data privacy laws such as the California Consumer Privacy Act ("CCPA"), as amended by the California Privacy Rights Act, the EU's General Data Protection Regulation ("EU GDPR"), and the EU GDPR as it forms part of United Kingdom law by virtue of section 3 of the European Union (Withdrawal) Act of 2018 ("UK GDPR") (the "EU GDPR" and the "UK GDPR" together, "GDPR").

These laws impose increasingly stringent and evolving regulatory frameworks related to the processing of personal data that increase our compliance obligations and exposure for any noncompliance. For example, where it applies, the GDPR requires stringent standards of data privacy and security concerning personal data, including limitations which could limit our ability to collect, use and share personal data (including health and medical information collected and processed in connection our relevant clinical trials and studies). In particular, the GDPR significantly restricts the transfer of personal data to the United States and other countries whose privacy laws are considered "inadequate". If there is no lawful manner for us to effect cross-border transfers of personal data in compliance with the GDPR, as applicable, or if the requirements for a compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate certain parts of our operations, increased exposure to regulatory actions, substantial fines and penalties, the inability to work with certain collaborators, partners, vendors and other third parties, and injunctions against our

processing or transferring of personal data necessary to operate our business. In addition, sanctions for breaches of the GDPR are significant: companies may face temporary or definitive bans on processing of personal data and other corrective actions; fines of up to 17.5 million pounds sterling under the UK GDPR / 20 million Euros under the EU GDPR, or, in each case, 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

Furthermore, we and the third parties with whom we work are subject to various and evolving federal, state, and foreign regulatory frameworks and other obligations related to cybersecurity that increase our compliance obligations and exposure for any noncompliance. For more information on the potential impact of these laws, including the GDPR, see the sections titled "Risk Factors—If our information technology systems or data, or those of third parties with whom we work, are or were compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse consequences" and "Risk Factors—We and the third parties with whom we work are subject to stringent and evolving obligations related to data privacy and security. These obligations include U.S. and foreign laws, regulations, and rules; contractual obligations; industry standards; and policies. Our (including the third parties with whom we work) actual or perceived failure to comply with such obligations could lead to regulatory investigations and actions (which could include civil or criminal penalties); private litigation (including class action claims) and mass arbitration demands; disruptions to our business operations; adverse publicity; and other adverse consequences that could negatively affect our operating results and business."

The U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act of 1977 ("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 United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Europe / Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we or our potential collaborators obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials.

Clinical Trials in the EU

In the EU, clinical trials are governed by the Clinical Trials Regulation (EU) No 536/2014 ("CTR"), which entered into application on January 31, 2022 repealing and replacing the former Clinical Trials Directive 2001/20 ("CTD"). The CTR is intended to harmonize and streamline clinical trial authorizations, simplify adverse-event reporting procedures, improve the supervision of clinical trials and increase transparency.

The CTR foresaw a three-year transition period that ended on January 31, 2025. Since this date, all new or ongoing trials are subject to the provisions of the CTR.

Certain requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Medicines used in clinical trials, must be manufactured in accordance with the guidelines on cGMP and in a GMP licensed facility, which can be subject to GMP inspections.

EU Review and approval process

In the EU, medicinal products can only be commercialized after a related marketing authorization ("MA") has been granted. To obtain an MA for a product in the EU, an applicant must submit a Marketing Authorization Application ("MAA") either under a centralized procedure administered by the EMA, or one of the procedures administered by the competent authorities of EU Member States (decentralized procedure, national procedure or mutual recognition procedure). An MA may be granted only to an applicant established in the EU.

Centralized procedure. The centralized procedure provides for the grant of a single MA, which is issued by the European Commission based on the opinion of the Committee for Medicinal Products for Human Use (the "CHMP") of the EMA and that is valid in all EU Member States, as well as Iceland, Liechtenstein and Norway (the European Economic Area ("EEA")). The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicines that contain a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that are highly innovative or for which a centralized process is in the interest of patients, authorization through the centralized procedure is optional on related approval. Under the centralized procedure the EMA's CHMP conducts the initial assessment of a product. The maximum timeframe for the evaluation of an MAA is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, a medicinal product targeting an unmet medical need is expected to be of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. Under the accelerated procedure the standard 210-day review period is reduced to 150 days (excluding clock stops). The CHMP can, however, revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

National authorization procedures. There are also two other possible routes to authorize medicinal products in several EU Member States, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- *Decentralized procedure*. Using the decentralized procedure, an applicant may apply for simultaneous authorizations in more than one EU country of medicinal products that have not yet been authorized in any EU Member State and that do not fall within the mandatory scope of the centralized procedure.
- *Mutual recognition procedure*. In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

An MA has, in principle, an initial validity of five years. 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 EU Member State in which the original MA was granted. The European Commission or the competent authorities of the EU Member States may decide on justified grounds relating to pharmacovigilance, to proceed with one further five year renewal period for the 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 EU market (for a centralized MA) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. In the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. An MA may also be granted "under exceptional circumstances" where the applicant can show that it is unable to provide comprehensive data on efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced.

Pediatric Development in the EU

In the EU, Regulation (EC) No 1901/2006 provides that all MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan ("PIP"), agreed with the EMA's Pediatric Committee. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the medicinal product for which MA is being sought. Once the MA is obtained in

all EU Member States and study results are included in the product information, even when negative, the product is eligible for a six-month extension to the Supplementary Protection Certificate , if any is in effect at the time of authorization or, in the case of orphan medicinal products, a two-year extension of orphan market exclusivity.

Data and Market Exclusivity in the EU

In the EEA, upon receiving marketing authorization, new active substances generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the date of authorization of the innovative product, after which a generic or biosimilar MAA can be submitted, and the innovator's data may be referenced. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. The overall ten-years of market exclusivity may, occasionally, be extended for a further year to a maximum of 11 years if, during the first eight years of those ten 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. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity and qualify for data exclusivity.

Orphan Designation in the EU

In the EU, Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a medicinal product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (i) the product is intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions; (ii) either (a) such conditions affect not more than 5 in 10,000 persons in the EU when the application is made, or (b) the product without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in developing the medicinal product; and (iii) there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition that has been authorized in the EU, or even if such method exists, the product will be of significant benefit to those affected by that condition.

Upon grant of a marketing authorization, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that the EMA cannot accept another marketing authorization application or accept an application to extend for a similar product and the European Commission cannot grant a marketing authorization for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP.

The period of market exclusivity may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria on the basis of which it received orphan medicinal product designation.

For other countries outside of the EU, such as the United Kingdom and countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country.

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

Human Capital Resources

In order to achieve the goals and expectations of our company, it is crucial that we continue to attract and retain top talent. To facilitate talent attraction and retention, we strive to make our company a safe and rewarding workplace, with opportunities for our employees to grow and develop in their careers, supported by strong compensation, benefits and health and wellness programs, and by programs that build connections between our employees.

As of December 31, 2024, we had 21 employees, including 15 in research and development and 6 in general and administrative functions. We believe our employee relations are good.

The success of our business is fundamentally connected to the well-being of our employees. Accordingly, we are committed to their health, safety and wellness. We provide our employees and their families with access to a

variety of innovative, flexible and convenient health and wellness programs, including benefits that provide protection and security so they can have peace of mind concerning events that may require time away from work or that impact their financial well-being; that support their physical and mental health by providing tools and resources to help them improve or maintain their health status and encourage engagement in healthy behaviors; and that offer choice where possible so they can customize their benefits to meet their needs and the needs of their families.

We provide compensation and benefits programs to help meet the needs of our employees. In addition to salaries, these programs include potential annual discretionary bonuses, stock awards, a 401(k) Plan, healthcare and insurance benefits, paid time off, family leave, and flexible work schedules, among others.

Corporate Information

We were initially formed as a limited liability company in Delaware in November 2014 under the name Spruce Biosciences LLC. In April 2016, Spruce Biosciences LLC converted into a Delaware corporation under the name Spruce Biosciences, Inc. Our principal executive offices are located at 611 Gateway Boulevard, Suite 740, South San Francisco, CA 94080. Our telephone number at that location is (415) 655-4168. Our corporate website address is www.sprucebiosciences.com. Information contained on, or that may be accessed through, our website is not incorporated by reference into this Annual Report and should not be considered a part of this Annual Report.

Available Information

We make available, free of charge through our website, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, and amendments to those reports, filed or furnished pursuant to Sections 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as soon as reasonably practicable after they have been electronically filed with, or furnished to, the SEC.

The SEC maintains an internet site (http://www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC.

Item 1A. Risk Factors.

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" before deciding whether to purchase, hold or sell shares of our common stock. The occurrence of any of the risks described below could harm our business, financial condition, results of operations, growth prospects, and/or stock price or cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report and those we may make from time to time. You should consider all of the risk factors described when evaluating our business.

Risks Related to Our Business and Industry

We have a limited operating history, have incurred significant net losses since our inception, and anticipate that we will continue to incur significant net losses for the foreseeable future, and such net losses are expected to increase as we continue our clinical development of, and seek regulatory approvals for, our product candidates, tralesinidase alfa, tildacerfont, SPR202, SPR204 and any future product candidates.

We are a late-stage biopharmaceutical company founded in 2014, and our operations to date have focused primarily on raising capital, establishing and protecting our intellectual property portfolio, organizing and staffing our company, business planning, and conducting preclinical and clinical development of, and manufacturing development for, our product candidates. Additionally, as an organization, we have not yet demonstrated an ability to successfully complete clinical development, obtain regulatory approvals, manufacture a commercial-scale product, or conduct sales and marketing activities necessary for successful commercialization. As we build our capabilities and expand our organization, we have not yet demonstrated an ability to overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. Consequently, any predictions about our future performance may not be as accurate as they would be if we had a history of successfully developing and commercializing biopharmaceutical products.

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effectiveness in the targeted indication or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any product revenue to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred significant net losses since our inception. If our product candidates are not successfully developed and approved, we may never generate any product revenue. For the years ended December 31, 2024 and 2023, we reported net losses of $53.0 million and $47.9 million, respectively. As of December 31, 2024, we had an accumulated deficit of $250.3 million.

We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our clinical development of, seek regulatory approvals for, and commercially launch tralesinidase alfa, tildacerfont and our other current and future product candidates, if approved. We may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our prior net losses and expected future net losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of increased expenses, or when, if at all, we will be able to achieve profitability.

We will need substantial additional financing to develop our product candidates and implement our operating plan. If we fail to obtain additional financing, we may be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Our operations have consumed substantial amounts of cash since our inception. We expect to continue to spend substantial amounts to continue the clinical development of, and seek regulatory approval for, tralesinidase alfa, tildacerfont and our other current and future product candidates. We will require significant additional amounts in order to prepare for commercialization, and, if approved, to launch and commercialize tralesinidase alfa, tildacerfont and our other current and future product candidates.

As of December 31, 2024, we had cash and cash equivalents of $38.8 million. In October 2020, we consummated our initial public offering ("IPO") and issued 6,900,000 shares of common stock for net proceeds of $93.4 million, after deducting underwriting discounts and commissions and offering expenses. In February 2023, we completed a private placement for net proceeds of $50.9 million. In April 2023, we received a $15.0 million upfront payment under the Kaken License Agreement.

Changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control.

We will require additional capital for the further development and commercialization of tralesinidase alfa, tildacerfont and our other current and future product candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate.

Additional funding may not be available on acceptable terms, or at all. In addition, we may not be able to access a portion of our existing cash and cash equivalents due to market conditions. For example, on March 10, 2023, the Federal Deposit Insurance Corporation ("FDIC") took control and was appointed receiver of Silicon Valley Bank ("SVB"). If other banks and financial institutions enter receivership or become insolvent in the future in response to financial conditions affecting the banking system and financial markets, our ability to access our existing cash and cash equivalents may be threatened and could have a material adverse effect on our business and financial condition. Further, as a result of geopolitical and macroeconomic events, the ongoing wars in Ukraine and Israel and related sanctions, the global credit and financial markets have experienced volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly or more dilutive. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back, or discontinue the development or commercialization of tildacerfont or other research and development initiatives. We also could be required to seek collaborators for our current product candidates and any future product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to our current product candidates and any future product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

Any of the above events could significantly harm our business, prospects, financial condition, and results of operations and cause the price of our common stock to decline.

We do not currently have sufficient working capital to fund our planned operations for the next twelve months and substantial doubt exists as to our ability to continue as a going concern.

As of December 31, 2024, we had incurred a net loss of $53.0 million and used $56.0 million of cash in operations. As of December 31, 2024, we had an accumulated deficit of $250.3 million and cash and cash equivalents of $38.8 million. We expect to continue to generate operating losses and have significant cash outflows from operating activities for at least the next few years. Until we can generate sufficient revenue, if ever, to fund our operations, we will need to finance future cash needs through public or private equity offerings, license agreements, debt financings or restructurings, collaborations, strategic alliances and marketing or distribution arrangements, and there can be no assurance that such arrangements will be available to us on a timely basis, or, if available, will be available on terms acceptable to us. Without alternative financing or proceeds from other strategic alternatives, we believe, based on our current operating plan, that our cash and cash equivalents as of December 31, 2024 will be insufficient to fund our operations and debt obligations for at least twelve months following the issuance date of our financial statements included elsewhere in this Annual Report. These conditions raise substantial doubt about our ability to continue as a going concern.

The perception of our ability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors and employees. If we are not able to obtain the necessary additional financing on a timely or commercially reasonable basis, we will be forced to delay or scale down some or all of our development activities (or perhaps even cease the operation of our business). If we are unable to continue as a going concern, our stockholders may lose some or all of their investment in the Company.

If we are unable to advance our product candidates in clinical development, obtain regulatory approval, and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

Human exposure to tralesinidase alfa has occurred in 3 clinical studies (201, 202, and 401) sponsored by Allievex. Study 201 was a completed Phase 1/2, first-in-human, multicenter, multinational, open-label, dose-escalation study. Study 250-202 was an extension study for patients who completed Study 201, and Study 401 was an extension study for patients who completed Study 202. Patients entered Study 201 by either completing Study 201's Part 1 dose-escalation study, or completing Study 901, an observational study of progressive MPS IIIB symptomatology.

In Studies 201 and 202, tralesinidase alfa was administered weekly by ICV infusion, and patients were evaluated in terms of neurocognitive function, behavior, sleep, quality of life (both of the patient and of the family/caregiver), MRI imaging characteristics, biochemical markers of disease burden and, in some cases, hearing. The primary objectives of these studies were to evaluate the safety and tolerability of tralesinidase alfa administered to patients with MPS IIIB via an ICV reservoir and catheter, and to evaluate the impact of tralesinidase alfa on cognitive function defined as communication skills in patients with MPS IIIB as assessed by the raw score and age-equivalent quotient ("AEq"). Patients in Study 202 were eligible for weekly or every other week dosing after Week 96. 22 patients enrolled in Study 201 and a total of 21 patients completed the study. 20 of these patients transitioned to Study 202. Study 401 was a Phase 3B/4 study to allow patients that completed Study 202 to continue receiving tralesinidase alfa for up to 3 additional years. The study was discontinued in October 2023 due to financial constraints of the product's prior sponsor.

Study 901 was a prospective, non-treatment study of MPS IIIB open to 1 – 10 year-old patients with cognitive developmental quotients ≥ 50 (determined by the BSID-III or KABC-II (each as defined below)) upon study entry. This study aimed to quantify MPS IIIB disease progression over time; to correlate changes in clinical features of the disease, in particular cognitive decline, with MRI characteristics and biochemical markers of disease burden; and to serve as a comparator for Studies 201 and 202. Following a screening period, patients were assessed every 12 weeks for up to 96 weeks. 22 patients enrolled and 20 patients matriculated into Study 201.

Study 902 was a prospective, non-treatment study of MPS IIIB that aimed to quantify the progression of cognitive decline in pediatric patients with MPS IIIB over time. The study enrolled patients regardless of age or baseline DQ. To this end, data collected from Study 902 will augment and extend data from Study 901. Data was prospectively collected from 44 patients for up to 192 weeks, with study visits occurring every 24 weeks.

In Studies 201 and 202, tralesinidase alfa was shown to significantly and durably normalize HS and HS-NRE levels over a five-year period. In Study 201, tralesinidase alfa was shown to normalize liver and spleen volume, while reducing cortical grey matter volume, reflecting removal of HS deposits from these target organs. We also believe that early intervention with tralesinidase alfa stabilizes cognitive decline in patients with MPSIIIB. In Study 201, patients with early disease, as defined by baseline cognition Bayley Scales of Infant and Toddler Development, Third Edition ("BSID-III") or the Kaufman Assessment Battery for Children, Second Edition ("KABC-II") Cognition AEq>40 months or Cognitive Disease Quotient>75, seven of ten patients (70%) demonstrated disease stability, or no meaningful loss of cognitive function at endpoint evaluation, as defined by BSID-III/KABC-11 cognition AEq ≥6 change from baseline. Three of twelve patients (25%) with more progressed disease demonstrated disease stability at endpoint evaluation.

In March 2024, in a type C meeting with the FDA, the FDA confirmed to Allievex that HS-NRE is deemed to be a biomarker reasonably likely to predict clinical benefit and could serve as a basis for accelerated approval. The FDA also confirmed that the completed clinical and nonclinical studies of tralesinidase alfa were sufficient for a biologics license application (BLA) submission and provided guidance around key design elements of a confirmatory Phase 3 trial (placebo-controlled 5-year study with a 2-year interim analysis in 14 patients), which must be initiated prior to potential accelerated approval of tralesinidase alfa. We intend to submit the BLA for tralesinidase alfa for the treatment of MPSIIIB in the first half of 2026.

In May 2024, we formed a strategic partnership with HMNC to investigate the potential of tildacerfont, a potent and highly selective, oral, small-molecule antagonist of the CRF_1receptor, and Cortibon, a companion diagnostic developed to identify major depressive disorder (MDD) patients most likely to benefit from CRF_1receptor antagonism. Cortibon was developed using DNA samples from patients that were enrolled in a large-scale randomized controlled trial where a CRF_1receptor antagonist was compared with the standard of care (escitalopram)

and placebo. Cortibon stratifies the patient sample with a sensitivity and specificity above 80% and post-hoc analysis suggests treatment benefit of a CRF_1receptor antagonist in the Cortibon-positive population.

HMNC and Spruce will collaborate in a Phase 2 proof-of-concept clinical trial called Tildacerfont as TAMARIND. TAMARIND's primary objective will be to explore efficacy of 400mg twice-daily tildacerfont versus placebo in improving depressive symptoms in MDD patients that are Cortibon-positive. Topline results from TAMARIND are anticipated in the first half of 2026.

The success of tralesinidase alfa, tildacerfont and our other current and future product candidates will depend on several factors, including the following:

- successful enrollment, site expansion and activation and patient engagement in our ongoing and planned clinical trials;
- successful completion of our ongoing and planned clinical trials with favorable results;
- acceptance by the FDA and EMA of the clinical trial design of our planned and ongoing clinical trials of tralesinidase alfa, tildacerfont and our other current and future product candidates;
- demonstrating safety and efficacy to the satisfaction of applicable regulatory authorities;
- the outcome, timing, and cost of meeting regulatory requirements established by the FDA, the European Commission, EMA, and other comparable foreign regulatory authorities;
- receipt of marketing approvals from applicable regulatory authorities, including one or more new drug applications ("NDAs") from the FDA, and maintaining such approvals;
- establishing commercial manufacturing capabilities and receiving/importing commercial supplies approved by the FDA and other regulatory authorities from any future third-party manufacturer;
- establishing sales, marketing, and distribution capabilities and commercializing tildacerfont, if approved, whether alone or in collaboration with others;
- establishing and maintaining patent and trade secret protection and regulatory exclusivity for tralesinidase alfa, tildacerfont and our other current and future product candidates;
- maintaining an acceptable safety profile of tildacerfont following approval; and
- maintaining and growing an organization of people who can develop and, if approved, commercialize, market, and sell tildacerfont to physicians, patients, healthcare payors, and others in the medical community.

If we do not achieve one or more of these factors, many of which are beyond our control, in a timely manner or at all, we could experience significant delays or an inability to obtain regulatory approvals or commercialize our product candidates.

Even if regulatory approvals are obtained, we may never be able to successfully commercialize our product candidates. In addition, we will need to transition at some point from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition. Accordingly, we may not be able to generate sufficient revenue through the sale of tildacerfont to continue our business.

We intend to seek FDA approval of TA-ERT for MPS IIIB through the accelerated approval pathway. If we are unable to obtain accelerated approval, we may be required to conduct additional preclinical studies or clinical trials beyond the confirmatory Phase 3 trial that we currently contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approval.

We intend to submit a BLA seeking accelerated approval based on existing clinical data, however there can be no assurance that such submission or application will be accepted for filing by the FDA or that approval will be granted on a timely basis, or at all. For example, in March 2024, in a type C meeting with the FDA, the FDA confirmed that HS-NRE is deemed to be a biomarker reasonably likely to predict clinical benefit and could serve as a basis for accelerated approval. The FDA also confirmed that the completed clinical and nonclinical studies of tralesinidase alfa were sufficient for a biologics license application BLA submission and provided guidance around key design elements of a confirmatory trial (placebo-controlled 5-year study with a 2-year interim analysis in 14 patients), which must be initiated prior to potential accelerated approval of tralesinidase alfa. Based, in part, on these

discussions, we intend to submit the BLA for tralesinidase alfa for the treatment of MPSIIIB in the first half of 2026. Failure to obtain accelerated approval would result in a longer time period to commercialization, if any, and would increase the cost of development and harm our competitive position in the marketplace.

Our clinical trials may fail to adequately demonstrate that our product candidates are well tolerated and provide sufficient clinical benefits for patients, which could prevent or delay regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of a product candidate, we must demonstrate through lengthy, complex, and expensive preclinical testing and clinical trials that a product candidate is both safe and effective for use in each target indication. Clinical trials often fail to demonstrate safety and efficacy of the product candidate studied for the target indication. Most product candidates that commence clinical trials are never approved by regulatory authorities for commercialization. We are seeking to develop treatments for MPS IIIB, MDD, congenital adrenal hyperplasia (CAH), and post-bariatric hypoglycemia (PBH). We intend to seek accelerated approval of TA-ERT for MPS IIIB based on existing clinical data. As a condition of seeking such approval of a BLA from the FDA, we will initiate a confirmatory Phase 3 trial, which must be initiated prior to potential accelerated approval of TA-ERT. We intend to submit the BLA for TA-ERT for the treatment of MPS IIIB in the first half of 2026. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of tralesinidase alfa and tildacerfont in other indications.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biopharmaceutical industry is characterized by intense competition and rapid innovation and our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis drug products that are more effective or less costly than tralesinidase alfa, tildacerfont, SPR202 and SPR204. We believe the key competitive factors that will affect the development and commercial success of our product candidates are, among other things:

- the efficacy, safety and tolerability profile of our product candidates relative to marketed products and product candidates in development by third parties;
- the time it takes for our product candidates to complete clinical development and receive marketing approval;
- the convenience of dosing;
- the price of our product candidates, including in comparison to branded or generic competitors;
- whether coverage and adequate levels of reimbursement are available under private and governmental health insurance plans, including Medicare;
- effectiveness of promotional support and high-touch patient initiatives;
- our ability to manufacture commercial quantities of our product candidates if they receive regulatory approval;
- our ability to negotiate preferential formulary status for our product candidates; and
- intellectual property protection.

Our commercial potential 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 products that we may develop. Our competitors' drugs may be more effectively marketed and sold than any drug we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated. We believe the key competitive factors affecting the success of our product candidates are likely to be efficacy, safety, and convenience.

Preclinical and clinical drug development involves a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of tralesinidase alfa, tildacerfont and our other current and future product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of any of our product candidates, we or our collaborators must conduct extensive trials to demonstrate the safety and efficacy of the product candidates in humans. Preclinical and clinical testing is expensive and difficult to design and implement, can take many years to complete, and its outcome is inherently uncertain. A failure of one or more preclinical or clinical trials can occur at any stage of testing. The results of preclinical studies and early clinical trials of tralesinidase alfa and tildacerfont, and preclinical studies of SPR202 and SPR204 may not be predictive of the results of later-stage clinical trials, and interim results of a trial do not necessarily predict final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. For example, we plan to use doses in our clinical trials for tralesinidase alfa and tildacerfont that may not be safe or efficacious doses. As such, our hypotheses of efficacy may not show the desired clinical results. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or safety profiles, notwithstanding promising results in earlier trials. Moreover, preclinical and clinical data is often susceptible to varying interpretations and analyses. We have faced significant setbacks as we conducted our two Phase 2b clinical trials for tildacerfont in adult patients with classic CAH, and we may continue to face such setbacks in our other development programs, which may delay or prevent regulatory approval of tildacerfont. For example, due to not meeting its primary efficacy endpoint, we terminated our CAHmelia-203 trial in March 2024 and our CAHmelia-204 trial in December 2024. Additionally, the prior sponsor of tralesinidase alfa, Allievex, discontinued clinical development due to financial constraints.

Further, if patients drop out of our clinical trials, miss scheduled doses or follow-up visits, or otherwise fail to follow clinical trial protocols, the integrity of data from our clinical trials may be compromised or not accepted by the FDA or other regulatory authorities, which would represent a significant setback for the applicable program.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may not be able to initiate or continue our clinical trials for tralesinidase alfa, tildacerfont and our other current and future product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA and comparable foreign regulatory authorities. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population especially in the case of an orphan indication, the proximity of patients to clinical sites, competition with other organizations or our own clinical trials for clinical trial sites or patients, the eligibility and exclusion criteria for the clinical trial, the design of the clinical trial, competing clinical trials, patient engagement, and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

In particular, one indication for which we are evaluating tralesinidase alfa is a rare neurodegenerative pediatric disorder with limited patient populations from which to draw participants in clinical trials. For example, we estimate the MPS-IIIB population in the United States is less than 200 patients. We are and will be required to identify and enroll a sufficient number of patients with the disorder under investigation for our clinical trials of tralesinidase alfa. Potential patients may not be adequately diagnosed or identified with the disorders which we are targeting or may not meet the entry criteria for our clinical trials. Additionally, other pharmaceutical companies with more resources and greater experience in drug development and commercialization are targeting these same disorders and are recruiting clinical trial patients from these patient populations, which may delay or make it more difficult to fully

enroll our clinical trials. Our inability to enroll a sufficient number of patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

Any delays in the commencement or completion, or termination or suspension, of our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue, and adversely affect our commercial prospects.

Before we can initiate clinical trials for our current product candidates or any future product candidates, we must submit the results of preclinical studies to the FDA, or comparable foreign regulatory authorities, along with other information, including information about chemistry, manufacturing and controls, and our proposed clinical trial protocol, as part of an IND or similar regulatory filing under which we must receive authorization to proceed with clinical development.

Before obtaining marketing approval from regulatory authorities for the sale of our current product candidates or any future product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our current product candidates and any future product candidates in humans. Clinical testing is expensive, time-consuming, and uncertain as to outcome. In addition, we may rely in part on preclinical, clinical and quality data generated by clinical research organizations ("CROs") and other third parties for regulatory submissions for our current product candidates and any future product candidates. While we have or will have agreements governing these third parties' services, we have limited influence over their actual performance. If these third parties do not make data available to us, or, if applicable, do not make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed, and we may need to conduct additional clinical trials or collect additional data independently. In either case, our development costs would increase.

We do not know whether our current or any future clinical trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA or comparable foreign regulatory authorities' failure to accept our proposed manufacturing processes and suppliers and/or requirement to provide additional information regarding our manufacturing processes before providing marketing authorization;
- obtaining regulatory authorizations to commence a clinical trial or reaching a consensus with regulatory authorities on clinical trial design or implementation;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining approval from one or more institutional review boards ("IRBs") or positive opinions from Ethics Committees ("ECs");
- IRBs or ECs refusing to approve or issuing a negative opinion, suspending, varying or terminating the clinical trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval or positive opinion of the clinical trial;
- changes to clinical trial protocols and related operationalization of such changes at clinical trial sites;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- acceptance by the FDA and EMA of the clinical trial design of our planned and ongoing clinical trials of tralesinidase alfa and tildacerfont;
- sites not timely activating, delaying screening activities, or deviating from clinical trial protocols;
- manufacturing sufficient quantities of tralesinidase alfa, tildacerfont or our other current and future product candidates or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trials at the rate we expect, or failing to return for post-treatment follow-up;

- subjects choosing an alternative treatment for the indications for which we are developing tralesinidase alfa, tildacerfont and our other current and future product candidates, or participating in competing clinical trials;
- lack of subject engagement in the clinical trials or subjects dropping out of a clinical trial;
- lack of adequate funding to continue the clinical trial, such as that experienced by Allievex in relation to the continued development of tralesinidase alfa;
- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of SAEs in clinical trials of the same class of agents conducted by other companies;
- a facility manufacturing our product candidates or any of its components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing practice ("cGMP"), regulations or other applicable requirements, or infections or cross-contaminations of our product candidates in the manufacturing process;
- any changes to our manufacturing process, suppliers or formulation that may be necessary or desired;
- third-party vendors not performing manufacturing and distribution services in a timely manner or to sufficient quality standards;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practice ("GCP"), or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or
- the impacts of contagious disease outbreaks on our ongoing and planned clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs or ECs of the institutions in which such trials are being conducted or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we have amended, and may need to further amend, clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to competent authorities, IRBs or ECs for reexamination, which may impact the costs, timing, or successful completion of a clinical trial.

Further, conducting clinical trials in foreign countries, which we are doing for tildacerfont and may do for any future product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve and have served as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or 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 trial. 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 tildacerfont.

If we experience delays in the completion of, or termination of, any clinical trial of tralesinidase alfa, tildacerfont or our other current and future product candidates, the commercial prospect of tralesinidase alfa, tildacerfont or our other current and future product candidates will be harmed, and our ability to generate product revenue will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of tralesinidase alfa, tildacerfont or our other current and future product candidates. Further, delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize tralesinidase alfa and tildacerfont and our competitors may be able to bring products to market before we do, and the commercial viability of tralesinidase alfa and tildacerfont could be significantly reduced. Any of these occurrences may harm our business, financial condition, and prospects significantly.

Tralesinidase alfa and tildacerfont are, and our other current and future product candidates will be, subject to extensive regulation and compliance obligations, which are costly and time-consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize tralesinidase alfa, tildacerfont and our other current and future product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing, and distribution of our product candidates subject to extensive regulation by the FDA in the United States and by comparable foreign regulatory authorities in foreign markets. In the United States, we are not permitted to market tralesinidase alfa, tildacerfont or any other current or future product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity, and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA has substantial discretion in the drug approval process, including the ability to delay, limit, or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed. Neither we nor any future collaborator is permitted to market tralesinidase alfa, tildacerfont or any other current or future product candidates in the United States until we receive approval of an NDA or BLA from the FDA. Similar requirements and risks are applicable in foreign markets. We have not previously submitted an NDA or BLA to the FDA, or similar drug approval filings to comparable foreign authorities.

Prior to obtaining approval to commercialize a product candidate in the United States or in foreign markets, we must demonstrate with substantial evidence from adequate and well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from non-clinical studies and clinical trials can be interpreted in different ways. Even if we believe the non-clinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities, as the case may be, may also require us to conduct additional preclinical studies or clinical trials for tralesinidase alfa, tildacerfont and any future product candidates either prior to or post-approval, or may object to elements of our clinical development program.

Tralesinidase alfa, tildacerfont and our other current and future product candidates could fail to receive regulatory approval for many reasons, including the following:

- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by people using drugs similar to tralesinidase alfa, tildacerfont and our other current and future product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;

- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for any of its proposed indications;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials may not be sufficient to satisfy the FDA or comparable foreign regulatory authorities to support the submission of an NDA, BLA or other comparable submissions in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere, requiring, in the case of adult patients with classic CAH, additional clinical trials beyond our ongoing Phase 2b clinical trial prior to any such approval;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Any of the above events could prevent us from achieving market approval of tralesinidase alfa, tildacerfont or our other current and future product candidates and could substantially increase the costs of commercializing tralesinidase alfa, tildacerfont or our other current and future product candidates. The demand for tralesinidase alfa, tildacerfont or any future product candidates could also be negatively impacted by any adverse effects of a competitor's product or treatment.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market tildacerfont and our other current and future product candidates, which would significantly harm our business, financial condition, results of operations, and prospects.

Even if we eventually complete clinical trials and receive approval of an NDA, BLA or foreign marketing application for tralesinidase alfa, tildacerfont and our other current and future product candidates, the FDA or comparable foreign regulatory authority may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, and/or the implementation of a risk evaluation and mitigation strategy ("REMS") or comparable foreign strategies which may be required to ensure safe use of the drug after approval. The FDA or the comparable foreign regulatory authority also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or comparable foreign regulatory authority may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

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

From time to time, we may publicly disclose interim, topline, or preliminary data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, topline, or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or topline

data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. Preliminary or top-line data may include, for example, data regarding a small percentage of the patients enrolled in a clinical trial, and such preliminary data should not be viewed as an indication, belief or guarantee that other patients enrolled in such clinical trial will achieve similar results or that the preliminary results from such patients will be maintained. As a result, such data should be viewed with caution until the final data are available. Adverse differences between preliminary, interim, or topline data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

Further, others, including regulatory authorities, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability, or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate, or our business. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain regulatory approval for, and commercialize, our product candidates and any future product candidates may be harmed, which could harm our business, operating results, prospects, or financial condition.

If the market opportunities for tralesinidase alfa, tildacerfont and our other current and future product candidates are smaller than we believe they are, our future revenue may be adversely affected, and our business may suffer.

If the size of the market opportunities in each of our target indications for our product candidates and any future product candidates is smaller than we anticipate, we may not be able to achieve profitability and growth. We focus our clinical development on treatments for neurological disorders. For example, we believe that tralesinidase alfa has the potential to bring therapeutic benefit to patients suffering from MPSIIIB. Given the relatively small number of patients who have MPSIIIB, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these disorders. In addition, our estimates of the patient populations for our target indications have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, and market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these disorders. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. For example, due to the lack of available treatment options, newborn screening programs have not been widely adopted for the detection of MPSIIIB. As a result, patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. In addition, the potentially addressable patient population for MPSIIIB may be limited or may not be amenable to treatment with tralesinidase alfa, if approved. Further, even if we obtain significant adoption and market penetration for tralesinidase alfa in MPSIIIB, we may never achieve profitability despite obtaining such significant market share, as other pharmaceutical companies with more resources and greater experience in drug development and commercialization are targeting this same disorder.

Obtaining and maintaining regulatory approval for a product candidate in one jurisdiction does not mean that we will be successful in obtaining regulatory approval for that product candidate in other jurisdictions.

Obtaining and maintaining regulatory approval for a product candidate in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, including a number of countries in

the EU, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our product candidates is also subject to approval.

As with the FDA, obtaining approval of a Marketing Authorization Application ("MAA") from the European Commission, following the related opinion of the Committee for Medicinal Products for Human Use, is a similarly lengthy and expensive process and the EMA has its own procedures for assessing product candidates. Regulatory authorities in jurisdictions outside of the United States and the EU also have requirements for approval for product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of tralesinidase alfa in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of tralesinidase alfa will be harmed, which would adversely affect our business, prospects, financial condition, and results of operations.

We currently have no marketing and sales organization and have yet to commercialize a product. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell tralesinidase alfa, tildacerfont and our other current and future product candidates, we may not be able to generate product revenues.

We currently do not have a commercial organization for the marketing, sales, and distribution of pharmaceutical products. To commercialize our product candidates and any future product candidates, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We intend to build a highly specialized commercial organization to support the commercialization of tralesinidase alfa, if approved, in the United States.

The establishment and development of our own sales force or the establishment of a contract sales force to market our product candidates and any future product candidates will be expensive and time-consuming and could delay any commercial launch. Moreover, we may not be able to successfully develop this capability. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts. To the extent we rely on third parties to commercialize our product candidates, if approved, we may have little or no control over the marketing and sales efforts of such third parties and our revenues from product sales may be lower than if we had commercialized tralesinidase alfa and tildacerfont and any future product candidates ourselves. In the event we are unable to develop our own marketing and sales force or collaborate with a third-party marketing and sales organization, we would not be able to commercialize tralesinidase alfa or any future product candidates.

Unfavorable U.S. and global economic and geopolitical conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the U.S. and global economies, the U.S. and global financial markets and adverse geopolitical and macroeconomic developments. U.S. and global market and economic conditions have been, and may continue to be, disrupted and volatile due to many factors, including component shortages and related supply chain challenges, outbreaks of contagious diseases, the wars in Ukraine and Israel and related sanctions, recent and potential future disruptions in access to bank deposits or lending commitments due to bank failures, and increasing inflation rates and the responses by central banking authorities to control such inflation, among others. General business and economic conditions that could affect our business, financial condition or results of operations include fluctuations in economic growth, debt and equity capital markets, liquidity of the global financial markets, access to our liquidity within the U.S. banking system, the availability and cost of credit, investor and consumer confidence, and the strength of the economies in which we, our manufacturers and our suppliers operate.

A severe or prolonged global economic downturn could result in a variety of risks to our business. For example, inflation rates, particularly in the United States, have increased to levels not previously seen in years, and increased inflation may result in increases in our operating costs (including our labor costs), reduced liquidity and limits on our ability to access credit or otherwise raise capital on acceptable terms, if at all. In addition, the U.S. Federal Reserve and equivalent foreign entities have raised, and may again raise, interest rates in response to concerns about inflation, which, coupled with reduced government spending and volatility in financial markets may have the effect of further increasing economic uncertainty and heightening these risks. Risks of a prolonged global

economic downturn are particularly true in Europe, which is undergoing a continued severe economic crisis. A weak or declining economy could also strain our suppliers and manufacturers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We have a banking relationship with SVB. SVB was closed on March 10, 2023 by the California Department of Financial Protection and Innovation, which appointed the FDIC as receiver. On March 12, 2023, the U.S. Treasury, Federal Reserve, and FDIC announced that SVB depositors will have access to all of their money starting March 13, 2023. On March 27, 2023, First Citizens Bank and Trust Company announced that it entered into an agreement with the FDIC to purchase out of FDIC receivership substantially all loans and certain other assets, and assume all customer deposits and certain other liabilities of Silicon Valley Bridge Bank, N.A. While we have not experienced any losses in such accounts, the recent failure of SVB potentially exposed us to significant credit risk prior to the completion by the FDIC of the resolution of SVB in a manner that fully protected all depositors. We are assessing how to prevent this exposure in the future, however, any potential future disruptions in access to bank deposits or lending commitments due to bank failures may expose us to significant credit risk.

In addition, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial institutions with which we have arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which we have financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

Additionally, financial markets around the world experienced volatility following the recent invasion of Ukraine by Russia. In response to the invasion, the United States, United Kingdom and EU, along with others, imposed significant new sanctions and export controls against Russia, Russian banks and certain Russian individuals and may implement additional sanctions or take further punitive actions in the future. The full economic and social impact of the sanctions imposed on Russia (as well as possible future punitive measures that may be implemented), as well as the counter measures imposed by Russia, in addition to the ongoing military conflict between Ukraine and Russia and related sanctions, which could conceivably expand into the surrounding region, remains uncertain; however, both the conflict and related sanctions have resulted and could continue to result in disruptions to trade, commerce, pricing stability, credit availability, supply chain continuity and reduced access to liquidity in both Europe and globally, and has introduced significant uncertainty into global markets. In particular, the ongoing Russia-Ukraine conflict and related sanctions has contributed to rapidly rising costs of living (driven largely by higher energy prices) in Europe and other advanced economies. Further, a weak or declining economy could strain our suppliers and manufacturers. Similarly, it is possible that the war in Israel may have similar effects. As a result, our business and results of operations may be adversely affected by the ongoing wars in Ukraine and Israel and related sanctions, particularly to the extent it escalates to involve additional countries, further economic sanctions or wider military conflict.

We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract, retain, manage and motivate highly qualified managerial, scientific, and medical personnel. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements in a timely manner could potentially harm our business, prospects, financial condition or results of operations.

We conduct our operations in South San Francisco, California. This region serves as the headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific, and development teams may terminate their employment with us on short notice. Although we have employment agreements and/or offer letters with our key employees, these arrangements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior scientific and medical personnel.

Many of the other biotechnology and pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. They may also provide more diverse opportunities and better chances for career advancement. Some of these characteristics are more appealing to high quality candidates than what we can offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can discover, develop and commercialize product candidates will be limited.

Use of tralesinidase alfa, tildacerfont or our other current and future product candidates could be associated with side effects, adverse events or other properties that could delay or prevent regulatory approval or result in significant negative consequences following marketing approval, if any.

As is the case with biopharmaceuticals generally, it is likely that there may be side effects and adverse events associated with the use of tralesinidase alfa, tildacerfont and our other current and future product candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by tralesinidase alfa, tildacerfont and our other current and future product candidates could cause us or regulatory authorities to interrupt, delay, terminate or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. For example, although tildacerfont has been assessed in over 400 subjects across ten completed clinical trials in which it has been well tolerated with no drug-related SAEs, in our proof-of-concept, dose-escalating Phase 2a clinical trial in adults with classic CAH, one patient experienced a grade one liver-related adverse event after 14 days of treatment at 1,000mg once daily. This patient had elevated levels of alanine transaminase ("ALT") between five and nine times the ULN, elevations in aspartate aminotransferase ("AST") less than five times the ULN, and no increases in bilirubin. The event resolved on its own without additional medical intervention. If drug-related SAEs are observed, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval for tildacerfont for any or all targeted indications. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition, and prospects significantly.

Furthermore, if tralesinidase alfa, tildacerfont and our other current and future product candidates receive marketing approval, and we or others later identify undesirable side effects caused by such product candidate, a number of potentially significant negative consequences could result, including:

- we may be forced to suspend marketing of that product, or decide to remove the product form the marketplace;
- regulatory authorities may withdraw approvals or suspend or change their approvals of such product or place restrictions on the way it is prescribed;
- regulatory authorities may require additional warnings on the label or limit access of that product to selective specialized centers with additional safety reporting and with requirements that patients be geographically close to these centers for all or part of their treatment;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way the product is administered;
- we could be subject to fines, injunctions, or the imposition of criminal or civil penalties;

- we could be sued and held liable for harm caused to patients; and
- the product may become less competitive, and our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of tralesinidase alfa, tildacerfont and our other current and future product candidates, if approved, and could significantly harm our business, results of operations, and prospects.

If we receive regulatory approval for tralesinidase alfa, tildacerfont and our other current and future product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with any product.

Any regulatory approvals that we receive may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including post-market studies or clinical trials, and surveillance to monitor safety and effectiveness. The FDA may also require us to adopt a REMS to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. We or our collaborators may also be required to adopt a REMS or engage in similar actions, such as patient education, certification of health care professionals, or specific monitoring, if we or others later identify undesirable side effects caused by any product that we develop alone or with collaborators. Comparable foreign regulatory authorities may impose similar requirements in their markets.

In addition, if the FDA or a comparable foreign regulatory authority approves a product candidate, the manufacturing, quality control, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export, and recordkeeping for the approved product will be subject to extensive and ongoing regulatory requirements. The FDA and comparable foreign regulatory authorities also require submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP requirements and GCP for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product candidate, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- issue warning letters or untitled letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners, or require other restrictions on the labeling or marketing of such products;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend, withdraw or modify regulatory approval;
- suspend, terminate or modify any ongoing clinical trials;
- require that we conduct post-market studies;
- refuse to approve pending applications or supplements to applications filed by us;
- grant approval for narrower indications than we requested;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize tralesinidase alfa, tildacerfont and our other current and future product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the U.S. Federal Trade Commission, the Department of Justice ("DOJ"), the Office of Inspector General of the U.S. Department of Health and Human Services ("HHS"), state attorneys general, members of the U.S. Congress, and the public. Additionally, advertising and promotion of any product candidate that obtains approval outside of the United States will be heavily scrutinized by comparable foreign entities and stakeholders. Violations, including actual or alleged promotion of our products for unapproved or off-label uses, are subject to enforcement letters, inquiries, and investigations, and civil and criminal sanctions by the FDA, DOJ, or comparable foreign authorities. Any actual or alleged failure to comply with labeling and promotion requirements may result in fines, warning letters, mandates to corrective information to healthcare practitioners, injunctions, or civil or criminal penalties.

The policies of the FDA and other regulatory authorities, including foreign regulatory authorities, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval for tralesinidase alfa, tildacerfont and our other current and future product candidates. For example, the U.S. Supreme Court's June 2024 decision in *Loper Bright Enterprises v. Raimondo* overturned the longstanding *Chevron* doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The *Loper* decision could result in additional legal challenges to regulations and guidance issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the *Loper* decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action or as a result of legal challenges, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition, and results of operations.

Changes in funding for the FDA and other government agencies, or comparable foreign regulatory authorities could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

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

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

If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Even if we obtain regulatory approval for tralesinidase alfa, tildacerfont and our other current and future product candidates, they may not gain market acceptance among physicians, patients, healthcare payors and others in the medical community.

Tralesinidase alfa, tildacerfont and our other current and future product candidates may not be commercially successful. The commercial success of Tralesinidase alfa, tildacerfont or our other current and future product candidates, if approved, will depend significantly on the broad adoption and use of such product by physicians and

patients for approved indications. The degree of market acceptance of tralesinidase alfa, tildacerfont or our other current and future products, if approved, will depend on a number of factors, including:

- the clinical indications for which such product candidate is approved;
- physicians and patients considering the product as a safe and effective treatment;
- the potential and perceived advantages of the product over alternative treatments;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities;
- the timing of market introduction of the product as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage and adequate reimbursement by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts and those of any collaboration or distribution partner on whom we rely for sales in foreign jurisdictions.

If tralesinidase alfa, tildacerfont or any other current or future product candidate is approved but fails to achieve market acceptance among physicians, patients, healthcare payors or others in the medical community, we will not be able to generate significant revenues, which would have a material adverse effect on our business, prospects, financial condition, and results of operations. Our commercial success also depends on coverage and adequate reimbursement by third-party payors, including government payors, which may be difficult or time-consuming to obtain, may be limited in scope and may not be obtained in all jurisdictions in which we may seek to market our product candidates. In addition, even if tralesinidase alfa, tildacerfont and any other current or future product candidate gains acceptance, the markets for the treatment of patients with our target indications may not be as significant as we estimate.

If tralesinidase alfa, tildacerfont and any other current or future product candidate is approved for marketing, and we are found to have improperly promoted off-label uses, or if physicians prescribe or use tralesinidase alfa, tildacerfont and any other current or future product candidates off-label, we may become subject to prohibitions on the sale or marketing of tralesinidase alfa, tildacerfont and any other current or future product candidates, significant fines, penalties, sanctions, or product liability claims, and our image and reputation within the industry and marketplace could be harmed.

The FDA, DOJ, and comparable foreign authorities strictly regulate the marketing and promotional claims that are made about pharmaceutical products following approval. In particular, a product may not be promoted for uses or indications that are not approved by the FDA or comparable foreign authorities as reflected in the product's approved labeling and Summary of Product Characteristics. However, if we receive marketing approval for tralesinidase alfa, tildacerfont and any other current or future product candidates, physicians can prescribe such product to their patients in a manner that is inconsistent with the approved label based on the physician's independent medical judgement. If we are found to have promoted such off-label uses, we may receive warning letters from the FDA and comparable foreign authorities, incur penalties, and become subject to significant liability, which would materially harm our business. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. If we become the target of such an investigation or prosecution based on our marketing and promotional practices, we could face similar sanctions, which would materially harm our business. In addition, management's attention could be diverted from our business operations, significant legal expenses could be incurred, and our reputation could be damaged. The FDA and other governmental authorities, including comparable foreign authorities, have also required that companies enter into consent decrees or permanent injunctions under which

specified promotional conduct is changed or curtailed in order to resolve enforcement actions. If we are deemed by the FDA, DOJ, or other governmental authorities, or comparable foreign regulatory authorities, to have engaged in the promotion of tralesinidase alfa, tildacerfont or any other current or future product candidate for off-label use, we could be subject to certain prohibitions or other restrictions on the sale or marketing and other operations or significant fines and penalties, and the imposition of these sanctions could also affect our reputation and position within the industry.

Coverage and reimbursement may be limited or unavailable in certain market segments for tralesinidase alfa, tildacerfont and our other current or future product candidates, which could make it difficult for us to sell tralesinidase alfa, tildacerfont and our other current or future product candidates profitably.

Successful sales of tralesinidase alfa, tildacerfont and any other current or future product candidates, if approved, depend on the availability of coverage and adequate reimbursement from third-party payors. Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from U.S. governmental healthcare programs, such as Medicare and Medicaid, or comparable foreign healthcare programs, and commercial payors is critical to new product acceptance, and we may not obtain such coverage or adequate reimbursement. Moreover, we focus our clinical development on treatments for serious disorders, some of which have relatively small patient populations. As a result, we must rely on obtaining appropriate coverage and reimbursement for these populations.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and the amount of reimbursement they will provide. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective, and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. We may not be able to provide data sufficient to obtain coverage and adequate reimbursement. If we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use tralesinidase alfa, tildacerfont or any other current or future product candidate unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost. Additionally, the reimbursement rates and coverage amounts may be affected by the approved label for tralesinidase alfa, tildacerfont or any other current or future product candidate. If coverage and reimbursement of our future products are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

In addition, the market for tralesinidase alfa, tildacerfont and any other current or future product candidates will depend significantly on access to third-party payors' drug formularies or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access through formulary controls or otherwise to a branded drug when a less costly generic equivalent or other alternative is available.

In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement for drug 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 tralesinidase alfa, tildacerfont and any other current or future product candidates to each payor separately, with no assurance that coverage and adequate reimbursement

will be obtained. Further, coverage policies and third-party reimbursement rates may change at any time. Therefore, even if favorable coverage and reimbursement status is attained, less favorable coverage policies and reimbursement rates may be implemented in the future.

We intend to seek approval to market tralesinidase alfa and tildacerfont in the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for tralesinidase alfa or tildacerfont, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of prescription pharmaceuticals and biologics is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval for a drug candidate. In addition, market acceptance and sales of a product will depend significantly on the availability of coverage and adequate reimbursement from third-party payors for a product and may be affected by existing and future health care reform measures.

Current and future legislation and healthcare reform measures may increase the difficulty and cost for us to obtain marketing approval for and commercialize tralesinidase alfa, tildacerfont and any other current or future product candidates and may affect the prices we may set.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures that may reduce or limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively the "Affordable Care Act"), was enacted in the United States. Among the provisions of the Affordable Care Act of importance to our potential product candidates are that it established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; expands eligibility criteria for Medicaid programs; increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program; created a new Medicare Part D coverage gap discount program; established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services ("CMS") to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

There have been executive, judicial and Congressional challenges to certain aspects of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. For example, on August 16, 2022, the Inflation Reduction Act of 2022 ("IRA") was signed into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges and amendments in the future. It is unclear how any such challenges and the healthcare reform measures of the second Trump administration will impact the Affordable Care Act and our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect until 2032, unless additional Congressional action is taken.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several recent Presidential executive orders, congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products.

At the federal level the IRA, among other things (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics that have been on the market for at least 7 years covered under Medicare and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that

outpace inflation. These provisions began to effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon reimbursement price of the first ten drugs that were subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. HHS will select up to fifteen additional drugs covered under Part D for negotiation in 2025. HHS has and will continue to issue and update guidance as these programs are implemented. In addition, in response to an October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the Center for Medicare and Medicaid Innovation which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework.

At the state level, individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, on January 5, 2024, the FDA approved Florida's Section 804 Importation Program ("SIP") proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted SIP proposals that are pending review by the FDA. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition, and prospects. In addition, regional healthcare authorities 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. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition, and prospects.

We expect that other healthcare reform measures that may be adopted in the future, particularly in light of the recent U.S. Presidential and Congressional elections, 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. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from third-party payors. The current Trump administration is pursuing policies to reduce regulations and expenditures across government including at HHS, the FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. These actions may include, for example, directives to reduce agency workforce, rescinding a Biden administration executive order tasking the Center for Medicare and Medicaid Innovation to consider new payment and healthcare models to limit drug spending and eliminating the Biden administration's executive order that directed HHS to establishing an AI task force and developing a strategic plan, and directing certain federal agencies to enforce existing law regarding hospital and price plan transparency and by standardizing prices across hospitals and health plans. Additionally, in its June 2024 decision in Loper Bright Enterprises v. Raimondo, the U.S. Supreme Court overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper Bright decision could result in additional legal challenges to current regulations and guidance issued by federal agencies applicable to our operations, including those issued by the FDA. Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program created under the IRA. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates, if approved.

Moreover, in order to obtain reimbursement for our products in some European countries, including some EU Member States, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. The Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal

impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States. In December 2021, Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted in the EU. This Regulation, which entered into force in January 2022, began to apply on January 12, 2025 through a phased implementation, with full implementation timelines extending to 2030. It is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at EU level for joint clinical assessments in these areas. The Regulation permits EU Member States to use common HTA tools, methodologies, and procedures across the EU to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement. If we are unable to maintain favorable pricing and reimbursement status in EU Member States for product candidates that we may successfully develop and for which we may obtain regulatory approval, any anticipated revenue from and growth prospects for those products in the EU could be negatively affected.

In addition, on April 26, 2023, the European Commission adopted a proposal for a new Directive and Regulation to revise the existing pharmaceutical legislation and on April 10, 2024, the Parliament adopted its related position. The proposed revisions remain to be agreed and adopted by the European Council. Moreover, on December 1, 2024, a new European Commission took office. The proposal could, therefore, still be subject to revisions. If adopted in the form proposed, the European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a number of changes to the regulatory framework governing medicinal product, including a decrease in data and market exclusivity for our product candidates in the EU, if approved, among other regulatory changes.

Our failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our product candidates internationally.

In order to market and sell our product candidates in other jurisdictions, we must obtain separate marketing approvals for those jurisdictions and comply with their numerous and varying regulatory requirements. We may not obtain foreign regulatory approvals on a timely basis, or at all. 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 regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, product reimbursement approvals must be secured before regulatory authorities will approve the product for sale in that country. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Our failure to obtain approval of our product candidates by foreign regulatory authorities may negatively impact the commercial prospects of such product candidates and our business prospects could decline. Also, if regulatory approval for our product candidates is granted, it may be later withdrawn. If we fail to comply with the regulatory requirements in international jurisdictions and receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential for our product candidates will be harmed and our business may be adversely affected.

Even if we obtain the necessary regulatory approvals, a variety of risks associated with marketing tralesinidase alfa, tildacerfont and any other current or future product candidates internationally could materially adversely affect our business.

We plan to seek regulatory approval for tralesinidase alfa, tildacerfont and any other current or future product candidates internationally. Even if we obtain such approvals, we will nevertheless be subject to additional risks related to operating in foreign countries, including:

- differing regulatory requirements in foreign countries, including differing reimbursement, pricing and insurance regimes;

- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers, price and exchange controls, and other 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 internationally;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the U.S. Foreign Corrupt Practices Act of 1977 ("FCPA") or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities internationally; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

If we fail to develop and commercialize additional product candidates, we may be unable to grow our business.

We intend to seek to in-license or acquire development and commercial-stage product candidates in disorders that have the potential to complement our existing portfolio. Our current product candidates are generally in-licensed from or derived from partnerships with other pharmaceutical companies. If we decide to pursue the development and commercialization of any additional product candidates, we may be required to invest significant resources to acquire or in-license the rights to such product candidates or to conduct drug discovery activities and we may be unable to in-license the rights on reasonable terms if at all. We do not currently have the necessary drug discovery personnel or expertise adequate to discover and develop an additional product candidate on our own. Any other product candidates will require additional, time-consuming development efforts, and significant financial resources, prior to commercial sale, including preclinical studies, extensive clinical trials, and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we may not be able to acquire, discover, or develop any additional product candidates, and any additional product candidates we may develop may not be approved, manufactured, or produced economically, successfully commercialized or widely accepted in the marketplace, or be more effective than other commercially available alternatives. Research programs to identify new product candidates require substantial technical, financial, and human resources whether or not we ultimately identify any candidates. If we are unable to develop or commercialize any other product candidates, our business and prospects will suffer.

We may form or seek strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such alliances or licensing arrangements.

We may form or seek strategic alliances, create joint ventures or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may

develop. We intend to establish commercial partnerships outside of the United States in selected foreign markets. Any of these relationships may require us to incur non-recurring and other charges, increase our near-and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. If we license products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. Following a strategic transaction or license, we may not achieve the revenues or cash flows that justifies such transaction. Any delays in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition, and results of operations.

We will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2024, we had 21 employees, all of whom are full-time. As our development and commercialization plans and strategies develop, and as we transition into operating as a public company, we expect to need additional development, managerial, operational, financial, sales, marketing, and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining, and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and regulatory review process for our product candidates and any future product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities. To date, we have used the services of outside vendors to perform tasks including clinical trial management, manufacturing, statistics and analysis, regulatory affairs, formulation development, and other drug development functions. Our growth strategy may also entail expanding our group of contractors or consultants to implement these tasks going forward. Because we rely on numerous consultants, effectively outsourcing many key functions of our business, we will need to be able to effectively manage these consultants to ensure that they successfully carry out their contractual obligations and meet expected deadlines. However, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for our product candidates and any future product candidates or otherwise advance our business. We may not be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and any future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our indebtedness to Silicon Valley Bank may limit our flexibility in operating our business and adversely affect our financial health and competitive position, and our obligations to Silicon Valley Bank are secured by substantially all of our assets, excluding our intellectual property assets. If we default on these obligations, Silicon Valley Bank could foreclose on our assets.

In September 2019, we entered into a Loan and Security Agreement (the "Loan Agreement") providing for a term loan (the "Term Loan") with SVB for an aggregate principal amount of $4.5 million. In March 2021, we entered into the First Amendment to Loan and Security Agreement (the "First Amendment"), which increased the aggregate principal amount of the Term Loan to up to $30.0 million, of which $20.0 million was immediately available under the first tranche (the "First Tranche") and $10.0 million was available under the second tranche through December 31, 2022 (the "Second Tranche") subject to the completion of certain clinical or financial milestones. In May 2022, we entered into the Second Amendment to Loan and Security Agreement (the "Second Amendment"), which amended the milestone upon which the Second Tranche commitment of $10.0 million would become available, added a liquidity covenant for the Second Tranche and amended the interest and prepayment terms. Commitments available under the Second Tranche of $10.0 million expired on December 31, 2022.

Repayment of principal on the First Tranche commenced in January 2023. As of December 31, 2024, we had $1.8 million outstanding under the Loan Agreement. Pursuant to the First Amendment, the Term Loan will mature on January 1, 2026.

All obligations under the Term Loan are secured by a first priority lien on substantially all of our assets, excluding intellectual property assets. We have agreed with SVB not to encumber our intellectual property assets, except as permitted under the Loan Agreement. As a result, if we default on any of our obligations under the Loan Agreement, SVB could foreclose on its security interest and liquidate some or all of the collateral, which would harm our business, financial condition, and results of operations and could require us to reduce or cease operations. In order to service this indebtedness and any additional indebtedness we may incur in the future, we need to generate cash from our operating activities. Our ability to generate cash is subject, in part, to our ability to successfully execute our business strategy, as well as general economic, financial, competitive, regulatory, and other factors beyond our control. Our business may not be able to generate sufficient cash flow from operations, and future borrowings or other financings may not be available to us in an amount sufficient to enable us to service our indebtedness and fund our other liquidity needs. To the extent we are required to use cash from operations or the proceeds of any future financing to service our indebtedness instead of funding working capital, capital expenditures or other general corporate purposes, we will be less able to plan for, or react to, changes in our business, industry, and in the economy generally. This could place us at a competitive disadvantage compared to our competitors that have less indebtedness.

The Loan Agreement contains certain covenants that limit our ability to engage in certain transactions that may be in our long-term best interest, including entering into a change in control transaction. The Loan Agreement also contains certain covenants that limit our ability to obtain additional debt financing, including incurring debt from third parties not permitted under the Loan Agreement or incurring liens or encumbrances on our property. While we have not previously breached and are currently in compliance with the covenants contained in the Loan Agreement, we may breach these covenants in the future. Our ability to comply with these covenants may be affected by events and factors beyond our control. In the event that we breach one or more covenants, SVB may choose to declare an event of default and require that we immediately repay all amounts outstanding under the Loan Agreement, terminate any commitment to extend further credit and foreclose on the collateral. In addition, if an event of default occurs under the Loan Agreement, SVB may, among other things, accelerate the Term Loan or do any acts it considers necessary or reasonable to protect its security interest in the collateral under the Term Loan. Events of default include the occurrence of a material adverse change in our business, operations, or condition (financial or otherwise). The occurrence of any of these events could have a material adverse effect on our business, financial condition, and results of operations.

For a more detailed description of the terms of the Loan Agreement, see the section titled “Item. 7 Management’s Discussion and Analysis of Financial Condition and Results of Operations—Material Agreements—Loan Agreement with Silicon Valley Bank” and Note 6 to our financial statements, each included elsewhere in this Annual Report.

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

We may seek additional capital through a combination of equity offerings, debt financings, strategic partnerships and alliances, and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or current or future product candidates, or grant licenses on terms unfavorable to us.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations, and those of our CROs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather

conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce tralesinidase alfa and tildacerfont. Our ability to obtain clinical supplies of tralesinidase alfa, tildacerfont and any other current or future product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. Our corporate headquarters is located in California near major earthquake faults and fire zones. The ultimate impact on us, our suppliers and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster.

Our employees, independent contractors, principal investigators, CROs, consultants, strategic partners, and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that employees, independent contractors, principal investigators, CROs, consultants, and vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) the rules of the FDA and other similar foreign regulatory bodies, including those rules that require the reporting of true, complete, and accurate information to the FDA and other similar foreign regulatory bodies; (ii) manufacturing standards; (iii) healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws or (iv) laws that require the true, complete, and accurate reporting of our financial information or data. These laws may impact, among other things, our current activities with principal investigators and research subjects, as well as proposed and future sales, marketing, and education programs. In particular, the promotion, sales, and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs, and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials.

If we obtain regulatory approval for tralesinidase alfa or tildacerfont and begin commercializing those products in the United States and in Europe, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal or comparable foreign healthcare programs, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Our relationships with customers, healthcare providers and third-party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other comparable foreign healthcare laws and regulations. If we or our employees, independent contractors, consultants, commercial partners, or vendors violate these laws, we could face substantial penalties.

Our relationships with customers, healthcare providers, and third-party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. These laws may impact, among other things, our clinical research program, as well as our proposed and future sales, marketing, and education programs. In particular, the promotion, sales and marketing of healthcare items and services is subject to extensive laws and regulations designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive, and other business arrangements. We may also be subject to federal, state and foreign laws governing the privacy and security of identifiable patient information. The U.S. healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person or entity from knowingly and willfully, offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the purchasing, leasing, ordering or arranging for the purchase, lease, or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that may be alleged to be intended to induce prescribing, purchases or recommendations, include any payments of more than fair market value, and may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, a person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation.
- federal civil and criminal false claims laws, including the federal civil False Claims Act, and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal government programs that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government, including federal healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act and the civil monetary penalties statute;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal civil and criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by any trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and their respective implementing regulations, which impose requirements on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, and their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information as well as their covered subcontractors; and
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

We may also be subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope. For example, we may be subject to the following: state and foreign anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, or that apply regardless of payor; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures, or drug pricing; state and local laws requiring the registration of pharmaceutical sales and medical representatives; and state and foreign laws, such as the EU GDPR governing the privacy and security of health information in some

circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Additionally, we may be subject to federal consumer protection and unfair competition laws, and equivalent foreign laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities, or our arrangements with physicians, could be subject to challenge under one or more of such laws. It is not always possible to identify and deter employee misconduct or business noncompliance, and the precautions we take to detect and prevent inappropriate conduct 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 or regulations. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If we or our employees, independent contractors, consultants, commercial partners and vendors violate these laws, we may be subject to investigations, enforcement actions and/or significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal or comparable foreign healthcare programs, contractual damages, public reprimands, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of tildacerfont outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If our information technology systems or data, or those of third parties with whom we work, are or were compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse consequences.

In the ordinary course of our business, we and the third parties with whom we work collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) proprietary, confidential, and sensitive data, including personal data (such as health-related data including in the context of clinical trials), intellectual property, and trade secrets (collectively, sensitive data). As a result, we and the third parties with whom we work face a variety of evolving threats, including but not limited to ransomware attacks, which could cause security incidents. Cyber-attacks, malicious internet-based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive data and information technology systems, and those of the third parties with whom we work. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer “hackers,” threat actors, “hacktivists,” organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation-state-supported actors.

Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties with whom we work may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our services.

We and the third parties with whom we work are subject to a variety of evolving threats, including but not limited to physical or electronic break-ins, social engineering attempts (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing and spam emails), malicious code (such as computer viruses and worms), malware (including as a result of advanced persistent threat intrusions), ransomware attacks, natural disasters, terrorism, war, server malfunctions, telecommunication and electrical failure, denial of service attacks (such as credential stuffing attacks), credential harvesting, personnel misconduct or error, supply-chain attacks, software bugs, attacks enhanced or facilitated by AI and other similar threats.

In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, loss of sensitive data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments.

Remote work has become more common and has increased risks to our information technology systems and data, as more of our personnel utilize network connections, computers, and devices outside our premises or network, including working at home, while in transit and in public locations. Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

In addition, our relationship with the third parties with whom we work could introduce new cybersecurity risks and vulnerabilities, including supply-chain attacks, and other threats to our business operations. We rely on third parties to operate critical business systems to process sensitive data in a variety of contexts, including, without limitation, cloud-based infrastructure, third-party research institution collaborators and other third parties to conduct clinical trials, data center facilities, encryption and authentication technology, employee email, and other functions. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. While we may be entitled to damages if the third parties with whom we work fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or that of the third parties with whom we work have not been compromised.

We have in the past and may continue to expend significant resources (including financial) and modify our business activities (including our clinical trial activities) to try to protect against security incidents and, as applicable, to detect, investigate, mitigate, contain and remediate security incidents. Additionally, certain data privacy and security obligations may require us to implement and maintain specific security measures or industry-standard or reasonable security measures to protect our information technology systems and sensitive data.

While we have implemented security measures designed to protect against and recover from security incidents, there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate and remediate vulnerabilities, in our information systems (such as our hardware and/or software, including that of third parties with whom we work). We may not, however, detect, mitigate and remediate all such vulnerabilities including on a timely basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident.

Any of the previously identified or similar threats have or could cause a security incident that resulted in or results in unauthorized, unlawful, or accidental acquisition, modification, destruction, alteration, encryption, access to, use or disclosure of, corruption of, or loss of sensitive data or our information technology systems, or those of the third parties with whom we work. A security incident has and could disrupt our ability (and that of third parties with whom we work) to provide our services.

In the event of a security incident, applicable data privacy and security obligations may require us, or we may voluntarily choose, to notify relevant stakeholders, such as consumers, partners, collaborators, government authorities, and the media or to take other actions, such as providing credit monitoring and identifying theft protection services. Such disclosures and related actions can be costly, and the disclosure or the failure to comply with such applicable requirements could lead to adverse consequences.

Security incidents (or perceived security incidents), may result in material adverse consequences, such as significant liabilities, regulatory and enforcement actions (including investigations, fines, penalties, audits and inspections), reputational damage, additional reporting requirements and/or oversight, restrictions on processing sensitive data (including personal data), litigation, indemnification obligations, negative publicity, monetary fund diversions, interruptions in our operations (including availability of data), diversion of management attention, financial loss, and other harms. For example, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in any regulatory approval or clearance efforts and significantly increase our costs to recover

or reproduce the data, and subsequently commercialize the product. Additionally, theft of our intellectual property or proprietary business information could require substantial expenditures to remedy.

Furthermore, our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. Additionally, we cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

We and the third parties with whom we work are subject to stringent and evolving obligations related to data privacy and security. These obligations include U.S. and foreign laws, regulations, and rules; contractual obligations; industry standards; and policies. Our (including the third parties with whom we work) actual or perceived failure to comply with such obligations could lead to regulatory investigations and actions (which could include civil or criminal penalties); private litigation (including class-action claims) and mass arbitration demands; disruptions to our business operations; adverse publicity; and other adverse consequences that could negatively affect our operating results and business.

We and the third parties with whom we work are or may become subject to federal, state, local, and foreign data privacy and security laws and regulations, as well as other rules, standards, policies and contractual or other obligations, relating to the processing of personal data, including data we collect about trial participants in connection with clinical trials. If we (including the third parties with whom we work) fail, or are perceived to have failed, to address or comply with any such obligations, this could result in enforcement actions that could include investigations, fines, penalties, audits and inspections, litigation (including class-action claims) and mass arbitration demands, additional reporting requirements and/or oversight, temporary or permanent bans on all or some processing of personal data, or orders to destroy or not use personal data.

In the United States, numerous federal, state, and local laws and regulations, including, as applicable, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act) and regulations, and other laws (e.g., wiretapping laws), that govern the processing of personal data apply to our operations and the operations of the third parties with whom we work. In addition, we obtain health information from third parties (including research institutions from which we obtain clinical trial data) that may be subject to privacy and security requirements under HIPAA, as amended by HITECH. If we violate HIPAA, we may be subject to significant administrative and civil penalties. Additionally, depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

In addition, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020 ("CPRA") (collectively "CCPA"), applies to personal data of consumers, business representatives, and employees who are California residents, and requires businesses (that are subject to the CCPA) to provide specific disclosures in privacy notices and honor requests of such individuals to exercise certain privacy rights. The CCPA provides for fines of up to $7,500 per intentional violation and allows private litigants affected by certain data breaches to recover significant statutory damages.

Numerous other states have also passed comprehensive privacy laws, and similar laws are being considered in several other states, as well as at the federal and local levels. We expect more states to pass similar laws in the future. The CCPA and other U.S. state comprehensive privacy laws exempt some data processed in the context of clinical trials, but these developments may further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties with whom we work.

Outside the United States, an increasing number of laws, regulations, and industry standards govern data privacy and security, including our processing of personal data. For example, our processing of personal data is or may become subject in certain circumstances to the EU GDPR and the United Kingdom's GDPR ("UK GDPR") (collectively, "GDPR"). The GDPR imposes stringent standards of data privacy and security concerning personal data and imposes potentially significant sanctions for non-compliance. For example, under the GDPR, companies may face temporary or definitive bans on processing of personal data and other corrective actions; fines of up to 20 million Euros under the EU GDPR. 17.5 million pounds sterling under the UK GDPR or, in each case, 4% of annual

global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

In the ordinary course of business, we transfer personal data from Europe and other jurisdictions to the United States and other countries outside Europe. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area ("EEA") and the UK have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it generally believes are inadequate. Other jurisdictions may adopt or have already adopted similarly stringent data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States and other 'inadequate' countries in compliance with law, as applicable, such as the European Commission's standard contractual clauses, the UK's International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto (which allow for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework and/or Extension), these mechanisms are subject to legal challenges, and there is no assurance that we can always satisfy or rely on these mechanisms to lawfully transfer personal data to the United States. If there is no lawful manner for us transfer personal data from the EEA, the UK or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with certain collaborators, partners, vendors and other third parties with whom we work, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data to recipients outside the EEA for allegedly violating the EU GDPR's cross-border data transfer limitations. Regulators in the United States are also increasingly scrutinizing certain personal data transfers and have and may further impose personal data transfer requirements or prohibitions on cross-border personal data transfers.

In addition to data privacy and security laws, we are bound by other contractual obligations related to data privacy and security, such as industry standards adopted by industry groups, and our efforts to comply with such obligations may not be successful. For example, trial participants about whom we or the third parties with whom we work to obtain information, as well as the third parties with whom we work who share this information with us, may contractually limit our ability to use and disclose the information. We also publish privacy policies and other statements regarding data privacy and security. Regulators are increasingly scrutinizing these types of policies and statements, and ff these policies or statements are found to be deficient, lacking in transparency, deceptive, unfair, misleading or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

Obligations related to data privacy and security (and individuals' data privacy and security expectations) are quickly changing, becoming increasingly stringent, and creating uncertainty. Compliance with data privacy and security obligations have in the past and could require us to take on more onerous requirements in our contracts, engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or the third parties with whom we work ability to operate in certain jurisdictions. Applicable data protection laws can be subject to differing applications and interpretations which may be inconsistent or conflict among jurisdictions.

Non-compliance (or perceived non-compliance) with applicable data privacy and security obligations, could result in significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims) and mass arbitration demands; additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. In particular, plaintiffs have become increasingly more active in bringing privacy-related claims against companies, including class claims and mass arbitration demands. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for monumental statutory damages, depending on the volume of data and the number of violations. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including, as relevant, clinical trials); inability to process personal data or to operate in certain jurisdictions; limited

ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of tralesinidase alfa, tildacerfont and any future product candidates.

We face an inherent risk of product liability as a result of the clinical testing of tralesinidase alfa, tildacerfont and any future product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if tralesinidase alfa, tildacerfont or any future product candidates causes or is perceived to cause 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, and 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 tralesinidase alfa and tildacerfont. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for tralesinidase alfa, tildacerfont and any future product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulatory authorities;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing, or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize tralesinidase alfa, tildacerfont and any future product candidates; or
- a decline in our share price.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry an aggregate of up to $10.0 million of product liability insurance covering our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If we determine that it is prudent to increase our product liability coverage due to the commercial launch of any approved product, we may be unable to obtain such increased coverage on acceptable terms, or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

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

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, and anti-corruption and anti-money laundering laws and regulations, including the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and

their employees, agents, clinical research organizations, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting or receiving, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products internationally once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, clinical research organizations, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. As of December 31, 2024, after reducing net operating losses ("NOLs") and tax credits for amounts not expected to be utilized, we had federal NOL carryforwards of approximately $128.1 million and state NOL carryforwards of approximately $123.0 million. The federal NOL carryforwards arising in taxable years beginning prior to 2018 will begin to expire in 2036 and state NOL carryforwards will begin to expire in 2036, unless previously utilized. We also have federal and state tax credit carryforwards totaling $32.3 million and $2.4 million, respectively. The federal tax credit carryforwards will begin to expire in 2036, unless previously utilized. The state tax credits will not expire.

Under the Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act"), federal NOL carryforwards generated in tax years beginning after December 31, 2017 may be carried forward indefinitely but may only be used to offset 80% of our taxable income annually. Similar rules may apply under state tax laws. Such limitations could result in the expiration of our carryforwards before they can be utilized and, if we are profitable, our future cash flows could be adversely affected due to our increased taxable income or tax liability. Our NOLs and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities and may become subject to annual limitations under Section 382 and 383 of the Internal Revenue Code of 1986, as amended. Under Section 382, certain cumulative changes in the ownership interest of significant stockholders over a rolling three-year period in excess of 50 percentage points (by value), could result in an ownership change that may limit our ability to utilize our NOL carryforwards and other tax attributes to offset future taxable income or tax liabilities. An ownership change analysis covering periods through December 31, 2023 concluded that an ownership change occurred in May 2016 and in August 2020. As a result of the ownership changes, we derecognized NOL-related deferred tax assets down to the amount expected to be realized. Our ability to use our remaining NOL carryforwards may be further limited if we experience a Section 382 ownership change as a result of future changes in our stock ownership. As of December 31, 2024, we recorded a full valuation allowance on our net deferred tax assets.

In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California recently enacted legislation that, with certain exceptions, suspends the ability to use California net operating losses to offset California income and limits the ability to use California business tax credits to offset California taxes, for taxable years beginning on or after January 1, 2024 and before January 1, 2027.

Changes in tax laws or regulations that are applied adversely to us may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Act, the CARES Act and the Inflation Reduction Act of 2022 enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities may affect us, and certain aspects of the changes could be repealed or modified in future legislation. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the CARES Act, the Inflation Reduction Act, or any other newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, and the deductibility of expenses under the Tax Act, the CARES Act, the Inflation Reduction Act or future reform legislation could have a material impact on the value of our net deferred tax assets,

could result in significant one-time charges, and could increase our future tax expense.

Risks Related to Our Reliance on Third Parties

We depend on intellectual property licensed from others, the termination of which could result in the loss of significant rights, which would harm our business.

We are dependent on technology, patents, know-how, and proprietary materials, both our own and licensed from others. For example, we entered into a license agreement with Lilly in May 2016 pursuant to which we were granted an exclusive, worldwide, royalty bearing, sublicensable license under certain technology, patent rights, know-how, and proprietary materials relating to certain CRF1 receptor antagonist compounds. Any termination of this license will result in the loss of significant rights and will restrict our ability to develop and commercialize tildacerfont. In addition, we entered into a license agreement with BioMarin Pharmaceutical Inc. in October 2019 pursuant to which we obtained a limited exclusivity, royalty bearing, and sublicensable license to certain technology, patent rights, know-how, and proprietary materials relating to certain enzyme replacement therapy products. We entered into a license agreement with HBM Alpha Therapeutics, Inc ("Harbour") in January 2025 pursuant to which we obtained a limited exclusivity, royalty bearing, and sublicensable license to certain technology, patent rights, manufacturing rights, know-how, and proprietary materials relating to certain compounds developed by Harbour. We also entered into an antibody license agreement with Twist Bioscience Corporation in December 2024, pursuant to which we obtained a license for purposes of evaluating certain antibodies for commercial development.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below under "Risks Related to Our Intellectual Property." If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize tralesinidase alfa, tildacerfont, and our other product candidates.

We currently rely on, and intend to continue relying on, third-party CROs in connection with our clinical trials for tralesinidase alfa and tildacerfont. We control or will control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with applicable protocol, legal, regulatory, and scientific standards, and our reliance on our CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these CROs fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, such regulatory authorities may determine that our clinical trials do not comply with the GCP regulations. In addition, our clinical trials must be conducted with drug product produced under cGMP regulations and will require a large number of test subjects. Our failure or any failure by our CROs to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of our CROs violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Our CROs are not our employees and, except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing preclinical, clinical and non-clinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could affect their performance on our behalf. If our CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, suspended, varied, delayed, or terminated and we may not be able to complete development of, obtain regulatory approval for or successfully commercialize tralesinidase alfa, tildacerfont and any future product candidates. As a result, our financial results and the

commercial prospects for tralesinidase alfa, tildacerfont and any future product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding CROs involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Although we carefully manage our relationships with our CROs, we may encounter challenges or delays in the future and these delays or challenges may have a material adverse impact on our business, prospects, financial condition, and results of operations.

In addition, quarantines, shelter-in-place, and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to infectious diseases could impact personnel at our CROs, which could disrupt our clinical timelines, which could have a material adverse impact on our business, prospects, financial condition, and results of operations.

We rely completely on third parties to manufacture our preclinical and clinical drug supplies and we intend to rely on third parties to produce commercial supplies of tralesinidase alfa, tildacerfont and any future product candidates, if approved, and these third parties may fail to obtain and maintain regulatory approval for their facilities, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.

We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our clinical drug supplies for use in the conduct of our clinical trials, and we lack the resources and the capability to manufacture tralesinidase alfa, tildacerfont and any future product candidates on a clinical or commercial scale. Instead, we rely on contract manufacturers for such production. In particular, we currently rely on a single-source manufacturer for drug product, and a single-source manufacturer for drug substance.

We do not currently have any long-term agreement with a manufacturer to produce raw materials, active pharmaceutical ingredients ("APIs"), and the finished products of tralesinidase alfa, tildacerfont or the associated packaging used in our current product format and we may rely on single source suppliers for clinical supply of API and drug products of tralesinidase alfa and tildacerfont. We will need to identify and qualify a third-party manufacturer prior to commercialization of tralesinidase alfa and tildacerfont, and we intend to enter into agreements for commercial production with third-party suppliers. Our reliance on third-party suppliers and manufacturers, including single-source suppliers, could harm our ability to develop tralesinidase alfa, tildacerfont and any future product candidates or to commercialize any product candidates that are approved. Further, any delay in identifying and qualifying a manufacturer for commercial production could delay the potential commercialization of tralesinidase alfa, tildacerfont and any future product candidates, and, in the event that we do not have sufficient product to complete our clinical trials, it could delay such trials.

The facilities used by our contract manufacturers to manufacture tralesinidase alfa, tildacerfont and any future product candidates must be approved by the applicable regulatory authorities, including the FDA or comparable foreign regulatory authorities, pursuant to inspections that will be conducted after an NDA, BLA or comparable foreign regulatory marketing application is submitted. We currently do not control the manufacturing process of tralesinidase alfa or tildacerfont and are completely dependent on our contract manufacturing partners for compliance with the FDA's and comparable foreign regulatory authorities' cGMP requirements for manufacture of both the active drug substances and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the FDA's and comparable foreign regulatory authorities' strict regulatory requirements, they will not be able to secure or maintain FDA or comparable foreign regulatory approval for the manufacturing facilities. In addition, we have limited control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authority does not approve these facilities for the manufacture of tralesinidase alfa, tildacerfont or any future product candidates or if it withdraws any such approval in the future, or if our suppliers or contract manufacturers decide they no longer want to supply or manufacture for us, we may need to find alternative manufacturing facilities, in which case we might not be able to identify manufacturers for clinical or commercial supply on acceptable terms, or at all, which would significantly impact our ability to develop, obtain regulatory approval for, or market tralesinidase alfa, tildacerfont and any future product candidates.

In addition, the manufacture of pharmaceutical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up and

validating initial production and absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state, and foreign regulations. Furthermore, if contaminants are discovered in our supply of tralesinidase alfa, tildacerfont or any future product candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Any stability or other issues relating to the manufacture of tralesinidase alfa, tildacerfont may occur in the future. In addition, quarantines, shelter-in-place, and similar government orders, or the perception that such orders, shutdowns, or other restrictions on the conduct of business operations could occur, related to infectious diseases could impact personnel at our third-party manufacturing facilities upon which we rely, or the availability or cost of materials, which could disrupt the supply chain for our product candidates. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide our product candidate to patients in clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

If we or our third-party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third-party manufacturers. Our manufacturers are subject to federal, state, and local laws and regulations in the United States governing the use, manufacture, storage, handling and disposal of medical, radioactive and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical, radioactive or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical radioactive or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development, and production efforts, which could harm our business, prospects, financial condition, or results of operations.

Social media platforms and AI-based platforms present new risks and challenges to our business.

As social media continues to expand, it also presents us with new risks and challenges. Social media is increasingly being used to communicate information about us, our programs and the diseases our product candidates are being developed to treat. Social media practices in the biopharmaceutical industry are evolving, creating uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the effectiveness of, or adverse experiences with, a product or a product candidate, which could result in reporting obligations or other consequences. Further, the accidental or intentional disclosure of non-public information by our workforce or others through media channels could lead to information loss. In addition, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us, our products, or our product candidates on any social media platform. The nature of social media prevents us from having real-time control over postings about us on social media. We may not be able to reverse damage to our reputation from negative publicity or adverse information posted on social media platforms or similar mediums. If any of these events were to occur or we otherwise fail to comply with application regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business including quick and irreversible damage to our reputation, brand image and goodwill. Additionally, AI-based platforms are increasingly being used in the biopharmaceutical industry. The use of AI platforms by people, including our vendors, suppliers and contractors, with access to our proprietary and confidential information, including trade secrets, may continue to increase and may lead to the release of such information, which may negatively impact our company, including our ability to realize the benefit of our intellectual property.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for TA-ERT, SPR202, tildacerfont, any future product candidates, and other proprietary technologies we develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize TA-ERT, SPR202, and tildacerfont, if approved, any future product candidates, and other proprietary technologies if approved, may be adversely affected.

Our commercial success will depend in part on our ability to obtain and maintain a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to TA-ERT, SPR202, tildacerfont, any future product candidates, and other proprietary technologies we develop. If we are unable to obtain or maintain patent protection with respect to TA-ERT, SPR202, and tildacerfont, any future product candidates, and other proprietary technologies we may develop, our business, financial condition, results of operations, and prospects could be materially harmed.

The patent position of biotechnology and pharmaceutical companies is highly uncertain and involves complex legal, scientific, and factual questions and has been the subject of frequent litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our patent applications may not result in patents being issued which protect our product candidates and uses thereof, any future product candidates, and other proprietary technologies we may develop or which effectively prevent others from commercializing competitive technologies and products. Further, no consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States or in many jurisdictions outside of the United States. Changes in either the patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be obtained or enforced in the patents that have been issued or may be issued from the applications we currently or may in the future own or license from third parties. Further, if any patents or applications we obtain or license are deemed invalid and unenforceable, our ability to commercialize or license our technology could be adversely affected.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators will be successful in protecting TA-ERT, SPR202, tildacerfont, any future product candidates and other proprietary technologies and their uses by obtaining, defending and enforcing patents. These risks and uncertainties include the following:

- the United States Patent and Trademark Office ("USPTO") and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable, or may otherwise not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with, or eliminate our ability to make, use and sell our potential product candidates and may limit, interfere with, or eliminate our ability to obtain patents related to our product candidates;
- other parties may have or may seek to design around our claims or develop technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications and patents, either by claiming the same composition of matter, methods or formulations or by claiming subject matter that could dominate our patent position;
- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any products or product candidates that we may develop;

- because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates, any future product candidates, and other proprietary technologies and their uses;
- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications for any application with an effective filing date before March 16, 2013; as such, subject matter covered in patents or patent applications that we or our licensors have filed before March 16, 2013 may be challenged and invalidated under an interference proceeding;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop, and market competing product candidates in those countries.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, or maintain all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection for such output. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in any of our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. Additionally, recent reforms and changes at government agencies of the United States and those of non-U.S. jurisdictions could increase the delays, uncertainties and costs surrounding the prosecution of our patent applications, and the maintenance, enforcement, or defense of our issued patents. For example, the ability of the USPTO and other applicable patent authorities to properly administer their functions is highly dependent on the levels of funding available to the agency and their ability to retain personnel and fill key leadership appointments, among various factors. Termination of employees or delays in replacing or hiring for positions could significantly impact the ability of the USPTO and other applicable patent authorities to fulfill their functions and could greatly impact our ability to timely and adequately prosecute or maintain our patent applications, and our ability to timely and adequately maintain, enforce, or defend our issued patents.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use TA-ERT, SPR202, tildacerfont, any future product candidates, and other proprietary technologies and erode or negate any competitive advantage we may have, which could have a material adverse effect on our financial condition and results of operations. For example:

- others may be able to make compounds that are similar to TA-ERT, SPR202, tildacerfont and any future product candidates but that are not covered by the claims of our patents;
- others may be able to make and use TA-ERT, SPR202, tildacerfont and any future product candidates in countries where valid enforceable patents are not obtained;
- we might not have been the first to make the inventions covered by our pending patent applications;
- we might not have been the first to file patent applications for these inventions;

- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents that we obtain may not provide us with any competitive advantages;
- we may not develop additional proprietary technologies that are patentable;
- our competitors might conduct research and development activities in countries where we do not have patent rights or where patent protection is weak and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our products;
- we cannot ensure that we will be able to successfully commercialize our products on a substantial scale, if approved, before the relevant patents that we own or license expire;
- others may obtain patents that cover the use or manufacture of TA-ERT, SPR202, or tildacerfont; or
- the patents of others may have an adverse effect on our business.

Others have filed, and in the future are likely to file, patent applications covering products and technologies that are similar, identical or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, opposition or invalidity proceedings before U.S. or non-U.S. patent offices.

We cannot be certain that the claims in our issued patents and pending patent applications covering our current product candidates, including TA-ERT, SPR202, or tildacerfont, or any future product candidates will be considered patentable by the USPTO, courts in the United States, or by patent offices or courts in foreign countries. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property internationally.

The strength of patents in the biotechnology and pharmaceutical fields involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our current product candidates and any future product candidates in the United States or in foreign countries. Even if such patents do successfully issue, third parties may challenge the ownership, validity, enforceability, or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful opposition to our patents could deprive us of exclusive rights necessary for the successful commercialization of our current product candidates and any future product candidates. Furthermore, even if they are unchallenged, our patents may not adequately protect our intellectual property, provide exclusivity for our current product candidates or any future product candidates or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents we hold with respect to our current product candidates or any future product candidates is threatened, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize, our current product candidates or any future product candidates.

For U.S. patent applications in which claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our participation in an interference proceeding may fail and, even if successful, may result in substantial costs and distract our management and other employees.

For U.S. patent applications containing a claim not entitled to priority before March 16, 2013, there is greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act ("America Invents Act") was signed into law. The America Invents Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO is developing regulations and procedures to govern the administration of the America Invents Act, and many of the substantive changes to patent law associated with the America Invents Act, and in particular, the "first to file" provisions, were enacted on March 16, 2013. This will require us to be cognizant going forward of the time

from invention to filing of a patent application and be diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions. It remains unclear what impact the America Invents Act will have on the operation of our business. As such, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, such as patent term adjustments, but the life of a patent and, correspondingly, the protection it affords is limited. Even if we or our licensors obtain patents covering our product candidates, when the terms of all patents covering a product expire, our business may become subject to competition from competitive products, including generic products. Given the amount of time required for the development, testing, and regulatory review and approval of new product candidates, patents protecting such candidates may expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Depending upon the timing, duration, and specifics of any FDA marketing approval of our product candidates, or any future product candidate we may develop, one or more of patents issuing from our U.S. patent applications may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984 ("Hatch-Waxman Amendments"). The Hatch-Waxman Amendments permit a patent extension term ("PTE") of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Similar patent term restoration provisions to compensate for commercialization delay caused by regulatory review are also available in certain foreign jurisdictions, such as in Europe under Supplemental Protection Certificate ("SPC"). If we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market our product candidates and any future product candidates under patent protection would be reduced. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Additionally, administrative changes at the USPTO or other applicable patent authorities, such as reduced hiring and/or funding, may result in delays in issuance of a patent or in accrual of patent term extension, thereby reducing the amount of patent term extension that could otherwise be received. Administrative changes (e.g., at the FDA or USPTO) may also lead to delays in review and analysis of regulatory submissions or requests for patent term extension, which could result in a patent term extension not being timely granted (e.g., before the expiration of the patent) and there may be no patent eligible for extension. Moreover, the applicable time period or the scope of patent protection afforded could be less than we project or request. In addition, to the extent we wish to pursue patent term extension based on a patent that we may license from a third party in the future, we may need the cooperation of that third party. If we are unable to obtain patent term extension, or the foreign equivalent, or if the term of any such extension is less than we project or request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed). If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties, such as our license agreement with Lilly, Antibody License Agreement with Twist and HBM License Agreement, or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to license agreements under which we are granted intellectual property rights that are important to our business and our product candidates. If we fail to comply with our obligations under the license agreements,

or we are subject to a bankruptcy, the license agreements may be terminated, in which event we would not be able to develop, commercialize or market our product candidates.

In January 2025, we entered into a Collaboration and License Agreement with HBM. Pursuant to the HBM License Agreement, we obtained an exclusive license to a specified product candidate developed by HBM in all countries outside of mainland China, Taiwan, Hong Kong, and Macau ("License"), for upfront consideration of $5.0 million and the issuance to HBM of a pre-funded warrant equal to 4.99% of our outstanding common stock as of the date of issuance of such warrant. Furthermore, we are obligated to pay HBM up to an aggregate of $390.0 million upon the achievement of certain development, regulatory, and sales milestones. In addition, we are required to pay to HBM certain mid to high-single digit tiered royalties on aggregate annual net sales of licensed products during the applicable royalty term, subject to certain customary reductions.

In December 2024, we entered into the Antibody License Agreement with Twist. Pursuant to the Antibody License Agreement, we obtained a license to certain intellectual property rights related to SPR204, a monoclonal antibody antagonist, controlled by Twist. At our election, we can pay an additional fee to extend the initial term of the research license. In addition, we have the exclusive option, upon payment of a one-time, non-refundable license fee, to acquire from Twist a license, with the right to sublicense, to (a) research and develop the antibody, (b) incorporate the antibody into products ("Products"), (c) commercialize such Products, and (d) control prosecution of the licensed patents and patent applications.

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

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

Further, our current licensors or any future licensor may not always act in our best interest. If disputes over intellectual property rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, our business, results of operations, financial condition, and prospects may be adversely affected. We may enter into additional licenses in the future and if we fail to comply with obligations under those agreements, we could suffer adverse consequences.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own, which are described below. If we, our current licensors, or any future licensor fail to adequately protect this intellectual property, our ability to commercialize our product candidates and any future product could be impeded.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on any issued patents and/or applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to foreign patent agencies. While an inadvertent lapse may sometimes be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or

complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market with similar or identical products or technology earlier than should otherwise have been the case, which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly on obtaining and enforcing patents. Our patent rights may be affected by developments or uncertainty in U.S. or foreign patent statutes, patent case law, USPTO rules and regulations or the rules and regulations of foreign patent offices. Obtaining and enforcing patents in the biotechnology and pharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States may, at any time, enact changes to U.S. patent law and regulations, including by legislation, by regulatory rule-making, or by judicial precedent, that adversely affect the scope of patent protection available and weaken the rights of patent owners to obtain patents, enforce patent infringement and obtain injunctions and/or damages. For example, the scope of patentable subject matter under 35 U.S.C. 101 has evolved significantly over the past several years as the Court of Appeals for the Federal Circuit and the U.S. Supreme Court issued various opinions, and the USPTO modified its guidance for practitioners on multiple occasions. Other countries may likewise enact changes to their patent laws in ways that adversely diminish the scope of patent protection and weaken the rights of patent owners to obtain patents, enforce patent infringement, and obtain injunctions and/or damages.

Further, the United States and other governments may, at any time, enact changes to law and regulation that create new avenues for challenging the validity of issued patents. For example, the America Invents Act created new administrative post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings that allow third parties to challenge the validity of issued patents. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the U.S. courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, 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. We cannot predict how decisions by the U.S. courts, the U.S. Congress or the USPTO may impact the value of our patent rights. For example, the U.S. Supreme Court held in *Amgen v. Sanofi* (2023) that a functionally claimed genus was invalid for failing to comply with the enablement requirement of the Patent Act. As such, our patent rights with functional claims may be vulnerable to third party challenges seeking to invalidate these claims for lacking enablement or adequate support in the specification. In addition, the Federal Circuit recently issued a decision, *In re Cellect, LLC* (2023) involving the interaction of patent term adjustment ("PTA"), terminal disclaimers, and obvious-type double patenting which may affect the patent term of any issued patents that rely on any PTA. The trend of these decisions along with resulting changes in patentability requirements being implemented by the USPTO could make it increasingly difficult for us to obtain and maintain patents on our products, and could jeopardize patent term adjustment or otherwise reduce patent term, reduce the scope of, or invalidate or render unenforceable our patent rights. 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, in the 2013 case *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents. For example, the Inflation Reduction Act ("IRA") passed by the U.S. Congress authorizes the Secretary of the Department of Health and Human Services ("HHS") to negotiate prices directly with participating manufacturers for selected medicines covered by Medicare even if these medicines are protected by an existing patent. For small molecule medicines, the process begins seven years after initial approval by the FDA. While we do

not believe that the IRA or its effects will impact our ability to obtain patents in the near future, we cannot be certain that it will not affect our patent strategy in the long term.

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

Patents are of national or regional effect. Filing, prosecuting, and defending patents on our product candidates, any future product candidates, and other proprietary technologies we develop in all countries throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights in the same manner and to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement of such patent protection is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The requirements for patentability may differ in certain countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval for a drug and its patent status. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors.

In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology or pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. For example, as of June 1, 2023, European patent applications and patents may be subjected to the jurisdiction of the Unified Patent Court (the "UPC"). In 2012, the European Union Patent Package (the "EU Patent Package") regulations were passed with the goal of providing a single pan-European Unitary Patent and a new European UPC for litigation involving European patents. The EU Patent Package was implemented on June 1, 2023. As a result, all European patents, including those issued prior to ratification of the EU Patent Package, now by default automatically fall under the jurisdiction of the UPC. European patent applications will have the option, upon grant of a patent, of becoming a Unitary Patent, which will be subject to the jurisdiction of the UPC. The UPC and Unitary Patent are significant changes in European patent practice. It is uncertain how the UPC will impact granted European patents in the biotechnology and pharmaceutical industries. Our European patent applications, if issued, could be challenged in the UPC. During the first seven years of the UPC's existence, the UPC legislation allows a patent owner to opt its European patents out of the jurisdiction of the UPC. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation in the UPC. As a single court system can invalidate a European patent, we, where applicable, may opt out of the UPC and as such, each European patent would need to be challenged in each individual country. We may decide to opt out future European patents from the UPC, but doing so may preclude us from realizing the benefits of the UPC. Moreover, if we do not meet all of the opt-out formalities and requirements under the UPC, our future European patents could remain under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patents, and allow for the possibility of a competitor to obtain pan-European injunctions. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates due to increased competition and, resultantly, on our financial condition, prospects and results of operations.

Geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent

maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees (including former employees of our licensors), collaborators or other third parties have an interest in our patents rights, trade secrets, or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. For example, we may have inventorship disputes arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business, financial condition, results of operations and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

Presently we have intellectual property rights, through licenses from third parties including Lilly, related to our product candidates. Because our program may require the use of additional proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license, on reasonable terms, proprietary rights related to any compositions, formulations, methods of use, processes or other intellectual property rights from third parties that we identify as being necessary for our product candidates. Even if we are able to obtain a license to such proprietary rights, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Where we obtain licenses from, grant licenses to, or collaborate with third parties, we may not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain the patents, covering technology that we license to or from third parties in certain countries or regions. Such activities, if controlled by us, may require the input of such third parties. Such activities, if controlled by such third parties, may require the input of us. However, in either case, such third parties may not cooperate with us even where such third parties are obligated to do so. We may not align on strategies for prosecuting the relevant patent applications or maintaining the relevant patents. For example, such third-party may not cooperate with us and may decide to prosecute the patent application in a manner that is inconsistent with the best interests of our business, or fails to comply with applicable laws and regulations. The validity and enforceability of such patents or any patents that may issue from such patent applications may be affected.

We may also require the cooperation of our licensors, licensees, and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and patent applications may not be prosecuted, maintained, and/or enforced in a manner consistent with the best interests of our business, or in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such patent applications. Moreover, if we do obtain necessary licenses, we will

likely have obligations under those licenses, including making royalty and milestone payments, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our business. Our business would suffer if any such licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical or similar to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

The licensing and acquisition of third-party proprietary rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party proprietary rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we may collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate an exclusive license to any of the institution's proprietary rights in technology resulting from the collaboration. Regardless of such option to negotiate a license, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer, on an exclusive basis, their proprietary rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us, either on reasonable terms, or at all. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment, or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights on commercially reasonable terms, our ability to commercialize our products, and our business, financial condition, and prospects for growth, could suffer.

Third-party claims alleging intellectual property infringement may prevent or delay our drug discovery and development efforts.

Our success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including *inter partes* review, interference and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. The America Invents Act introduced new procedures including *inter partes* review and post grant review. The implementation of these procedures brings uncertainty to the possibility of challenges to our patents in the future and the outcome of such challenges. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our activities related to our product candidates may give rise to claims of infringement of the patent rights of others.

The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always 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. We cannot assure you that any of our current or future product candidates will not infringe existing or future patents. We may not be aware of patents that have already issued that a third party might assert are infringed by one of our current or future product candidates.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be currently pending third-party patent applications which may later result in issued patents that our product candidates, any future product candidates, and other proprietary technologies may infringe, or which such third parties claim are infringed by the use of our technologies. Parties making claims against us for infringement or misappropriation of their intellectual property rights may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates or future product candidates. Defense of these claims, regardless of their merit, could involve substantial expenses and could be a substantial diversion of management and other employee resources from our business. If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. In the future, we may agree to indemnify our commercial collaborators against certain intellectual property infringement claims brought by third parties.

We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. We cannot be certain that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction, because:

- some patent applications in the United States may be maintained in secrecy until the patents are issued;
- patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived;
- pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates, and any future product candidates or the use of our technologies, our product candidates, and any future product candidates;
- identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases, and the difficulty in assessing the meaning of patent claims;
- patent applications in the United States are typically not published until 18 months after the priority date; and
- publications in the scientific literature often lag behind actual discoveries.

Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. Further, we may incorrectly determine that our technologies, products, or product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or internationally that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our products or product candidates.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours, and others may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and future approved products or impair our competitive position. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Any such patent application may have priority over our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application

on inventions similar to ours, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar invention prior to our own invention, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications and may be entitled to priority over our applications in such jurisdictions.

Any claims of patent infringement asserted by third parties would be time-consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing our product candidates or any future product candidates until the asserted patent expires or is finally held invalid, unenforceable, or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property;
- require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be willfully infringing; and/or
- require us to enter into royalty or license agreements, which may not be available on commercially reasonable terms, or at all.

Although no third party has asserted a claim of patent infringement against us as of the date of this prospectus, others may hold proprietary rights that could prevent our product candidates from being marketed. For example, we are aware of issued patents that claim a method of treatment based upon a general mode of action. While we believe that these patents are difficult to enforce and that we would have valid defenses to these claims of patent infringement, we cannot be certain that we would prevail in any dispute, and we cannot be certain how an adverse determination would affect our business.

It is possible that a third party may assert a claim of patent infringement directed at any of our product candidates. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our products, treatment indications, or processes could subject us to significant liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our product candidates. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly. Even if we were able to obtain a license, the rights may be nonexclusive, which may give our competitors access to the same intellectual property.

Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates, treatment indications, or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology.

Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may in the future pursue invalidity proceedings with respect to third-party patents. The outcome following legal assertions of invalidity is unpredictable. Additionally, we may be subject to claims of patent infringement during those proceedings, and delays caused by the federal agencies may increase the time period that we are subject to such claims. For example, administrative changes, including reduced personnel and budgets experienced by the Patent and Trial Appeal Board, could further delay our ability to timely challenge any such patents. Even if resolved in our favor, these legal proceedings may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such proceedings adequately. Some of these third parties may be able to sustain the costs of such proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent proceedings could compromise our ability to compete in the marketplace. If we do not prevail in the patent proceedings the third parties may assert a claim of patent infringement directed at our product candidates.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees or consultants have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industries, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates and other proprietary technologies. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition 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 become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damage, which could adversely affect our business. 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 our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

Our patents or pending patent applications, or the patents or pending patent applications that we license, may be challenged in the courts or administrative bodies in the United States and other foreign jurisdictions. Such proceedings to challenges in enforceability or validity could result in the revocation of, cancellation of or amendment to our owned and in-licensed patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensing partners and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

Third parties including competitors may infringe, misappropriate or otherwise violate our patents, patents that may issue to us in the future, or the patents of our licensors that are licensed to us. To counter infringement or unauthorized use, we may need to or choose to file infringement claims, which can be expensive and time-consuming. We may not be able to prevent, alone or with our licensors, infringement, misappropriation, or other violation of our intellectual property, particularly in countries where the laws may not protect those rights as fully as in the United States.

If we choose to go to court to stop another party from using the inventions claimed in our patents, that individual or company has the right to ask the court to rule that such patents are invalid, unenforceable, or should not be enforced against that third party for any number of reasons. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements for patentability, including, but not limited to, lack of novelty, obviousness, lack of written description, indefiniteness, or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution, i.e., committed inequitable conduct.

Third parties may also raise similar claims before the USPTO, even outside the context of litigation or infringement. Such mechanisms could include re-examination, post-grant review, inter partes review, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). For example, we are currently a party to Requests for Director Review from a Final Written Decision in two post-grant reviews of U.S. Patent Nos. 10,849,908 B2 and 11,007,201 B2, a post-grant review of U.S. Patent No. 12,115,166 B2, an opposition proceeding with the European Patent Office with respect to EP Patent No. 3,678,649, and a Revocation Proceeding with respect to EP Patent No. 3,678,649. We may be subject to new or additional third-party pre-issuance submission of prior art to the USPTO or become involved in other post-grant review procedures, derivations, reexaminations, or *inter partes review* proceedings, in the United States or oppositions or similar proceedings in foreign jurisdictions, challenging our patent rights. The legal threshold for initiating such proceedings may be low, so that even proceedings with a low probability of success might be initiated. An adverse determination in any such challenges 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 technology and products, or limit the duration of the patent protection of our technology and products.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development or manufacturing partnerships that would help us bring any future product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace. 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 this type of litigation. Intellectual property litigation or administrative proceedings are very costly and time-consuming and could interfere with our ability to sell and market our products. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they

have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patent, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors, and inventions agreements with employees, consultants, and advisors, to protect our trade secrets and other proprietary information. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and these agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer, or third party with authorized access. Our security measures may not prevent an employee, consultant or customer from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome is unpredictable. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties

typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors, and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our products and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our future trademarks or trade names may be unable to be obtained, challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights, or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

Moreover, any name we have proposed to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. Similar requirements exist in Europe. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. 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.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our products.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements, including our Collaboration and License Agreement with HBM Alpha Therapeutics, and Antibody License Agreement with Twist Bioscience Corporation, will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our products or may elect not to continue or renew development or commercialization programs based on trial or test results, changes in their strategic focus due to the acquisition of competitive products, availability of funding, or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates and any future product candidates;
- a collaborator with marketing, manufacturing, and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development, or commercialization of our current or future products or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future products;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property;
- we may not be able to obtain intellectual property rights in technologies or products resulting from the collaboration; under certain situations, the collaborators may provide us with an option to negotiate a license to such developed technologies or products, however, we may not be able to negotiate such license; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Risks Related to Ownership of Our Common Stock

If we fail to meet all applicable requirements of the Nasdaq Capital Market ("Nasdaq") and Nasdaq determines to delist our common stock, the delisting could adversely affect the market liquidity of our common stock and the market price of our common stock could decrease.

On April 26, 2024, we received a letter from Nasdaq Listing Qualifications, notifying us that, for the previous 30 consecutive business day period prior to the date of the letter, the closing bid price for our common stock was below $1.00. In accordance with Listing Rule 5810(c)(3)(A) we were provided an initial period of 180 calendar days, or until October 23, 2024, to regain compliance with Nasdaq's bid price requirement. On October 10, 2024, we applied to transfer our listing from the Nasdaq Global Select Market to the Nasdaq Capital Market (the "Transfer"). On October 24, 2024, Nasdaq Listing Qualifications notified us that the Transfer was approved, effective October 28, 2024, and that, in connection with the Transfer, we were eligible for an additional 180 calendar day period, or until April 21, 2025 (the "Extended Compliance Date"), to regain compliance with the minimum closing bid price requirement. If, at any time before the Extended Compliance Date, the bid price for our common stock closes at $1.00 or more for a minimum of 10 consecutive business days (the "Minimum Bid Price Requirement"), we will regain compliance with the bid price requirement, unless Nasdaq Listing Qualifications staff exercise their discretion to extend this 10-day period pursuant to Nasdaq rules. In connection with obtaining approval for the Transfer, we notified Nasdaq Listing Qualifications in writing of our intention to regain compliance with the Minimum Bid Price Requirement by effecting a reverse stock split, if necessary. We can provide no assurance that any action taken by us to restore compliance with Nasdaq's Minimum Bid Price Requirement would

prevent our common stock from dropping below the Nasdaq Minimum Bid Price Requirement or prevent future non-compliance with the listing requirements of Nasdaq Listing Qualifications.

If we are unable to satisfy the Nasdaq Listing Qualifications criteria for continued listing, our common stock would be subject to delisting. Should our common stock be delisted from Nasdaq, we can provide no assurance that we will be able to re-list our common stock on a national securities exchange or that there will be an active market for these securities on the OTC market. A delisting of our common stock could negatively impact us by, among other things, reducing the liquidity and market price of our common stock; reducing the number of investors willing to hold or acquire our common stock, which could negatively impact our ability to raise equity financing; decreasing the amount of news and analyst coverage of us; resulting in a determination that the common stock is a "penny stock" which would require brokers trading in the common stock to adhere to more stringent rules, possibly resulting in a reduced level of trading activity in the secondary trading market for shares of common stock; limiting our ability to issue additional securities or obtain additional financing in the future; and impairing our ability to provide equity incentives to our employees. In addition, delisting from Nasdaq may negatively impact our reputation and, consequently, our business.

An active, liquid and orderly trading market for our common stock may not be sustained.

Prior to the closing of our IPO in October 2020, there was no public market for shares of our common stock. An active trading market for our shares may not be sustained. You may not be able to sell your shares quickly or at the market price if trading in shares of our common stock is not active. As a result of these and other factors, you may be unable to resell your shares of our common stock. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

The trading price of our common stock has been, and may continue to be volatile, and you could lose all or part of your investment.

The trading price of our common stock has been, and is likely to continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. For example, the closing price of our common stock from January 1, 2024 to April 11, 2025 has ranged from a low of $0.27 to a high of $5.49. These factors include:

- the commencement, enrollment or results of our ongoing and planned clinical trials of tralesinidase alfa, tildacerfont or any future clinical trials we may conduct of tralesinidase alfa, tildacerfont and any future product candidates, or changes in the development status of tildacerfont, tralesinidase alfa and any future product candidates;
- acceptance by the FDA and EMA of the clinical trial design of our planned and ongoing clinical trials of tralesinidase alfa and tildacerfont;
- any delay in our regulatory filings for tralesinidase alfa, tildacerfont and any future product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- adverse results or delays in clinical trials as a result of outbreaks of contagious diseases, patient engagement, protocol amendments or otherwise;
- our decision to initiate a clinical trial, not to initiate a clinical trial, or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval for tralesinidase alfa, tildacerfont and any future product candidates;
- changes in laws or regulations applicable to tralesinidase alfa, tildacerfont and any future product candidates, including but not limited to clinical trial requirements for approvals;
- the failure to obtain coverage and adequate reimbursement of tralesinidase alfa, tildacerfont and any future product candidates, if approved;
- changes in the structure of healthcare payment systems;

- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- our inability to establish collaborations if needed;
- our failure to commercialize tralesinidase alfa, tildacerfont and any future product candidates;
- unanticipated serious safety concerns related to the use of tralesinidase alfa, tildacerfont and any future product candidates;
- introduction of new products or services offered by us or our competitors, or the release or publication of clinical trial results from competing product candidates;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- the size and growth, if any, of the markets for MPS-IIIB (Sanfilippo Syndrome Type B), major depressive disorder, and other disorders that we may target;
- actual or anticipated variations in quarterly or annual operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- fluctuations in the market valuation of companies perceived by investors to be comparable to us;
- overall performance of the equity markets;
- issuances of debt or equity securities;
- sales of our common stock by us, our insiders or our other stockholders in the future;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- geopolitical and macroeconomic conditions, including relating to contagious disease outbreaks, the ongoing wars in Ukraine and Israel, and recent and potential future disruptions in access to bank deposits or lending commitments due to bank failures; and
- other events or factors discussed in this “Risk Factors” section and elsewhere in this Annual Report, many of which are beyond our control.

In addition, the stock market in general, and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this “Risk Factors” section, could have a dramatic and negative impact on the market price of our common stock.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which could harm our business, operating results or financial condition.

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

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, pursuant to the Loan Agreement, we are prohibited from paying cash dividends without the prior written consent of SVB, and future debt instruments may materially restrict our ability to pay dividends on our common stock. Any return to stockholders would therefore be limited to the appreciation, if any, of their stock.

Our principal stockholders and management own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval.

Our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding capital stock, beneficially own shares representing a significant percentage of our common stock. Therefore, these stockholders have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

We are an emerging growth company and a smaller reporting company, and the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of certain exemptions from various public company reporting requirements, including being permitted to provide only two years of audited financial statements, in addition to any required financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Annual Report, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We may take advantage of these exemptions until December 31, 2025, or until we are no longer an emerging growth company, whichever is earlier. We will cease to be an emerging growth company prior to the end of such five-year period if certain earlier events occur, including if we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, our annual gross revenues exceed $1.235 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to use this extended transition period under the JOBS Act until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company, which would allow us to take

advantage of many of the same exemptions available to emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 ("Sarbanes-Oxley Act"), and reduced disclosure obligations regarding executive compensation. We will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter. Investors may find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

As a result of being a public company, we are obligated to develop and maintain proper and effective internal control over financial reporting, and any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our common stock.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of Nasdaq. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls over financial reporting. We must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in this Annual Report, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. Prior to our IPO, we have never been required to test our internal controls within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act 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 market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities.

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

As a public company, we have incurred and will continue to incur significant legal, accounting, and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly, and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act ("Dodd-Frank Act") was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Emerging growth companies and smaller reporting companies are exempted from certain of these requirements, but we may be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to continue to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a

material adverse effect on our business, financial condition, and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

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 intend to sell shares, could reduce the market price of our common stock. As of December 31, 2024, there were 42,231,285 shares of our common stock outstanding.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, Rule 144 and Rule 701 under the Securities Act of 1933, as amended ("Securities Act"). If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

In February 2023, we entered into a securities purchase agreement with several institutional and accredited investors, including holders of more than 5% of our total common stock outstanding on the date of the securities purchase agreement, pursuant to which we issued and sold 16,116,000 shares of common stock, pre-funded warrants to purchase 800,000 shares of common stock, and warrants to purchase 12,687,000 shares of common stock. All of the pre-funded warrants have been exercised. Pursuant to the securities purchase agreement, we have registered for resale such securities. If these additional shares of common stock, and the shares of common stock issued or issuable pursuant to such pre-funded warrants and warrants, are resold, or if it is perceived that they will be resold, in the public market, the trading price of our common stock could decline.

Further, certain holders of shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to the Shelf Registration, Sales Agreement and our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that we will need significant additional capital in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities, and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. For example, in February 2022 we filed a registration statement on Form S-3, as amended, declared effective in February 2022, covering the sale of up to $200.0 million of our securities (the "Shelf Registration"), which expired February 2025. Further, in February 2022, we entered into an Open Market Sales Agreement℠ (the "Sales Agreement") with Jefferies, LLC ("Jefferies"), pursuant to which we could have sold shares of common stock having an aggregate offering price of up to $21.0 million under the Shelf Registration through Jefferies acting as the sales agent and/or principal. The Shelf Registration expired in February 2025, and no further sales may be made under the Sales Agreement. Prior to the expiration of the Shelf Registration, we did not issue any shares of common stock pursuant to the Sales Agreement. In addition, in February 2023, we entered into a securities purchase agreement with several institutional and accredited investors, including holders of more than 5% of our total common stock outstanding on the date of the securities purchase agreement, pursuant to which we issued and sold 16,116,000 shares of common stock, pre-funded warrants to purchase 800,000 shares of common stock, all of which have been exercised, and warrants to purchase 12,687,000 shares of common stock. If we sell additional shares of common stock, convertible securities or other equity securities, investors may be materially diluted by subsequent

sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock.

Pursuant to our 2020 Plan, our management is authorized to grant stock options and other stock awards to our employees, directors and consultants. Additionally, the number of shares of our common stock reserved for issuance under our 2020 Plan will automatically increase on January 1 of each year continuing through and including January 1, 2030, by 5% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our board of directors. In addition, pursuant to our 2020 Employee Stock Purchase Plan, the number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year continuing through January 1, 2030, by the lesser of (i) 1% of the total number of shares of our common stock outstanding on the last day of the calendar month before the date of the automatic increase, and (ii) 441,280 shares; provided that before the date of any such increase, our board of directors may determine that such increase will be less than the amount set forth in clauses (i) and (ii). Unless our board of directors elects not to increase the number of shares available for future grant each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president, or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer, or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware (and any appellate court therefrom) is the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative claim or cause of action brought on our behalf; (ii) any claim or cause of action for breach of a fiduciary duty owed by any of our current or former directors, officers, or other employees to us or our stockholders; (iii) any claim or cause of action against us or any of our current or former directors, officers, or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws; (iv) any claim or cause of action seeking to interpret, apply, enforce, or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws (in each case as may be amended from time to time); (v) any claim or cause of action as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and (vi) any claim or cause of action against us or any of our current or former directors, officers, or other employees governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants. These provisions would not apply to claims or causes of action brought to enforce a duty or liability created by the Securities Act and the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation and our amended and restated bylaws further provide that, to the fullest extent permitted by law, the federal district courts of the United States of America is the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation and our amended and restated bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions and the provisions may not be enforced by a court in those other jurisdictions.

These exclusive 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 and may discourage these types of lawsuits. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation or bylaws has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. If a court were to find either exclusive forum provision contained in our amended and restated certificate of incorporation or amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could seriously harm our business.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Risk Management and Strategy

We have implemented and maintain various information security processes designed to identify, assess and manage material risks from cybersecurity threats to our critical computer networks, third party hosted services, communications systems, hardware and software, and our critical data, including intellectual property, confidential information that is proprietary, strategic or competitive in nature, and personal health information (including clinical trial data) ("Information Systems and Data").

Our information technology function, which is led by Samir Gharib, our President, Chief Financial Officer, and Chief Compliance Officer, helps identify, assess and manage the Company's cybersecurity threats and risks. Our information technology function works to identify and assess risks from cybersecurity threats by monitoring and evaluating our threat environment and the Company's risk profile using various methods including, employing both automated and manual tools and controls; conducting threat and vulnerability assessments; utilizing third-party services to monitor our information technology infrastructure; and performing internal audits.

Depending on the environment, we implement and maintain various technical, physical, and organizational measures, processes, standards and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example: risk assessments, incident detection and response policies, network security controls for certain systems (including as applicable data segregation, data encryption, access controls, physical security, and systems threat monitoring), disaster recovery and business continuity plans, vendor risk management program, and dedicated cybersecurity staff and employee training.

Our assessment and management of material risks from cybersecurity threats are integrated into the Company's overall risk management processes. For example, cybersecurity risk is addressed as a component of the Company's enterprise risk management program and the information technology function works with management to prioritize our risk management processes and mitigate cybersecurity threats that are more likely to lead to a material impact to our business. Additionally, Mr. Gharib and the audit committee of the board of directors evaluate material risks from cybersecurity threats against our overall business objectives and reports to the board of directors, which evaluates our overall enterprise risk.

We use third-party service providers to assist us from time to time to identify, assess, and manage material risks from cybersecurity threats, including for example cybersecurity software providers and managed cybersecurity service providers.

We use third-party service providers to perform a variety of functions throughout our business, such as application providers, hosting companies, contract research organizations, contract manufacturing organizations, and supply chain providers. We have a vendor management program to manage cybersecurity risks associated with our use of service providers. The program includes, as applicable, risk assessment for certain vendors, security questionnaires, review of certain vendors' security programs and security assessments, and imposition of cybersecurity-related contractual obligations for some vendors. Depending on the nature of the services provided, the sensitivity of the Information Systems and Data at issue, and the identity of the provider, our vendor management process may involve different levels of assessment designed to help identify cybersecurity risks associated with a provider and we may impose contractual obligations related to cybersecurity on the provider.

For a description of the risks from cybersecurity threats that may materially affect the Company and how they may do so, see our risk factors under Part 1. Item 1A. Risk Factors in this Annual Report, including the sections titled "Risk Factors— If our information technology systems or data, or those of third parties with whom we work, are or were compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse consequences" and "Risk Factors— We and the third parties with whom we work are subject to stringent and evolving obligations related to data privacy and security. These obligations include U.S. and foreign laws, regulations, and rules; contractual obligations; industry standards; and policies. Our (including the third parties with whom we work) actual or perceived failure to comply

with such obligations could lead to regulatory investigations and actions (which could include civil or criminal penalties); private litigation (including class-action claims) and mass arbitration demands; disruptions to our business operations; adverse publicity; and other adverse consequences that could negatively affect our operating results and business."

Governance

Our board of directors addresses the Company's cybersecurity risk management as part of its general oversight function. The audit committee of the board of directors is responsible for overseeing Company's cybersecurity risk management processes, including oversight and mitigation of risks from cybersecurity threats.

Our cybersecurity risk assessment and management processes are implemented and maintained by certain Company management, including Mr. Gharib, who oversees enterprise risk management and information security for the Company.

Mr. Gharib is responsible for hiring information security personnel, integrating cybersecurity risk considerations into the Company's overall risk management strategy, and communicating key priorities to relevant personnel. Mr. Gharib is also responsible for approving budgets, helping prepare for cybersecurity incidents, approving cybersecurity processes, and reviewing security assessments and other security-related reports.

Our incident response and vulnerability management processes and policies are designed to escalate certain cybersecurity incidents to members of management depending on the circumstances, including Mr. Gharib and the Chief Executive Officer. Mr. Gharib works with the Company's incident response team to help the Company mitigate and remediate cybersecurity incidents of which they are notified. In addition, the Company's incident response and vulnerability management processes and policies include reporting to the audit committee of the board of directors for certain cybersecurity incidents.

The audit committee receives periodic reports from Mr. Gharib concerning the Company's significant cybersecurity threats and risk and the processes the Company has implemented to address them. The audit committee also receives various reports, summaries or presentations related to cybersecurity threats, risk and mitigation.

Item 2. Properties.

Our corporate headquarters are located at 611 Gateway Boulevard, Suite 740, South San Francisco, California 94080, where we occupy approximately 6,500 square feet of office space pursuant to a lease entered in December 2022, which began in December 2022 and expires in February 2028.

We believe our existing facility meets our current needs.

Item 3. Legal Proceedings.

In January 2025, Neurocrine Biosciences, Inc. ("Neurocrine") filed suit in the United States District Court for the District of Delaware against us, seeking to invalidate one of our patents. In addition, Neurocrine has initiated administrative proceedings against other Spruce patents in the U.S. Patent Office, and both judicial and administrative proceedings against Spruce patents in other jurisdictions. We currently believe that none of the claims or actions pending against us is likely to have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations. Given the unpredictability inherent in litigation, however, we cannot predict the outcome of these matters.

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 traded on the Nasdaq Capital Market under the symbol "SPRB" since October 28, 2024. Between October 9, 2020 and October 27, 2024, our common stock was traded on the Nasdaq Global Select Market. Prior to October 9, 2020, there was no public market for our common stock.

Holders of Common Stock

As of April 11, 2025, we had 42,231,285 shares of common stock outstanding held by 33 holders of record, one of which was Cede & Co., a nominee for Depository Trust Company ("DTC"). All of the shares of our common stock held by brokerage firms, banks and other financial institutions as nominees for beneficial owners are deposited into participant accounts at DTC and are therefore considered to be held of record by Cede & Co. as one stockholder. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Securities Authorized for Issuance Under Equity Compensation Plans

See Item 12 of Part III of this Annual Report for information about our equity compensation plans which is incorporated by reference herein.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. In addition, pursuant to the Loan Agreement with Silicon Valley Bank, as amended, we are prohibited from paying cash dividends without the prior written consent of Silicon Valley Bank and future debt instruments may materially restrict our ability to pay dividends on our common stock. Any future determination related to dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

Item 6. Reserved.

Not applicable.

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

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our financial statements and the related notes to those statements included later in this Annual Report. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates, beliefs and expectations that involve risks and uncertainties. Our actual results and the timing of events could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report, particularly in Item 1A. "Risk Factors" and "Special Note Regarding Forward-Looking Statements." Unless otherwise indicated, all references in this Annual Report to "Spruce," the "company," "we," "our," "us" or similar terms refer to Spruce Biosciences, Inc.

Overview

We are a biopharmaceutical company focused on developing and commercializing novel therapies for neurological disorders with significant unmet medical need. We have a diverse portfolio of product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are either no approved therapies treating the underlying disease or suboptimal treatment options. We were founded in April 2016 and are led by a management team experienced in the development and commercialization of groundbreaking therapeutics.

Since our inception in November 2014, we have focused primarily on raising capital, establishing and protecting our intellectual property portfolio, organizing and staffing our company, business planning, and conducting preclinical and clinical development of, and manufacturing development for, our product candidate, tildacerfont. We have no products approved for commercial sale and have not generated any product revenue to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. Our ability to generate product revenue sufficient to achieve profitability, if ever, will depend on the successful development of tildacerfont and any future product candidates.

Given that a relatively small number of clinicians and specialists treat a large proportion of the patients with MPS IIIB, we believe this market can be effectively addressed with a modest-sized and targeted patient-centric field team, alongside various high-touch patient initiatives. We plan to seek strategic collaborations to benefit from the resources of biopharmaceutical companies specialized in either relevant disease areas or geographies in markets outside the United States.

We rely, and expect to continue to rely, on third parties for the manufacture of our investigational products for preclinical studies and clinical trials, as well as for commercial manufacture if our investigational products, including TA-ERT, obtain marketing approval. We also rely, and expect to continue to rely, on third parties to package, label, store, and distribute tildacerfont, if marketing approval is obtained. We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment, and personnel while also enabling us to focus our expertise and resources on the development of tildacerfont.

Since inception, we have incurred significant losses and negative cash flows from operations. During the years ended December 31, 2024 and 2023, we incurred net losses of $53.0 million and $47.9 million, respectively, and used $56.0 million and $33.3 million of cash in operations, respectively. As of December 31, 2024, we had an accumulated deficit of $250.3 million, and we do not expect positive cash flows from operations for the foreseeable future. We expect to continue to incur significant and increasing losses for the foreseeable future, and our net losses may fluctuate significantly from period to period, depending on the timing of expenditures on our planned research and development activities.

Since inception through December 31, 2024, we have raised aggregate gross proceeds of $293.1 million, including $103.5 million from our initial public offering ("IPO") in October 2020, $116.0 million from the sale of our redeemable convertible preferred stock, $5.0 million from the issuance of debt, $53.6 million from a private placement financing in February 2023, and the $15.0 million upfront payment from Kaken received in April 2023. As of December 31, 2024, we had cash and cash equivalents of $38.8 million.

Without alternative financing or proceeds from other strategic alternatives, we believe, based on our current operating plan, that our cash and cash equivalents as of December 31, 2024 will be insufficient to fund our operations and debt obligations for at least 12 months following the issuance date of our financial statements

included elsewhere in this Annual Report.

We expect our expenses will increase significantly in connection with our ongoing activities, as we:

- pursue regulatory approval of TA-ERT in patients with MPSIIIB;
- build a highly specialized commercial organization to support the commercialization of TA-ERT, if approved, in the United States;
- seek strategic collaborations to benefit from the resources of biopharmaceutical companies specialized in either relevant disease areas or geographies in markets outside the United States;
- advance TA-ERT through a planned confirmatory study in patients with MPSIIB and expanded access programs;
- expand manufacturing capacity to accommodate anticipated global demand of TA-ERT, if approved, for the treatment of MPSIIIB;
- advance clinical development of tildacerfont in MDD;
- advance pre-clinical and clinical development of SPR202 in CAH;
- advance pre-clinical and clinical development of SPR204 in PBH;
- implement operational, financial, and management information systems;
- hire additional personnel; and
- obtain, maintain, expand, and protect our intellectual property portfolio.

Global economic and business activities continue to face widespread macroeconomic uncertainties, including recent and potential future disruptions in access to bank deposits or lending commitments due to bank failures, labor shortages, inflation and monetary supply shifts, recession risks and potential disruptions from the ongoing wars in Ukraine and the Middle East and related sanctions.

The extent of the impact of these factors on our operational and financial performance, including our ability to execute our business strategies and initiatives in the expected time frame, will depend on future developments, which are uncertain and cannot be predicted; however, any continued or renewed disruption resulting from these factors could negatively impact our business.

Material Agreements

Loan Agreement with Silicon Valley Bank

In September 2019, we entered into a Loan and Security Agreement, as subsequently amended (the "Loan Agreement"), with SVB providing for a term loan (the "Term Loan") for an aggregate principal amount of $4.5 million.

In March 2021, we entered into a First Amendment to Loan and Security Agreement (the "First Amendment") which increased the aggregate principal amount of the Term Loan to $30.0 million, of which $20.0 million was immediately available under the first tranche (the "First Tranche") and $10.0 million was available under the second tranche through December 31, 2022 (the "Second Tranche") subject to the completion of certain clinical or financial milestones. Pursuant to the First Amendment, the Term Loan will mature on January 1, 2026 (the "Maturity Date").

In May 2022, we entered into a Second Amendment to Loan and Security Agreement (the "Second Amendment") which amended the milestones for the Second Tranche, added a liquidity covenant for the Second Tranche and amended the interest and prepayment terms.

As of December 31, 2024 and 2023, the outstanding principal was comprised of $1.8 million and $3.4 million, respectively, under the First Tranche. Repayment of principal under the First Tranche commenced in January 2023. Commitments available under the Second Tranche of $10.0 million expired on December 31, 2022.

The Loan Agreement provided for monthly cash interest-only payments following the funding date of each respective tranche and continuing thereafter through December 31, 2022. The Term Loan is subject to a floating per annum interest rate equal to the greater of (a) 0.50% above the Prime Rate (as defined in the Loan Agreement) or (b)

3.75%. Following the interest-only period, the outstanding Term Loan balance is payable in (i) 37 consecutive monthly payments after the end of the interest-only period and continuing on the same day of each month thereafter, in amounts that would fully amortize such Term Loan balance, as of the first business day of the first month following the amended interest-only period, over the repayment period, plus (ii) monthly payments of accrued but unpaid interest.

The final payment is due on the Maturity Date and includes all outstanding principal plus accrued unpaid interest and an end of term payment totaling $0.3 million, which is 6.0% of the original funded principal amount of the First Tranche (the "Supplemental Final Payment"). We may prepay amounts outstanding under the Term Loan at any time provided certain notification conditions are met, in which case, all outstanding principal plus accrued and unpaid interest, the Supplemental Final Payment, a prepayment fee of 1% or 2% of the principal amount of the First Tranche, and any bank expenses become due and payable.

Components of Results of Operations

Collaboration Revenue

To date, all of our revenue has been derived from the Kaken License Agreement, pursuant to which we granted Kaken the exclusive right to develop and commercialize tildacerfont for CAH in Japan.

We will recognize royalty and milestone revenues under the Kaken License Agreement if and when appropriate under the relevant accounting rules (see Note 8 to our financial statements). We have not generated any revenues from the commercial sale of approved products and we do not expect to generate revenues from the commercial sale of our product candidates for at least the foreseeable future, if ever.

Operating Expenses

We classify operating expenses into two main categories: (i) research and development expenses and (ii) general and administrative expenses.

Research and Development Expenses

Our research and development expenses consist of external and internal expenses incurred in connection with our research activities and development programs.

These expenses include:

- external expenses, consisting of:
  - clinical development—expenses associated with clinical research organizations ("CROs") engaged to manage and conduct clinical trials, in-process research and development and other outside services;
  - preclinical studies—expenses associated with preclinical studies and clinical pharmacology;
  - manufacturing—expenses associated with contract manufacturing; labeling, packaging, and distribution of clinical trial supplies, and other outside services;
  - other research and development—expenses associated with business operations, quality and regulatory compliance; and
- internal expenses, consisting of personnel, including expenses for salaries, bonuses, benefits, stock-based compensation, as well as allocation of certain expenses.

To date, these expenses have been incurred primarily to advance tildacerfont and acquire TA-ERT. These expenses will primarily consist of personnel costs, expenses for the conduct of clinical trials, manufacturing costs for clinical drug supply, and in-process research and development. We expect that significant additional spending will be required to progress TA-ERT through clinical development and potential regulatory approval and advancing our other investigational product candidates through clinical and pre-clinical development.

Research and development expenses are recognized as they are incurred, including licenses of intellectual property that have no alternative future use at the time of the acquisition. If deposits are required by external vendors, a portion of the deposit is included as a prepaid expense until the activity has been performed or when the goods have been received to amortize the deposit to expense in the statements of operations and comprehensive loss.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs, including salaries, bonuses, benefits, and stock-based compensation expense, for executive, finance, and other administrative functions. General and administrative expenses also include legal fees, professional fees, insurance costs, facility costs not otherwise included in research and development expenses, and public company expenses such as costs associated with compliance with the rules and regulations of the SEC, and those of the Nasdaq Stock Market LLC ("Nasdaq") listing rules.

We expect that our general and administrative expenses will continue to increase in the foreseeable future as additional administrative personnel and services are required to manage these functions of a public company, and as we advance tildacerfont through clinical development and potential regulatory approval.

Interest Expense

Interest expense consists of interest incurred and non-cash amortization of debt discount and issuance costs in connection with the Term Loan.

Interest and Other Income, Net

Interest and other income, net primarily consists of interest income earned on our cash, cash equivalents and investments.

Results of Operations

Comparisons of the Year Ended December 31, 2024 and 2023

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

	Year Ended December 31,		
	2024	2023	Change
Collaboration revenue	$ 4,911	$ 10,089	$ (5,178)
Operating expenses:			
Research and development	46,418	49,432	(3,014)
General and administrative	14,644	12,650	1,994
Total operating expenses	61,062	62,082	(1,020)
Loss from operations	(56,151)	(51,993)	(4,158)
Interest expense	(307)	(483)	176
Interest and other income, net	3,422	4,557	(1,135)
Net loss	$ (53,036)	$ (47,919)	$ (5,117)

Collaboration Revenue

During the years ended December 31, 2024 and 2023, we recognized $4.9 million and $10.1 million, respectively, as collaboration revenue under the Kaken License Agreement.

Research and Development Expenses

The following table sets forth research and development expenses for the periods presented (in thousands):

	Year Ended December 31,		
	2024	2023	Change
External expenses:			
Clinical development	$ 27,824	$ 32,354	$ (4,530)
Manufacturing	7,748	3,855	3,893
Preclinical studies	31	490	(459)
Other research and development	860	1,272	(412)
Internal expenses:			
Personnel	9,637	11,130	(1,493)
Facilities and other	318	331	(13)
Total research and development expenses	$ 46,418	$ 49,432	$ (3,014)

Research and development expenses decreased by $3.0 million during the year ended December 31, 2024 compared to the year ended December 31, 2023.

The decrease in clinical development expenses of $4.5 million was primarily driven by (i) a decrease of $8.5 million due to the termination of the CAHmelia-203 study, (ii) a decrease of $2.5 million due to completion of the POWER study, (iii) a decrease of $3.8 million due to completion of enrollment in the CAHmelia-204 study, partially offset by (iv) clinical development costs related to the Allievex asset purchase of $8.9 million and (v) an increase of $1.0 million related to additional dose ranging cohorts in the CAHptain-205 clinical trial.

The increase in manufacturing expenses of $3.9 million was primarily driven by manufacturing costs related to the Allievex asset purchase of $5.9 million, partially offset by a decrease of $1.0 million related to the termination of the CAHmelia-203 study.

The decrease in personnel related expenses of $1.5 million was primarily driven by a decrease of $1.3 million in salaries due to reduced headcount, partially offset by an increase of $0.5 million in stock-based compensation expense.

General and Administrative Expenses

General and administrative expenses increased by $2.0 million during the year ended December 31, 2024 compared to the year ended December 31, 2023, primarily due to an increase of $2.5 million in legal professional services, partially offset by a decrease of $0.3 million in insurance costs for directors and officers.

Interest Expense

Interest expense decreased by $0.2 million during the year ended December 31, 2024 compared to the year ended December 31, 2023 due to the decrease in the interest rate and the decrease in the principal balance on the Term Loan year over year.

Interest and Other Income, Net

Interest and other income, net decreased by $1.1 million during the year ended December 31, 2024 compared to the year ended December 31, 2023 due to a decrease in cash and cash equivalents year over year.

Liquidity and Capital Resources

Liquidity

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from operations. We anticipate that we will continue to incur net losses for the foreseeable future. As of December 31, 2024, we had an accumulated deficit of $250.3 million. As of December 31, 2024, we had cash and cash equivalents of $38.8 million. Since inception through December 31, 2024, we have raised aggregate gross proceeds of $293.1 million, including $103.5 million from our IPO in October 2020, $116.0 million from the sale of our redeemable convertible preferred stock, $5.0 million from the issuance of debt, $53.6 million from a private placement financing in February 2023, and $15.0 million from the Kaken upfront payment received in April 2023.

Until we can generate sufficient revenue, if ever, to fund our operations, we will need to finance future cash needs through public or private equity offerings, license agreements, debt financings or restructurings, collaborations, strategic alliances and marketing or distribution arrangements, and there can be no assurance that such arrangements will be available to us on a timely basis, or, if available, will be available on terms acceptable to us. Without alternative financing or proceeds from other strategic alternatives, we believe, based on our current operating plan, that our cash and cash equivalents as of December 31, 2024 will be insufficient to fund our operations and debt obligations for at least 12 months following the issuance date of our financial statements included elsewhere in this Annual Report. These conditions raise substantial doubt about our ability to continue as a going concern.

Funding Requirements

To date, we have not generated any product revenue. We do not expect to generate any meaningful revenue unless and until we obtain regulatory approval and commercialize TA-ERT or any future product candidates, and we do not know when, or if at all, that will occur. We will continue to require additional capital to develop tildacerfont and fund operations for the foreseeable future. Our primary uses of cash are to fund our operations, which consist

primarily of research and development expenses related to our clinical development programs, and to a lesser extent, general and administrative expenses.

At this time, we cannot reasonably estimate or know the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, tildacerfont or any of our future product candidates. We expect our research and development expenses to increase significantly in the foreseeable future as we continue to invest in activities related to the clinical development and commercialization of TA-ERT, as we pursue regulatory approval of TA-ERT for the treatment of MPSIIIB. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and we may never succeed in achieving regulatory approval for TA-ERT in patients with MPSIIIB.

We may seek to raise capital through equity or debt financings, collaborative agreements, potentially including agreements to out-license rights to develop and commercialize TA-ERT, or other arrangements with other companies, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the progress, costs, trial design, results of, and timing of our ongoing and planned clinical trials of our product candidates;
- the outcome, costs and timing of seeking and obtaining FDA and any other regulatory approvals;
- the number and characteristics of product candidates that we may pursue;
- our ability to manufacture sufficient quantities of our product candidates;
- our plan to expand our research and development activities;
- the costs associated with manufacturing our product candidates and establishing clinical and commercial supplies, and sales, marketing, and distribution capabilities;
- our ability to enter into favorable out-licensing agreements for the development and commercialization of our product candidates;
- the costs associated with commercialization;
- the costs of acquiring, licensing, or investing in product candidates;
- our ability to maintain, expand, and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense, and enforcement of any patents or other intellectual property rights;
- our need and ability to retain key management and hire scientific, technical, business, and medical personnel;
- the effect of competing products and product candidates and other market developments;
- the timing, receipt, and amount of sales from our product candidates and any future product candidates, if approved;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems;
- the economic and other terms, timing of, and success of any collaboration, licensing, or other arrangements which we may enter in the future; and
- the effects of the disruptions to and volatility in the credit and financial markets in the United States and worldwide from geopolitical and macroeconomic events, including the wars in Ukraine and Israel and related sanctions, and recent and potential future disruptions in access to bank deposits or lending commitments due to bank failures.

If we raise additional funds by issuing equity securities, our stockholders will experience dilution. If we raise additional capital through debt financing, we may be subject to covenants that restrict our operations including

limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments, and engage in certain merger, consolidation, or asset sale transactions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders.

We may be unable to raise additional funds or to enter into such agreements or arrangements on favorable terms, or at all. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and the disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from macroeconomic events, the wars in Ukraine and Israel and related sanctions, and recent and potential future disruptions in access to bank deposits or lending commitments due to bank failures, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back, or discontinue the development or commercialization of our product candidates or other research and development initiatives. We also could be required to seek collaborators for our product candidates and any future product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to our product candidates and any future product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

The amount and timing of our future funding requirements will depend on many factors including the pace and results of our development efforts. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

Material Cash Requirements

As of December 31, 2024, future payments of principal and interest on the Term Loan, which commenced repayment in January 2023 and matures in January 2026, were $1.8 million. For a description of the terms of the Loan Agreement, see the section titled “Material Agreements — Loan Agreement with Silicon Valley Bank” above.

As of December 31, 2024, the total undiscounted lease payments for our non-cancelable operating lease for office space, which terminates in February 2028 unless renewed, was $1.2 million.

We enter into contracts in the normal course of business with third-party contract manufacturing organizations and CROs for clinical trials, non-clinical studies, drug substance and product manufacturing and other services for operating purposes. These contracts are generally cancelable by us upon prior written notice after a certain period. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation.

We have also entered into license and collaboration agreements under which we are obligated to make aggregate milestone payments upon the achievement of specified milestones as well as royalty payments. As of December 31, 2024, we were unable to estimate the timing or likelihood of achieving these milestones or generating future product sales. For a description of the terms of our license and collaboration agreements, see “Item 1. Business — License and Collaboration Agreements” above.

Summary Statements of Cash Flows

The following table sets forth the primary sources and uses of cash, cash equivalents, and restricted cash for the periods presented below (in thousands):

	Year Ended December 31,		
	2024	2023	Change
Net cash used in operating activities	$ (55,964)	$ (33,275)	$ (22,689)
Net cash provided by investing activities	—	55,777	(55,777)
Net cash provided by (used in) financing activities	(1,622)	49,140	(50,762)
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ (57,586)	$ 71,642	$ (129,228)

Cash Used in Operating Activities

Net cash used in operating activities increased by $22.7 million during the year ended December 31, 2024 compared to the year ended December 31, 2023. Net cash used in fiscal 2024 includes cash paid of $10.6 million for the Allievex asset purchase which was offset by a decrease in payments driven by the termination of the CAHmelia-203 study and completion of the studies for CAHmelia-204, CAHmelia-205 and POWER. Additionally, cash used in fiscal 2023 was offset by the receipt of the $15.0 million upfront payment under the Kaken License Agreement in April 2023.

Cash Used in Investing Activities

For the year ended December 31, 2024, no cash was provided by investing activities.

For the year ended December 31, 2023, net cash provided by investing activities was $55.8 million, consisting primarily of proceeds from maturities of investments of $67.7 million offset by purchases of investments of $11.9 million.

Cash Provided by Financing Activities

For the year ended December 31, 2024, net cash used in financing activities was $1.6 million, consisting primarily of principal payments on the Term Loan of $1.6 million.

For the year ended December 31, 2023, net cash provided by financing activities was $49.1 million, consisting primarily of net proceeds received from the February 2023 private placement of $50.9 million, offset by principal payments on the Term Loan of $1.6 million.

Segments

We operate and manage our business as one operating segment, which is the business of developing and commercializing novel therapies for serious neurological disorders with significant unmet medical need.

Critical Accounting Estimates

Our accounting policies are more fully described in Note 2 of the financial statements to this Annual Report. As disclosed in Note 2, the preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions about future events that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ significantly from those estimates. We believe that the following discussion addresses our most critical accounting estimates, which are those that are most important to the portrayal of our financial condition and results of operations and require management's most difficult, subjective and complex judgments.

Contingent Liabilities in Accrued Research and Development Expenses

We evaluate contingencies based on information currently available and will establish accruals for those matters when a contingency is considered probable and the related amount is reasonably estimable. As of December 31, 2024, we have accrued contingent liabilities of $4.8 million related to the Allievex Purchase Agreement that are deemed both probable and estimable. We have estimated the amount of liabilities based on the amounts owed by Allievex to external vendors and through discussions with internal personnel and the external vendors. Accruals are periodically reviewed and may be adjusted as circumstances change. Although we do not expect our estimates to be materially different from amounts actually accrued, our estimates may materially vary.

Revenue Recognition

We recognize revenue allocated to the Kaken License Agreement from non-refundable, up-front fees at the point in time when the license is transferred to the licensee and the licensee can use and benefit from the license. As the license is bundled with other distinct or combined obligations, we use judgment to assess the nature of the performance obligation to determine whether the performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. As the performance obligation is satisfied over time, we evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. We utilize the cost-based input method over the respective performance period. If the actual costs vary from our estimates, we adjust the recognition of revenue based on the updated measure of progress each reporting period. Although we do not expect our

estimates to be materially different from amounts actually incurred, our projections of costs relative to the actual costs incurred may materially vary and may result in reporting amounts that are too high or too low in any particular period.

JOBS Act

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012 ("JOBS Act"). The JOBS Act permits emerging growth companies to take advantage of an extended transition period to comply with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. We have elected to use this extended transition period under the JOBS Act until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We could be an emerging growth company until December 31, 2025, although circumstances could cause us to lose that status earlier, including if we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act or if we have total annual gross revenue of $1.235 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three year period before that time, we would cease to be an emerging growth company immediately.

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

Interest Rate Risk

Our cash and cash equivalents as of December 31, 2024 consisted of $38.8 million in bank deposits and money market funds. Previously, we have held U.S treasury securities and corporate bonds. Such interest-earning instruments carry a degree of interest rate risk. The goals of our investment policy are capital preservation, liquidity, safeguarding of capital and total return. We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate exposure. While we believe our cash and cash equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. Additionally, the interest rate for our Term Loan is variable.

As of December 31, 2024 and 2023, a hypothetical 1% change in interest rates would not have had a material effect on our financial statements. We do not currently engage in hedging transactions to manage our exposure to interest rate risk.

Foreign Currency Exchange Risk

Our operations include activities in the United States. In addition, we contract with vendors that are located outside of the United States and certain invoices are denominated in foreign currencies. While our operating results are exposed to changes in foreign currency exchange rates between the U.S. dollar and various foreign currencies, there was no material impact on our results of operations for any periods presented herein.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein. While we are seeing, and expect to continue to see, inflation due to geopolitical and macroeconomic, as of December 31, 2024, we do not expect anticipated changes in inflation to have a material effect on our business, financial condition or results of operations for future reporting periods.

Item 8. Financial Statements and Supplementary Data.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm (BDO USA, P.C., San Jose, California, PCAOB ID #243)	100
Balance Sheets	101
Statements of Operations and Comprehensive Loss	102
Statements of Stockholders' Equity	103
Statements of Cash Flows	104
Notes to Financial Statements	105

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Stockholders and Board of Directors
Spruce Biosciences, Inc.
South San Francisco, California

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Spruce Biosciences, Inc. (the "Company") as of December 31, 2024 and 2023, the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Going Concern Uncertainty

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has insufficient cash and cash equivalents to fund its planned operations and debt obligations for at least 12 months following the date of these financial statements, which raises substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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.

/s/ BDO USA, P.C.

We have served as the Company's auditor since 2020.

San Jose, California

April 15, 2025

SPRUCE BIOSCIENCES, INC.
BALANCE SHEETS
(in thousands, except share and per share amounts)

	December 31,	
	2024	2023
ASSETS		
Current assets:		
Cash and cash equivalents	$ 38,753	$ 96,339
Prepaid expenses	3,177	3,876
Other current assets	2,276	1,968
Total current assets	44,206	102,183
Right-of-use assets	934	1,181
Other assets	69	582
Total assets	$ 45,209	$ 103,946
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,295	$ 3,332
Accrued expenses and other current liabilities	12,329	14,600
Term loan, current portion	1,622	1,622
Deferred revenue	—	4,911
Total current liabilities	15,246	24,465
Lease liabilities, net of current portion	736	1,019
Term loan, net of current portion	124	1,717
Other liabilities	282	236
Total liabilities	16,388	27,437
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized and no shares issued or outstanding as of December 31, 2024 and 2023	—	—
Common stock, $0.0001 par value; 200,000,000 shares authorized as of December 31, 2024 and 2023; 42,231,285 and 41,029,832 shares issued and outstanding as of December 31, 2024 and 2023, respectively	4	4
Additional paid-in capital	279,085	273,737
Accumulated deficit	(250,268)	(197,232)
Total stockholders' equity	28,821	76,509
Total liabilities and stockholders' equity	$ 45,209	$ 103,946

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

SPRUCE BIOSCIENCES, INC.
STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2024	2023
Collaboration revenue	$ 4,911	$ 10,089
Operating expenses:		
Research and development	46,418	49,432
General and administrative	14,644	12,650
Total operating expenses	61,062	62,082
Loss from operations	(56,151)	(51,993)
Interest expense	(307)	(483)
Interest and other income, net	3,422	4,557
Net loss	(53,036)	(47,919)
Other comprehensive gain, net of tax:		
Unrealized gain on available for sale securities	—	558
Total comprehensive loss	$ (53,036)	$ (47,361)
Net loss per share, basic and diluted	$ (1.29)	$ (1.24)
Weighted-average shares of common stock outstanding, basic and diluted	41,264,948	38,510,220

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

SPRUCE BIOSCIENCES, INC.
STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance as of January 1, 2023	23,601,004	$ 3	$ 218,354	$ (558)	$ (149,313)	$ 68,486
Exercise of pre-funded warrants	800,000	—	8	—		8
Exercise of common stock options	54	—	1	—	—	1
Issuance of common stock related to employee stock purchase plan	162,791	—	169	—	—	169
Issuance of common stock related to vesting of restricted stock units, net of tax withholdings	349,983	—	(311)	—		(311)
Issuance of common stock and warrants, net of offering costs of $2,721	16,116,000	1	50,894	—		50,895
Stock-based compensation	—	—	4,622	—		4,622
Unrealized loss on available for sale securities	—	—	—	558	—	558
Net loss	—	—	—	—	(47,919)	(47,919)
Balance as of December 31, 2023	41,029,832	4	273,737	—	(197,232)	76,509
Exercise of common stock options	120,328	—	180	—	—	180
Issuance of common stock related to employee stock purchase plan	158,569	—	66	—	—	66
Issuance of common stock related to vesting of restricted stock units, net of tax withholdings	922,556	—	(246)	—	—	(246)
Stock-based compensation	—	—	5,348	—	—	5,348
Net loss	—	—	—	—	(53,036)	(53,036)
Balance as of December 31, 2024	42,231,285	$ 4	$ 279,085	$ —	$ (250,268)	$ 28,821

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

SPRUCE BIOSCIENCES, INC.
STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2024	2023
Cash flows from operating activities		
Net loss	$ (53,036)	$ (47,919)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	5,348	4,622
Depreciation and amortization	46	70
Net accretion of discount on available-for-sale securities	—	(636)
Non-cash lease expense	247	230
Loss on disposal of property and equipment	2	2
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	391	(2,636)
Other assets	494	96
Accounts payable	(2,037)	1,906
Accrued expenses and other current liabilities	(2,271)	6,255
Deferred revenue	(4,911)	4,911
Other liabilities	(237)	(176)
Net cash used in operating activities	(55,964)	(33,275)
Cash flows from investing activities		
Proceeds from maturities of investments	—	67,665
Purchases of investments	—	(11,881)
Purchases of property and equipment	—	(7)
Net cash provided by investing activities	—	55,777
Cash flows from financing activities		
Proceeds from issuance of common stock and warrants	—	53,616
Proceeds from issuance of common stock related to employee stock purchase plan	66	169
Proceeds from exercise of pre-funded warrants	—	8
Proceeds from exercise of common stock options	180	1
Payment of offering costs	—	(2,721)
Repayment of term loan	(1,622)	(1,622)
Tax withholding payments on restricted stock units	(246)	(311)
Net cash provided by (used in) financing activities	(1,622)	49,140
Net increase (decrease) in cash, cash equivalents, and restricted cash	(57,586)	71,642
Cash, cash equivalents, and restricted cash at beginning of period	96,374	24,732
Cash, cash equivalents, and restricted cash at end of period	$ 38,788	$ 96,374
Reconciliation of cash, cash equivalents, and restricted cash		
Cash and cash equivalents	$ 38,753	$ 96,339
Restricted cash, long-term (included in other assets)	35	35
Total cash, cash equivalents, and restricted cash	$ 38,788	$ 96,374
Supplemental cash flow data:		
Cash paid for interest on term loan	$ 225	$ 369
Supplemental disclosure of non-cash investing and financing activities:		
Deferred offering costs included in accrued expenses	$ —	$ 51
Right-of-use asset recognized in exchange for lease liability	$ —	$ 11

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

SPRUCE BIOSCIENCES, INC.
NOTES TO FINANCIAL STATEMENTS

1. Organization and Principal Activities

Description of Business

Spruce Biosciences, Inc. (the "Company") is a late-stage biopharmaceutical company focused on developing and commercializing novel therapies for neurological disorders with significant unmet medical need. The Company is located in South San Francisco, California and was incorporated in the state of Delaware in April 2016.

Private Placement of Common Stock and Warrants

In February 2023, the Company entered into a Securities Purchase Agreement (the "Purchase Agreement") with certain institutional investors (the "Purchasers"), pursuant to which the Company agreed to sell and issue (i) 16,116,000 shares of the Company's common stock ("Common Stock"), (ii) pre-funded warrants to purchase 800,000 shares of Common Stock (the "Pre-Funded Warrants") to a Purchaser and (iii) 12,687,000 warrants to purchase Common Stock (the "Standard Warrants" and together with the Pre-Funded Warrants, the "Warrants") in a private placement transaction (the "Private Placement"). The total gross proceeds to the Company were approximately $53.6 million, which does not include any proceeds that may be received upon exercise of the Standard Warrants.

Liquidity and Capital Resources

The Company has incurred significant losses and negative cash flows from operations. During the year ended December 31, 2024, the Company incurred a net loss of $53.0 million and used $56.0 million of cash in operations. As of December 31, 2024, the Company had an accumulated deficit of $250.3 million and does not expect positive cash flows from operations in the foreseeable future. The Company has funded its operations primarily through the issuance and sale of equity securities, debt and collaboration revenue.

The accompanying financial statements have been prepared assuming the Company will continue as a going concern, which assumes the realization of assets and satisfaction of liabilities and commitments in the normal course of business. Without alternative financing or proceeds from other strategic alternatives, the Company believes that based on its current operating plan, its cash and cash equivalents of $38.8 million as of December 31, 2024 will be insufficient to fund its planned operations and debt obligations for at least 12 months following the issuance date of these financial statements. The Company's ability to continue as a going concern will require the Company to raise additional capital to fund the Company's operations and there can be no assurance that additional financing will be available to the Company or that such financing, if available, will be available on terms acceptable to the Company. Accordingly, there is substantial doubt about the Company's ability to continue as a going concern for at least 12 months following the issuance date of these financial statements.

In order to meet these additional cash requirements, the Company may seek to out-license rights to develop and commercialize its investigational product candidates or sell additional equity or issue debt, convertible debt or other securities that may result in dilution to its stockholders. If the Company raises additional funds through the issuance of debt or convertible debt securities, these securities could have rights senior to those of its shares of Common Stock and could contain covenants that restrict its operations. There can be no assurance that the Company will be able to obtain additional equity or debt financing on terms acceptable to it, if at all. Additional debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include covenants limiting or restricting the Company's ability to take specific actions such as incurring debt, making capital expenditures or declaring dividends. The Company's failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on its business, results of operations, and financial condition.

2. Summary of Significant Accounting Policies

Basis of Presentation

The financial statements and accompanying notes have been prepared in accordance with generally accepted accounting principles in the United States ("U.S. GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented. Certain prior period amounts in the balance sheet and the statement of cash flows have been reclassified to conform to the current period presentation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities and expenses as well as related disclosure of contingent assets and liabilities. Significant estimates and assumptions reflected in these financial statements include, but are not limited to, accrued research and development expenses, revenue recognition, stock-based compensation, and uncertain tax positions. The Company bases its estimates on its historical experience and on assumptions that it believes are reasonable; however, actual results could significantly differ from those estimates.

Risks and Uncertainties

Any product candidates developed by the Company will require approvals from the U.S. Food and Drug Administration ("FDA") or foreign regulatory agencies prior to commercial sales. There can be no assurance that the Company's current and future product candidates will meet desired efficacy and safety requirements to obtain the necessary approvals. If approval is denied or delayed, it may have a material adverse impact on the Company's business and its financial statements.

The Company is subject to a number of risks similar to other late-stage biopharmaceutical companies including, but not limited to, dependency on the clinical success of the Company's product candidates, ability to obtain regulatory approval of its product candidates, the need for substantial additional financing to achieve its goals, uncertainty of broad adoption of its approved products, if any, by physicians and consumers, significant competition, untested manufacturing capabilities, and dependence on key individuals and sole source suppliers.

Global economic and business activities continue to face widespread macroeconomic and geopolitical uncertainties, including recent and potential future disruptions in access to bank deposits or lending commitments due to bank failures, labor shortages, inflation and monetary supply shifts, recession risks and potential disruptions from the ongoing wars in Ukraine and Israel and related sanctions. The Company continues to actively monitor the impact of these macroeconomic and geopolitical factors on its financial condition, liquidity, operations, and workforce. The extent of the impact of these factors on the Company's operational and financial performance, including its ability to execute its business strategies and initiatives in the expected time frame, will depend on future developments, which are uncertain and cannot be predicted; however, any continued or renewed disruption resulting from these factors could negatively impact the Company's business.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to significant concentration of credit risk, consist primarily of cash and cash equivalents. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and cash equivalents to the extent recorded in the balance sheets.

Segment Reporting

The Company operates and manages its business as one reportable and operating segment, which is the business of developing and commercializing novel therapies for serious neurological and disorders with significant unmet medical need. The Company's chief executive officer, who is the chief operating decision maker ("CODM"), reviews financial information on an aggregate basis for allocating and evaluating financial performance. All long-lived assets are maintained in the United States of America.

The Company's segment revenue is derived from a collaboration and license agreement with Kaken Pharmaceutical Co, Ltd. (see Note 8). The CODM assesses performance and decides how to allocate resources based on net loss. Net loss is used to monitor budget versus actual results. The measure of segment revenue, segment net loss and segment expenses is reported on the statement of operations. The measure of segment assets is reported on the balance sheet as total assets.

Cash and Cash Equivalents

The Company considers all highly liquid investments with remaining maturities at the date of purchase of three months or less to be cash equivalents. Cash equivalents, which consist of amounts invested in money market funds, are stated at fair value.

Restricted Cash

The Company had $35 thousand of restricted cash as of December 31, 2024 and 2023, which is related to collateralized cash in connection with letters of credit issued on behalf of the Company for the security deposits required under operating leases. Short-term restricted cash is included in other current assets on the balance sheets and long-term restricted cash is included in other assets on the balance sheets.

Fair Value of Financial Instruments

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability, or an exit price, in the principal or most advantageous market for that asset or liability in an orderly transaction between market participants on the measurement date. Fair value measurement establishes a fair value hierarchy that requires an entity to maximize the use of observable inputs, where available, and minimize the use of unobservable inputs when measuring fair value.

The Company determined the fair value of financial assets and liabilities using the fair value hierarchy that describes three levels of inputs that may be used to measure fair value, as follows:

- Level 1—Quoted prices in active markets for identical assets and liabilities;
- Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities; and
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company’s financial instruments primarily consist of cash and cash equivalents, prepaid expenses, accounts payable, term loan, and accrued expenses. The carrying value of cash and cash equivalents, prepaid expenses, 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. The estimated fair value of the term loan is based on market observable interest rates, which is considered a Level 2 fair value measurement.

Investments

The Company’s investments are classified as available-for-sale and carried at estimated fair values and reported in cash equivalents. Management determines the appropriate classification of the investments at the time they are acquired and evaluates the appropriateness of such classifications at each balance sheet date. Investments with contractual maturities greater than 12 months are considered long-term investments.

For available-for-sale debt securities in an unrealized loss position, the Company first assesses whether it intends to sell, or it is more likely than not that it will be required to sell the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the security’s amortized cost basis is written down to fair value and recognized in interest and other income, net in the statement of operations and comprehensive loss. If neither criteria is met, the Company evaluates whether the decline in fair value is related to credit-related factors or other factors. In making this assessment, management considers the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and adverse conditions

specifically related to the security, among other factors. Credit-related impairment losses, limited by the amount that the fair value is less than the amortized cost basis, are recorded through an allowance for credit losses in interest and other income, net.

Any unrealized losses from declines in fair value below the amortized cost basis as a result of non-credit factors are recognized in accumulated other comprehensive loss, net of tax as a separate component of stockholders' equity, along with unrealized gains. Realized gains and losses and declines in fair value, if any, on available-for-sale securities are included in interest and other income, net in the statement of operations and comprehensive loss.

For purposes of identifying and measuring credit-related impairments, the Company's policy is to exclude applicable accrued interest from both the fair value and amortized cost basis of the related security. The Company has elected to write-off uncollectible accrued interest receivable balances in a timely manner, which is defined by the Company as when interest due becomes 90 days delinquent. The accrued interest write-off will be recorded by reversing interest income. Accrued interest receivable is recorded in other current assets on the balance sheets.

Leases

The Company determines if an arrangement includes a lease at inception. Right-of-use assets and lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the commencement date. The right-of-use asset includes any lease payments made on or before the lease commencement date, less lease incentives received. The incremental borrowing rate is used in determining the present value of future payments. The Company utilizes its incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. The lease terms may include options to extend or terminate the lease. Lease expense for operating leases is recognized on a straight-line basis over the non-cancelable lease term. Variable lease expense relates primarily to office lease common area maintenance, insurance, and property taxes, is expensed as incurred, and is excluded from the calculation of the lease liability and right-of-use-asset.

The Company has elected not to recognize a right-of-use asset and lease liability for short-term leases. A short-term lease is a lease with an expected lease term of 12 months or less and which does not include an option to purchase the underlying asset that the lessee is reasonably certain to exercise. Lease agreements that include lease and non-lease components are accounted for as a single lease component.

Property and Equipment, Net

Property and equipment are stated at cost less accumulated depreciation and are included in other assets on the balance sheets. Depreciation expense is calculated using the straight-line method over the estimated useful life of the respective asset and begins at the time the asset is placed into service. Maintenance and repairs are charged to expense as incurred, and improvements are capitalized.

The useful lives of property and equipment are as follows:

Computer and office equipment	3 years
Computer software	3 years
Furniture and fixtures	5 years
Manufacturing machinery and equipment	7 years
Leasehold improvements	Lesser of lease term or 15 years

Long-Lived Assets

Long-lived assets, such as property and equipment are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be fully recoverable. If circumstances require a long-lived asset or asset group to be tested for possible impairment, the Company first compares undiscounted cash flows expected to be generated by that asset or asset group to its carrying value. If the carrying value of the long-lived asset or asset group is not recoverable on an undiscounted cash flow basis, an impairment is recognized to the extent that the carrying value exceeds its fair value. Fair value is determined through various valuation techniques including discounted cash flow models, quoted market values and third-party independent appraisals, as considered necessary. There were no such impairment losses during the years ended December 31, 2024 and 2023.

Accrued Research and Development Expenses

Clinical trial costs are charged to research and development expense as incurred. The Company accrues for expenses resulting from contracts with clinical research organizations ("CROs"), consultants, and clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to us under such contracts. The Company's policy is to reflect the appropriate expense in the financial statements by matching the appropriate expenses with the period in which services and efforts are expended.

The CRO contracts generally include pass-through fees including, but not limited to, regulatory expenses, investigator fees, laboratory fees and other miscellaneous costs. The Company determines accrual estimates through reports from and discussion with clinical personnel and outside service providers as to the progress or state of completion of trials, or the services completed. The Company estimates accrued expenses as of each balance sheet date based on the facts and circumstances known at that time. The clinical trial accrual is dependent, in part, upon the receipt of timely and accurate reporting from the CROs and other third-party vendors.

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 associated with licensing agreements to acquire exclusive licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternate commercial use are expensed as incurred. Payments made to third parties under these arrangements in advance of the performance of the related services by the third parties are recorded as prepaid expenses until the services are rendered.

Revenue Recognition

The Company recognizes revenues when, or as, the promised goods or services are transferred to customers in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those services. To determine revenue recognition for arrangements, the Company performs the following five steps: (1) identify the contract(s) with a customer; (2) identify the performance obligation(s) in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligation(s) in the contract; and (5) recognize revenue when (or as) the performance obligation(s) are satisfied.

The Company has entered into a licensing and collaboration agreement that primarily includes the following: (i) upfront cash consideration; (ii) payments associated with achieving certain milestones; and (iii) royalties based on specified percentages of net product sales, if any. At the initiation of an agreement, the Company analyzes each unit of account within the contract to determine if the counterparty is a customer in the context of the unit of account.

At contract inception, the Company assesses the goods or services promised and enforceable in a contract with a customer and identifies those distinct goods and services that represent a performance obligation. If a promised good or service is not distinct, the Company combines that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct. Promised goods and services that are not material in the context of the contract are not considered performance obligations. Additional goods or services that are exercisable at a customer's discretion are assessed to determine if they provide a material right to the customer and if so, they are considered performance obligations.

The transaction price is the amount of consideration to which the Company expects to be entitled in exchange for transferring promised goods or services to a customer. The consideration promised in a contract with a customer

may include fixed amounts, variable amounts, or both. Non-refundable upfront payments are considered fixed consideration and included in the transaction price. At the inception of arrangements that include variable consideration, the Company uses judgment to estimate the amount of variable consideration to include in the transaction price using the most likely method. If it is probable that a significant revenue reversal will not occur, then the estimated amount is included in the transaction price. Milestone payments that are not within the Company's or the licensee's control, such as regulatory approvals, are not included in the transaction price until those approvals are received. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and if the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied. At the end of each reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint and, as necessary, adjusts the estimate of the overall transaction price. Any adjustments will be recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

If it is determined that multiple performance obligations exist, the transaction price is allocated at the inception of the agreement to all identified performance obligations based on the relative standalone selling prices, unless the consideration is variable and meets the criteria to be allocated entirely to one or more, but not all, performance obligations in the contract. Other components of the transaction price are allocated based on the relative standalone selling price, over which the Company applies significant judgment. The Company develops assumptions that require judgment to determine the standalone selling price for license-related performance obligations under the adjusted market assessment approach, which may include forecasted revenues, development timelines, discount rates and probabilities of success.

Revenue is recognized when, or as, the Company satisfies a performance obligation. The Company recognizes revenue over time by measuring the progress toward complete satisfaction of the relevant performance obligation using an appropriate input method based on the nature of the good or service promised to the customer. The Company uses judgment to assess the nature of the performance obligation to determine whether the performance obligation is satisfied over time or at a point in time. The selection of the method to measure progress towards completion requires judgment and is based on the nature of the products or services to be provided.

If a customer pays consideration, or the Company has an unconditional right to the consideration, before the satisfaction of the revenue recognition criteria, the amounts are recorded as deferred revenue in the Company's balance sheet. The current portion of deferred revenue represents the amount of the performance obligation that is expected to be satisfied within the next twelve months. Amounts recognized as revenue prior to receipt or before they are due are recorded as contract assets in the Company's balance sheet, excluding any amounts presented as accounts receivable. If the Company has an unconditional right to receive consideration, the contract assets are accounted for as accounts receivable and presented separately from contract assets. A net contract asset or liability is presented for each contract with a customer.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses include, but are not limited to, purchases of acquired in-process research and development, personnel costs, fees paid to external entities that conduct certain non-clinical and clinical development activities on our behalf, manufacturing costs, outside service and consulting costs, and allocated overhead, including rent. Assets acquired that are utilized in research and development that have no alternative future use are also expensed as incurred. Purchases of acquired in-process research and development are included as an operating activity on the statements of cash flow.

Stock-Based Compensation

The Company accounts for stock-based compensation using a fair value-based method, which requires the recognition of compensation expense for costs related to all stock-based payments including stock options, restricted stock units ("RSUs") and purchase rights under the Employee Stock Purchase Plan ("ESPP"). The Company estimates the fair value of stock options and purchase rights granted under the ESPP on the date of grant using the Black-Scholes option pricing model, which is impacted by the fair value of the Company's common stock, as well as changes in assumptions regarding a number of variables. The model requires management to make a number of assumptions which include the following:

- *Expected Term*. The expected term is based on the simplified method, as the Company's stock options have the following characteristics: (i) granted at-the-money; (ii) exercisability is conditioned upon service through the vesting date; (iii) termination of service prior to vesting results in forfeiture; (iv) limited exercise period following termination of service; and (v) options are non-transferable and non-hedgeable, or "plain vanilla" options, and the Company has limited history of exercise data. For the ESPP, the expected term is based on the term of the purchase period.
- *Expected Volatility*. The expected volatility is estimated using a combination of historical volatilities of the Company's stock and that of comparable publicly traded biopharmaceutical companies. In evaluating similarity, the Company considered factors such as market capitalization, stage of development, area of specialty, and stock-specific attributes. The Company will continue to apply this process and analyze the historical stock price volatility and expected term assumptions as more historical data for the Company's common stock becomes available.
- *Risk-Free Interest Rate*. The risk-free interest rate is based on U.S. Treasury constant maturity rates with remaining terms similar to the expected term of the options.
- *Expected Dividend Rate*. The Company has never paid any dividends and does not plan to pay dividends in the foreseeable future, and, therefore, used an expected dividend rate of zero in the valuation model.
- *Forfeitures*. The Company accounts for forfeitures as they occur.

The fair value of RSUs, including RSUs subject to performance-based vesting conditions, is based on the grant-date fair value of the Company's stock price.

The Company recognizes compensation expense on a straight-line basis over the requisite service period of the award, which is generally the vesting period. The Company accounts for forfeitures as they occur.

For options and RSUs that vest upon the satisfaction of certain performance conditions, the Company recognizes compensation expense when it becomes probable that the performance conditions will be met. When the criteria are deemed probable of being met, the Company records cumulative compensation expense in the period the performance criteria are deemed probable of being met and recognizes the remaining compensation expense on a straight-line basis over the remaining period for which the performance criteria are expected to be completed.

Income Taxes

The Company accounts for income taxes under the asset and liability method. The Company estimates actual current tax exposure together with assessing temporary differences resulting from differences in accounting for reporting purposes and tax purposes for certain items, such as accruals and allowances not currently deductible for tax purposes. These temporary differences result in deferred tax assets and liabilities. In general, deferred tax assets represent future tax benefits to be received when certain expenses previously recognized in the Company's statements of operations and comprehensive loss become deductible expenses under applicable income tax laws or when net operating loss or credit carryforwards are utilized. Accordingly, realization of the Company's deferred tax assets is dependent on future taxable income against which these deductions, losses and credits can be utilized.

The Company assesses the likelihood that the Company's deferred tax assets will be recovered from future taxable income, and to the extent the Company believes that recovery is not likely, the Company establishes a valuation allowance. The assessment of whether or not a valuation allowance is required often requires significant judgment, including the forecast of future taxable income and on-going prudent and feasible tax planning initiatives. Based upon the weight of available evidence, the Company has determined that net deferred tax assets should be fully offset by a valuation allowance. When the Company establishes or reduces the valuation allowance against its net deferred tax assets, its provision for income taxes will increase or decrease, respectively, in the period such determination is made.

The Company accounts for uncertainty in income taxes in accordance with Accounting Standards Codification 740. Tax positions are evaluated in a two-step process, whereby the Company first determines whether it is more likely than not that a tax position will be sustained upon examination by tax authorities, including resolutions of any related appeals or litigation processes, based on technical merit. If a tax position meets the more-likely-than-not recognition threshold, it is then measured to determine the amount of benefit to be recognized in the financial statements. The tax position is measured as the largest amount of benefit that is greater than 50% likely of being realized upon ultimate settlement. The Company's policy is to recognize interest and penalties related to the

underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to unrecognized tax benefits.

Comprehensive loss

Comprehensive loss represents the net loss for the period and other comprehensive income. Other comprehensive loss reflects certain gains and losses that are recorded as a component of stockholders' equity and are not reflected in the statements of operations. The Company's other comprehensive loss consists of changes in unrealized gains and losses on available-for-sale investments, net of tax. There was no income tax effect related to unrealized gains and losses during the years ended December 31, 2024 and 2023.

Net Loss per Share

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common stock and potentially dilutive securities outstanding for the period. For purposes of the diluted net loss per share calculation, outstanding stock options, RSUs, and shares expected to be issued pursuant to the ESPP are considered to be potentially dilutive securities. Because the Company has reported a net loss for all periods presented, diluted net loss per share is the same as basic net loss per share for those periods.

Emerging Growth Company Status

The Company is an emerging growth company ("EGC") as defined in the Jumpstart Our Business Startups Act of 2012 ("JOBS Act") and may take advantage of reduced reporting requirements that are otherwise applicable to public companies. Section 107 of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies are required to comply with those standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards.

Recent Accounting Pronouncements Adopted

In November 2023, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update 2023-07, *Improvements to Reportable Segment Disclosures* ("ASU 2023-07") which is intended to improve reportable segment disclosure requirements, primarily through additional disclosures about significant segment expenses, including for single reportable segment entities. ASU 2023-07 is effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. ASU 2023-07 should be applied retrospectively to all prior periods presented in the financial statements. The Company adopted the standard for the fiscal year beginning January 1, 2024 and the adoption did not have any impact to the Company's financial statements.

Recent Accounting Pronouncements - Not Yet Adopted

In December 2023, the FASB issued Accounting Standards Update 2023-09, *Income Taxes - Improvements to Income Tax Disclosures* ("ASU 2023-09") requiring enhancements and further transparency to certain income tax disclosures, most notably the tax rate reconciliation and income taxes paid. ASU 2023-09 is effective for fiscal years beginning after December 15, 2024 on a prospective basis and retrospective application is permitted. The Company is evaluating the impact of the adoption of this standard on the Company's financial statements and related disclosures.

In November 2024, the FASB issued Accounting Standards Update 2024-03, *Income Statement-Reporting Comprehensive Income-Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses* ("ASU 2024-03"), which requires disaggregated information about certain income statement expense line items on an annual and interim basis. ASU 2024-03 is effective for annual periods beginning after December 15, 2026 and interim reporting periods within annual reporting periods beginning after December 15,

2027. Early adoption is permitted and can be applied prospectively or retrospectively. The Company is evaluating the impact of the adoption of this standard on the Company's financial statements and related disclosures.

3. Fair Value Measurements

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company classifies money market funds as Level 1 investments as the Company uses quoted prices in active markets for identical assets to determine the fair value.

The following table summarizes the Company's financial assets measured at fair value on a recurring basis by level within the fair value hierarchy (in thousands):

		December 31, 2024			
	Fair Value Hierarchy Level	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	Level 1	$ 37,802	$ —	$ —	$ 37,802
Total cash equivalents		$ 37,802	$ —	$ —	$ 37,802

		December 31, 2023			
	Fair Value Hierarchy Level	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	Level 1	$ 95,875	$ —	$ —	$ 95,875
Total cash equivalents		$ 95,875	$ —	$ —	$ 95,875

There were no debt or equity securities as of December 31, 2024 and 2023.

The estimated fair value of the term loan was $2.0 million and $3.6 million as of December 31, 2024 and 2023, respectively, and was based on market observable interest rates, a Level 2 input.

The Company did not have any financial liabilities recorded at fair value on a recurring or non-recurring basis as of December 31, 2024 and 2023.

4. Balance Sheet Components

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2024	2023
Accrued research and development expenses	$ 10,635	$ 10,832
Accrued compensation and benefits	882	3,101
Accrued general and administrative expenses	529	416
Lease liabilities, current portion	283	251
Total accrued expenses and other current liabilities	$ 12,329	$ 14,600

As of December 31, 2024, accrued research and development expenses were primarily related to the Allievex asset purchase (see Note 8).

5. Leases

The Company leases space under a non-cancelable operating lease, which requires the Company to pay base rent, real estate taxes, insurance, general repairs, and maintenance.

In December 2022, the Company entered into a non-cancelable operating lease for approximately 6,500 square feet of office space in South San Francisco, California, which commenced in December 2022 and expires in

February 2028 (the "South San Francisco Lease"). Total minimum rental payments for the South San Francisco Lease are $1.7 million over the lease term. The Company has an option to extend the lease term of the South San Francisco Lease for an additional three years which has not been included in the lease term as it is not reasonably certain that the Company will exercise this option. The Company will also be responsible for the payment of additional rent to cover the Company's share of the annual operating and tax expense for the building. Under the terms of the South San Francisco Lease, the Company issued a letter of credit to the landlord of $29 thousand, which is collateralized by a restricted cash deposit of $35 thousand.

Other information related to the operating lease was as follows (dollar amounts in thousands):

	Year Ended December 31,	
	2024	2023
Operating lease costs	$ 336	$ 337
Cash paid for operating lease liabilities	$ 344	$ 251
Weighted average remaining lease term (years)	3.2	4.2
Weighted average discount rate	8.0%	8.0%

Variable lease expense for the years ended December 31, 2024 and 2023 was immaterial.

Future minimum lease commitments under the Company's leases as of December 31, 2024 were as follows (in thousands):

Year ending December 31,	
2025	354
2026	365
2027	376
2028	64
Total undiscounted lease payments	1,159
Less: present value discount	(140)
Total lease liabilities	$ 1,019
Lease liabilities, current portion*	$ 283
Lease liabilities, net of current portion	736
Total lease liabilities	$ 1,019

** included in accrued expenses and other current liabilities on the balance sheets*

6. Term Loan

In September 2019, the Company entered into a Loan and Security Agreement, as subsequently amended (the "Loan Agreement") with Silicon Valley Bank ("SVB") providing for a term loan (the "Term Loan") for an aggregate principal amount of $4.5 million.

In September 2019 and in connection with the Loan Agreement, the Company issued a warrant to purchase up to an aggregate of 49,609 shares of Common Stock at $1.44 per share. The Company determined the initial fair value of the warrant to be $0.1 million using the Black-Scholes option-pricing model. The fair value of the warrant was recorded to equity and as a debt discount, which was being amortized to interest expense using the effective interest method over the term of the Term Loan. In November 2020, the warrant was net-exercised for 46,358 shares of Common Stock.

In March 2021, the Company entered into a First Amendment to Loan and Security Agreement (the "First Amendment"), which increased the aggregate principal amount of the Term Loan to $30.0 million, of which $20.0 million was immediately available under the first tranche ("First Tranche") and $10.0 million was available under the second tranche through December 31, 2022 ("Second Tranche"), subject to the completion of certain

clinical or financial milestones. Pursuant to the First Amendment, the Term Loan will mature on January 1, 2026 (the "Maturity Date").

In May 2022, the Company entered into a Second Amendment to Loan and Security Agreement (the "Second Amendment"), which amended the milestones for the Second Tranche, added a liquidity covenant for the Second Tranche and amended the interest and prepayment terms.

As of December 31, 2024, the carrying value of the Term Loan was $1.7 million, consisting of the outstanding principal under the First Tranche of $1.8 million, less unamortized debt discount and issuance costs of $11 thousand which are being amortized using the effective interest method over the life of the Term Loan. Commitments available under the Second Tranche of $10.0 million expired on December 31, 2022.

The Loan Agreement provided for monthly cash interest-only payments following the funding date of each respective tranche and continuing thereafter through December 31, 2022. The Term Loan is subject to a floating per annum interest rate equal to the greater of (a) 0.50% above the Prime Rate (as defined in the Loan Agreement) or (b) 3.75%. Following the interest-only period, the outstanding Term Loan balance is payable in (i) 37 consecutive monthly payments after the end of the interest-only period and continuing on the same day of each month thereafter, in amounts that would fully amortize such Term Loan balance, as of the first business day of the first month following the amended interest-only period, over the repayment period, plus (ii) monthly payments of accrued but unpaid interest. As of December 31, 2024 and 2023, the stated interest rate of the Term Loan was 8.0% and 9.0%, respectively.

The final payment is due on the Maturity Date and includes all outstanding principal plus accrued unpaid interest and an end of term payment totaling $0.3 million, which is 6.0% of the original funded principal amount of the First Tranche (the "Supplemental Final Payment"). The Company may prepay amounts outstanding under the Term Loan at any time provided certain notification conditions are met, in which case, all outstanding principal plus accrued and unpaid interest, the Supplemental Final Payment, a prepayment fee of 1% or 2% of the principal amount of the First Tranche, and any bank expenses become due and payable.

The Company is subject to customary affirmative and restrictive covenants under the Loan Agreement. The Company's obligations under the Loan Agreement are secured by a first priority security interest in substantially all of its current and future assets, other than intellectual property. The Company also agreed not to encumber its intellectual property assets, except as permitted by the Loan Agreement.

The Loan Agreement also contains customary indemnification obligations and customary events of default, including, among other things, the Company's failure to fulfill certain obligations under the Loan Agreement and the occurrence of a material adverse change in its business, operations, or condition (financial or otherwise), a material impairment of the prospect of repayment of any portion of the loan, or a material impairment in the perfection or priority of lender's lien in the collateral or in the value of such collateral. In the event of default by the Company under the Loan Agreement, the lender would be entitled to exercise their remedies thereunder, including the right to accelerate the debt, upon which the Company may be required to repay all amounts then outstanding under the Loan Agreement. As of December 31, 2024, the Company was in compliance with all covenants under the Loan Agreement and there has been no material adverse change.

As of December 31, 2024, future payments of principal and interest are as follows (in thousands):

Year ending December 31,	
2025	1,704
2026	136
Total	$ 1,840
Less: interest	(83)
Term loan, gross	$ 1,757
Less: unamortized debt issuance costs	(11)
Less: term loan, current portion	(1,622)
Term loan, net of current portion	$ 124

7. Commitments and Contingencies

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business. The Company evaluates the likelihood of an unfavorable outcome in legal or regulatory proceedings to which it is a party and records a loss contingency on an undiscounted basis when it is probable that a liability has been incurred and the amount of the loss can be reasonably estimated. These judgments are subjective and based on the status of such legal proceedings, the merits of the Company's defenses, and consultation with legal counsel. Actual outcomes of these legal proceedings may differ materially from the Company's estimates. The Company estimates accruals for legal expenses when incurred as of each balance sheet date based on the facts and circumstances known to the Company at that time.

See Note 8 for discussion over contingent liabilities related to the Allievex asset purchase as well as other commitments associated with the Company's license and collaboration agreements.

Legal Matters

The Company's industry is characterized by frequent claims and litigation, including claims regarding intellectual property. As a result, the Company may be subject to various legal proceedings from time to time. The results of any future litigation cannot be predicted with certainty, and regardless of the outcome, litigation can have an adverse impact on the Company because of defense and settlement costs, diversion of management resources and other factors. The Company was not subject to any material legal proceedings during the years ended December 31, 2024 and 2023 and management is not aware of any pending or threatened litigation that, individually or in the aggregate, could have a material adverse effect on the Company's business, financial condition or results of operations.

8. License and Purchase Agreements

Eli Lilly and Company

In May 2016, the Company entered into a license agreement (the "Lilly License Agreement"), with Eli Lilly and Company ("Lilly"). Pursuant to the terms of the Lilly License Agreement, Lilly granted the Company an exclusive, worldwide, royalty bearing, sublicensable license under certain technology, patent rights, know-how and proprietary materials related to certain compounds, to research, develop, and commercialize such compounds for all pharmaceutical uses.

As partial consideration for the rights granted to the Company under the Lilly License Agreement, the Company made a one-time upfront payment to Lilly of $0.8 million during the year ended December 31, 2016, which was recorded as research and development expense as there was no alternative use due to the early stage of the technology. The Company is also required to pay Lilly up to an aggregate of $23.0 million upon the achievement, during the time the Lilly License Agreement remains in effect, of certain milestones relating to the clinical development and commercial sales of products licensed under the Lilly License Agreement. Such payments are for predetermined fixed amounts, are paid only upon the first occurrence of each event, and are due shortly after achieving the applicable milestone. In addition, the Company is required to pay Lilly tiered royalties on annual worldwide net sales with rates ranging from mid-single-digits to sub-teens. No additional amounts were paid by the Company to Lilly during any of the periods presented, nor were due as of such dates pursuant to the Lilly License Agreement.

The Lilly License Agreement will remain in effect, unless earlier terminated, until the expiration of the royalty payment obligations. Royalties are payable on a product-by-product and country-by-country basis from the first commercial sale of the product until the later of (i) the tenth anniversary of the date of first commercial sale in such country, (ii) the expiration in such country of the last-to-expire licensed patent having a valid claim covering the manufacture, use or sale of the licensed product as commercialized in such country, and (iii) the expiration of any data or regulatory exclusivity period for the licensed product in such country.

Kaken Pharmaceutical Co. Ltd.

On January 5, 2023, the Company entered into a collaboration and license agreement (the "Kaken License Agreement") with Kaken Pharmaceutical Co. Ltd. ("Kaken"). Under the terms of the Kaken License Agreement, the Company granted to Kaken the exclusive right to develop, manufacture and commercialize the Company's product

candidate, tildacerfont, for the treatment of CAH in Japan. Pursuant to the Kaken License Agreement, Kaken will be responsible for securing and maintaining regulatory approvals necessary to commercialize tildacerfont in Japan. The Company will retain all rights to tildacerfont in all other geographies.

Pursuant to the Kaken License Agreement, Kaken made an upfront payment to the Company of $15.0 million in April 2023. In addition to the upfront payment, the Company is entitled to receive up to an aggregate of approximately $65.0 million (at exchange rates in effect on the date of the Kaken License Agreement) upon the achievement of specified milestones related to the development, regulatory approval and commercialization of tildacerfont in Japan, including the achievement of specified net sales thresholds, if approved. Kaken has agreed to pay the Company a non-creditable, non-refundable specified purchase price for each unit of Company-manufactured product supplied to Kaken for commercial sale. In addition, the Company will also be entitled to receive a royalty for each unit of non-Company manufactured product sold equal to a range of double-digit percentages up to the mid-twenties based on annual net sales of tildacerfont in Japan. Both the purchase price for each unit and the royalty rate are subject to reduction in certain circumstances as specified in the Kaken License Agreement. Kaken's obligation to pay royalties will continue for ten years after the first commercial sale in Japan or, if later, until the expiration of regulatory exclusivity of tildacerfont or the expiration of the last valid claim of a Company-licensed patent covering tildacerfont in Japan.

The Company identified a combined performance obligation consisting of the license and know-how granted to Kaken as well as certain non-contingent research and development activities. The Company determined that the transaction price at the inception of the Kaken License Agreement consisted of the upfront payment of $15.0 million. The transaction price was recognized as revenue using the cost-based input method over the estimated period of its non-contingent research and development obligations, which was approximately two years. The transaction price has been fully recognized as of December 31, 2024 as the performance obligation was satisfied.

During the years ended December 31, 2024 and 2023, the Company recognized collaboration revenue of $4.9 million and $10.1 million, respectively.

HMNC Holding GmbH

In May 2024, the Company entered into a license, development and option agreement (the "HMNC Agreement") with HMNC Holding GmbH ("HMNC"). Under the terms of the HMNC Agreement, HMNC will fund and conduct a Phase 2 proof-of-concept study of tildacerfont in MDD patients, who will be screened using Cortibon Genetic Selection Tool ("Cortibon"), HMNC's proprietary genetic selection tool.

The Company has an option to in-license exclusive worldwide rights to Cortibon after completion of the study, if results are positive. If the Company exercises its option, it will be responsible for the future worldwide development and commercialization of tildacerfont and Cortibon for the treatment of MDD under a collaboration framework that leverages HMNC's ongoing expertise in precision psychiatry and companion diagnostics. Pursuant to the license terms, HMNC would be entitled to receive certain milestone payments and tiered royalties on net sales of tildacerfont in MDD.

No amounts were paid to the Company during any of the periods presented, nor were due as of such dates pursuant to the HMNC Agreement.

Allievex Corporation

On October 4, 2024, the Company entered into that certain Asset Purchase Agreement (the "Allievex Purchase Agreement") with AVX (ABC), LLC, a Delaware limited liability company, in its sole and limited capacity as the assignee for the benefit of creditors of Allievex Corporation ("Allievex"). Pursuant to the Allievex Purchase Agreement, the Company acquired all intellectual property and inventory relating to Allievex's product candidates and that certain Exclusive License Agreement, by and between BioMarin Pharmaceutical Inc. ("BioMarin") and Allievex, dated October 22, 2019 (the "BioMarin License Agreement").

As consideration, the Company paid $5.0 million to Allievex in November 2024. The Company will also assume certain liabilities of Allievex of $11.7 million, of which $5.6 million was paid as of December 31, 2024 and the remaining $6.1 million is included in accrued expenses and other current liabilities on the balance sheet. The amount accrued includes certain contingent liabilities that are deemed both probable and estimable. The Company has also recorded an estimated receivable of $1.9 million in other current assets on the balance sheet as contingent consideration expected to be returned related to the assumed liabilities. The receivable is contingent upon the

completion of the Allievex bankruptcy proceedings and has been recorded as the Company deems the amount to be both probable and estimable. The Company also incurred transaction costs of $0.3 million.

The Company concluded that the assets purchased in conjunction with the Allievex Purchase Agreement represent an asset acquisition whereby the underlying assets comprise in-process research and development assets with no alternative future use. Therefore, the aggregate net acquisition cost of $15.1 million, related to the upfront cash payment, the liabilities assumed and the estimated contingent consideration expected to be returned, was recognized as acquired in-process research and development expense, which is reported as a component of research and development expense for the year ended December 31, 2024.

The Company also assumed the obligations of Allievex to pay BioMarin up to an aggregate of $88.0 million upon the achievement of certain development and regulatory milestones (up to $22.5 million for the first MPSIIIB product) and up to an aggregate of $100.0 million per licensed product upon the achievement of certain sales milestones. In addition, the Company is required to pay to BioMarin certain (i) high-single digit to low-double digit tiered royalties on aggregate annual net sales of licensed MPS IIIB products and (i) mid-to-high single digit tiered royalties on aggregate annual net sales of licensed products other than MPS IIIB products, in each case during the applicable royalty term, subject to certain customary reductions and floors.

The Company may terminate the BioMarin License Agreement at any time for convenience upon prior written notice provided within a specified period of time. BioMarin may terminate the BioMarin License Agreement upon written notice if we (i) challenge the validity, enforceability or scope of any of the patents licensed by us under the BioMarin License Agreement, subject to certain conditions, or (ii) cease all material research and development activity for any licensed product for a specified period of time, subject to certain exceptions. Either the Company or BioMarin may also terminate the BioMarin License Agreement (i) in the event the other party shall have materially breached its obligations thereunder and such default shall have continued for a specified period after written notice thereof or (ii) upon the bankruptcy or insolvency of the other party.

Twist Bioscience Corporation

On December 20, 2024, the Company entered into an antibody license agreement (the "Twist Antibody License Agreement") with Twist Bioscience Corporation ("Twist"). Under the terms of the Twist License Agreement, the Company obtained (i) a license for purposes of evaluating a certain antibody during the research term and (ii) an exclusive option to acquire an exclusive, non-transferable and royalty-bearing world-wide license, with the right to sublicense, to (a) research and develop the antibody, (b) incorporate the antibody into products and (c) commercialize such products (the "Twist Option"). The Twist Option can be exercised during the research term, which is initially six months.

As consideration, the Company paid $0.5 million to Twist in February 2025. The Company can extend the research term by an additional six months by making an extension payment of $0.5 million. The Company can exercise the Twist Option by making an exercise payment of $1.5 million. As of December 31, 2024, the research term will expire in June 2025.

The Company concluded that the rights acquired under the Twist License Agreement have no alternative future use. Therefore, the consideration paid of $0.5 million was recognized as acquired in-process research and development expense, which is reported as a component of research and development expense for the year ended December 31, 2024. The consideration of $0.5 million is included in accrued expenses and other current liabilities on the balance sheet of December 31, 2024.

The Company is also required to pay Twist up to an aggregate of $5.0 million upon the achievement of certain regulatory milestone and up to $125.0 million per product upon the achievement of certain sales milestones by each such product. In addition, the Company is required to pay Twist tiered royalties on annual net sales with rates ranging in the mid to high-single digit. No additional amounts were paid by the Company to Twist nor were due as of December 31, 2024 pursuant to the Twist License Agreement.

The Twist License Agreement will remain in effect until the expiration of the research term except if the Company exercises the Twist Option, then the Twist License Agreement will remain in effect, unless earlier terminated, until the expiration of the royalty payment obligations. Royalties are payable on a product-by-product and country-by-country basis from the first commercial sale of the product until expiration.

9. Capital Structure

Common Stock

As of December 31, 2024 and 2023, the Company was authorized to issue 200,000,000 shares of $0.0001 par value common stock, respectively. Holders of the Company's common stock are entitled to dividends if and when declared by the Board of Directors of the Company ("Board of Directors"). The holder of each share of common stock is entitled to one vote. As of December 31, 2024, no dividends were declared.

Common stock reserved for future issuance, on an as converted basis, consisted of the following:

	December 31,	
	2024	2023
Common Stock warrants, issued and outstanding	12,687,000	12,687,000
Stock options, issued and outstanding	3,523,655	4,097,376
Restricted and performance stock units, issued and outstanding	2,239,710	3,497,663
Shares available for future issuance under 2020 Equity Incentive Plan	2,001,335	77,631
Shares available for future issuance under 2020 Employee Stock Purchase Plan	926,767	675,038
Total shares reserved	21,378,467	21,034,708

10. Stock-Based Compensation

Equity Incentive Plans

The Company adopted the 2020 Equity Incentive Plan (the "2020 Plan") in October 2020. The 2020 Plan is a successor to and continuation of the Amended and Restated 2016 Equity Incentive Plan (the "2016 Plan") and provides for the granting of stock options, stock appreciation rights, restricted stock, restricted stock units, and other stock or cash-based awards to individuals who are then employees, officers, directors or consultants. A total of 2,647,684 shares of common stock were approved to be initially reserved for issuance under the 2020 Plan. In addition, the number of shares of common stock available for issuance under the 2020 Plan will be automatically increased on the first day of each calendar year during the ten-year term of the 2020 Plan, beginning with January 1, 2021 and ending with January 1, 2030, by an amount equal to 5% of the outstanding number of shares of the Company's common stock on December 31st of the preceding calendar year or such lesser amount as determined by the Company's Board of Directors. Following the effectiveness of the 2020 Plan, no further grants will be made under the 2016 Plan; however, shares subject to awards granted under the 2016 Plan will continue to be governed by the 2016 Plan.

The Board of Directors determines the per share exercise price of each stock option, which for ISOs shall not be less than 100% of the fair market value of a share on the date of grant; provided that the exercise price of an ISO granted to a stockholder who at the time of grant owns stock representing more than 10% of the voting power of all classes of stock (a 10% stockholder) shall not be less than 110% of the fair market value of a share on the date of grant.

The Board of Directors determines the period over which options vest and become exercisable. Options granted to new employees generally vest over a four-year period: 25% of the shares vest on the first anniversary from the vesting commencement date of the option and an additional 1/48th of the shares vest on each monthly anniversary thereafter, subject to the employee's continuous service through each vesting date.

The Board of Directors also determines the term of options, provided the maximum term for ISOs granted to a 10% stockholder must be no longer than five years from date of grant and the maximum term for all other options must be no longer than ten years from date of grant. If an option holder's service terminates, options generally terminate three months from the date of termination except under certain circumstances, such as death or disability.

Under the 2020 Plan and the 2016 Plan, individuals can be granted the ability to early exercise their options. There were no shares, related to the early exercise of options, subject to repurchase by the Company as of

December 31, 2024. As of December 31, 2024, 2,001,335 shares remained available for issuance under the 2020 Plan and no shares remained available for issuance under the 2016 Plan.

A summary of the Company's stock option activity and related information is as follows (in thousands, except share and per share amounts):

	Outstanding Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value
Balance as of December 31, 2023	4,097,376	$ 3.19	7.2	$ 3,050
Granted	210,000	$ 0.75		
Exercised	(120,328)	$ 1.50		
Forfeited	(663,393)	$ 2.28		
Balance as of December 31, 2024	3,523,655	$ 3.27	6.7	$ —
Vested and expected to vest as of December 31, 2024	3,523,655	$ 3.27	6.7	$ —
Vested and exercisable as of December 31, 2024	2,838,093	$ 3.47	6.3	$ —

The aggregate intrinsic values of options outstanding and exercisable were calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock as of the respective balance sheet date. The total intrinsic value of options exercised was $0.3 million and immaterial for the years ended December 31, 2024 and 2023, respectively. The total fair value of options vested was $2.1 million and $4.0 million for the years ended December 31, 2024 and 2023, respectively.

Restricted Stock Units ("RSUs")

A summary of the Company's RSU activity and related information is as follows (in thousands, except share and per share amounts):

	Number of RSUs	Weight-Average Grant Date Fair Value
Balance as of December 31, 2023	3,497,663	$ 1.59
Granted	1,698,400	$ 1.59
Vested	(1,423,890)	$ 1.94
Forfeited	(1,532,463)	$ 1.49
Balance as of December 31, 2024	2,239,710	$ 1.59

For the year ended December 31, 2023, the weighted average fair value of RSUs granted was $1.59 per share. The total fair value of RSUs vested was $2.8 million and $0.9 million for the years ended December 31, 2024 and 2023, respectively.

During the year ended December 31, 2024, the Company granted 1,698,400 RSUs, including 903,050 RSUs subject to time-based vesting in installments through August 2028 and 795,350 RSUs subject to performance-based vesting conditions related to the satisfaction of certain clinical development milestones.

As of December 31, 2024, the Company has 512,800 RSUs outstanding subject to performance-based vesting conditions, of which none are considered probable of achievement.

Employee Stock Purchase Plan

The Company's Board of Directors adopted and the Company's stockholders approved the 2020 Employee Stock Purchase Plan (the "ESPP") in October 2020. The ESPP allows eligible employees to purchase shares of the Company's common stock at a discount through payroll deductions of up to 15% of their eligible compensation. At the end of each purchase period, employees are able to purchase shares at 85% of the lower of the fair market value of the Company's common stock as of the offering date or the applicable purchase date. A total of 220,640 shares of common stock were approved to be initially reserved for issuance under the ESPP. In addition, the number of shares of common stock available for issuance under the ESPP will be automatically increased on the first day of each

calendar year during the first ten-years of the term of the ESPP, beginning with January 1, 2021 and ending with January 1, 2030, by an amount equal to the lessor of (i) 1% of the outstanding number of shares of the Company's common stock on December 31st of the preceding calendar year, (ii) 441,280 shares of common stock or (iii) such lesser amount as determined by the Board of Directors.

Except for the initial offering period, the ESPP provides for 24-month offering periods starting every January 1st and July 1st, each consisting of four six-month purchase periods. As of December 31, 2024, 926,767 shares of common stock remained available for issuance under the ESPP.

Stock-Based Compensation Expense

For the years ended December 31, 2024 and 2023, the weighted-average fair value of options granted was $0.64 and $1.65 per share, respectively.

The Company estimated the fair value of stock options and purchase rights under ESPP using the Black-Scholes option-pricing model, with the following weighted-average assumptions:

	2024		2023	
	Options	ESPP	Options	ESPP
Expected term (in years)	5.5	1.4	5.6	1.4
Expected volatility	118.1%	222.8%	87.8%	104.6%
Risk-free interest rate	4.5%	5.1%	3.7%	5.4%
Expected dividend rate	0.0%	0.0%	0.0%	0.0%

The following table summarizes stock-based compensation expense related to stock options, RSUs and ESPP that is included in the Company's statements of operations and comprehensive loss (in thousands):

	Year Ended December 31,	
	2024	2023
Research and development	$ 2,013	$ 1,547
General and administrative	3,335	3,075
Total stock-based compensation expense	$ 5,348	$ 4,622

As of December 31, 2024, there was approximately $2.8 million of total unrecognized stock-based compensation expense related to awards that are expected to vest, which is expected to be recognized over an estimated weighted-average vesting term of 1.4 years.

11. Income Taxes

The Company did not have any income tax expense for the years ended December 31, 2024 and 2023. The reconciliation of the federal statutory income tax rate to the Company's effective tax rate is as follows:

	December 31,	
	2024	2023
Federal statutory income tax rate	21.0 %	21.0 %
Nondeductible expenses	(2.9)	(5.3)
Tax credits	17.9	23.8
Stock-based compensation	—	(0.8)
Change in valuation allowance	(34.3)	(35.0)
Change in state apportionment - deferred tax impact	—	(3.7)
Prior year true up	(1.7)	—
Effective tax rate	— %	— %

Deferred Tax Assets and Liabilities

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's net deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2024	2023
Deferred tax assets:		
Net operating loss carryforwards	$ 35,484	$ 33,400
Capitalized research and experimental costs	15,518	11,744
Accruals	696	626
Intangible assets	2,617	77
Tax credits	29,808	20,292
Lease liability	214	267
Other	1,209	991
Total gross deferred tax assets	85,546	67,397
Valuation allowance	(85,349)	(67,148)
Total deferred tax assets	197	249
Deferred tax liabilities:		
Lease right-of-use asset	(196)	(248)
Other	(1)	(1)
Total deferred tax liabilities	(197)	(249)
Total net deferred tax assets	$ —	$ —

Management regularly assesses the ability to realize deferred tax assets recorded based upon the weight of available evidence, including such factors as recent earnings history and expected future taxable income on a jurisdiction by jurisdiction basis. In the event that the Company changes its determination as to the amount of realizable deferred tax assets, the Company will adjust its valuation allowance with a corresponding impact to the provision for income taxes in the period in which such determination is made. The Company's management believes that, based on a number of factors, it is more likely than not, that all or some portion of the deferred tax assets will not be realized; and accordingly, for the year ended December 31, 2024, the Company has provided a valuation allowance against the Company's U.S. net deferred tax assets. The valuation allowance increased by $18.2 million during the year ended December 31, 2024, primarily due to an increase in tax credits (primarily related to orphan drug), an increase in current year capitalization of Section 174 research and experimental costs and the addition of an IP intangible for tax purposes associated with the Allievex asset purchase. The valuation allowance increased by $16.8 million during the year ended December 31, 2023, primarily due to an increase in the net operating loss (primarily from pre-tax book loss) and the current year capitalization of Section 174 research and experimental costs.

As of December 31, 2024, the Company had net operating loss carryforwards for federal and state income tax purposes of approximately $128.1 million and $123.0 million, respectively, both of which will begin to expire in 2036 with the exception of $120.9 million of the Company's federal net operating losses that carry over indefinitely.

As of December 31, 2024, the Company had federal general business credit and state research and development credit carryforwards of approximately $32.3 million and $2.4 million, respectively. The federal general business credit carryforwards will begin to expire in 2036 while the California research credit carryforwards have an indefinite life.

The Internal Revenue Code of 1986, as amended, imposes restrictions on the utilization of net operating losses in the event of an "ownership change" of a corporation. Accordingly, a company's ability to use net operating losses may be limited as prescribed under Internal Revenue Code Section 382 ("IRC Section 382"). Events which may cause limitations in the amount of the net operating losses that the Company may use in any one year include, but are not limited to, a cumulative ownership change of more than 50% over a three-year period. Utilization of the federal and state net operating losses may be subject to substantial annual limitation due to the ownership change limitations provided by the IRC Section 382 and similar state provisions.

The Company files income tax returns in the U.S. federal jurisdiction and California state jurisdiction. The Company is not currently under audit by the Internal Revenue Service or any other similar state, local, or foreign authority. All tax years remain open to examination by major taxing jurisdictions to which the Company is subject.

Uncertain Income Tax Positions

The Company had approximately $4.3 million and $3.2 million of unrecognized tax benefits as of December 31, 2024 and 2023, respectively. No liability related to uncertain tax positions is recorded in the financial statements due to the fact the liabilities have been netted against deferred attribute carryovers. The unrecognized tax benefits would not impact the annual effective tax rate if recognized because the Company has recorded a valuation allowance on its deferred tax assets. The Company does not expect the amount of unrecognized tax benefits to materially change in the next 12 months. As of December 31, 2024 and 2023, the Company has not recognized any tax-related penalties or interest in its financial statements.

A reconciliation of the beginning and ending balance of the unrecognized tax benefits is as follows (in thousands):

	December 31,	
	2024	2023
Balance at the beginning of the period	$ 3,240	$ 2,959
Increases based on tax positions related to current period	870	956
Increases based on tax positions related to prior period	365	1,520
Decreases based on tax positions related to prior period	(127)	(2,195)
Balance at the end of the period	$ 4,348	$ 3,240

12. 401(k) Retirement Savings Plan

In December 2017, the Company adopted a plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan") for all employees who have met certain eligibility requirements. Under the 401(k), employees may elect to contribute a portion of their eligible compensation, subject to certain limitations. During the years ended December 31, 2024 and 2023, the Company incurred expense of $0.1 million.

13. Net Loss Per Share

The following table sets forth the computation of the basic and diluted net loss per share (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2024	2023
Numerator:		
Net loss	$ (53,036)	$ (47,919)
Denominator:		
Weighted-average shares of common stock outstanding	41,264,948	38,510,220
Net loss per share, basic and diluted	$ (1.29)	$ (1.24)

Basic net loss per share was the same as diluted net loss per share for all periods as the inclusion of potentially dilutive securities would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations were as follows:

	December 31,	
	2024	2023
Shares subject to outstanding Standard Warrants	12,687,000	12,687,000
Shares subject to outstanding common stock options	3,523,655	4,097,376
Shares subject to outstanding RSUs	2,239,710	3,482,663
Estimated shares issuable under the ESPP	316,122	126,151
Total	18,766,487	20,393,190

14. Subsequent Events

On January 15, 2025, the Company entered into a collaboration and license agreement (the "HBM License Agreement") with HBM Alpha Therapeutics, Inc. ("HBM"). Under the terms of the HBM License Agreement, HBM granted the Company a limited exclusivity, royalty bearing, and sublicensable license to certain technology, patent rights, manufacturing rights, know-how, and proprietary materials relating to certain compounds developed by HBM. As consideration, in January 2025, the Company made a one-time upfront payment to HBM of $5.0 million and issued a pre-funded warrant that will be equal to 4.99% of the Company's outstanding common stock as of the date of issuance of such warrant. The Company is also required to pay HBM development and regulatory milestone payments, sales milestone payments and royalties on net sales.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's ("SEC's") rules and forms, and that such information is accumulated and communicated to the Company's management, including its chief executive officer and chief financial officer, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our management, with the participation of our chief executive officer and our chief financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024. Based on the evaluation of our disclosure controls and procedures as of December 31, 2024, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, 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 in the United States.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

As of December 31, 2024, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013). Based on this assessment, our management concluded that, as of December 31, 2024, our internal control over financial reporting was effective based on those criteria.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting due to an exemption established by the JOBS Act for "emerging growth companies" and because we qualify as a "non-accelerated filer" (i.e., we do not qualify as either an "accelerated filer" or a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act).

Changes in Internal Controls over Financial Reporting

There has been no change in our internal control over financial reporting during the quarter ended December 31, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

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 will be set forth under the captions "Proposal 1 Election of Directors" and "Information Regarding the Board and Corporate Governance" in the Company's definitive Proxy Statement for its 2025 Annual Stockholder Meeting, to be filed with the SEC within 120 days after December 31, 2024, and is incorporated herein by reference

Code of Conduct and Insider Trading Policy

We maintain a Code of Conduct that applies to all our employees, officers and directors. This includes our principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions. The full text of our Code of Conduct is posted on our website at www.sprucebiosciences.com. The information on our website is not incorporated by reference into this Annual Report or our Proxy Statement. We intend to disclose on our website any future amendments of our Code of Conduct or waivers that exempt any principal executive officer, principal financial officer, principal accounting officer or controller, persons performing similar functions or our directors from provisions in the Code of Conduct.

We have adopted an Insider Trading Policy governing the purchase, sale and/or other dispositions of our securities by our directors, officers and employees. A copy of the Insider Trading Policy is filed as an exhibit to this Annual Report. In addition, it is our practice to comply with the applicable laws and regulations relating to insider trading.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires the Company's directors and executive officers, and persons who own more than ten percent of a registered class of the Company's equity securities, to file with the SEC initial reports of ownership and reports of changes in ownership of common stock and other equity securities of the Company. Officers, directors and greater than 10% stockholders are required by SEC regulation to furnish the Company with copies of all Section 16(a) forms they file.

Due to administrative delays, each of Dr. Szwarcberg, Dr. Charlton and Mr. Gharib failed to timely file three Form 4 reports reflecting the vesting and net settlement of certain RSUs.

Item 11. Executive Compensation.

The information required by this item will be set forth under the captions "Executive Compensation" and "Information Regarding the Board and Corporate Governance" in the Company's definitive Proxy Statement for its 2025 Annual Stockholder Meeting, to be filed with the SEC within 120 days after December 31, 2024, 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 will be set forth under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" in the Company's definitive Proxy Statement for its 2025 Annual Stockholder Meeting, to be filed with the SEC within 120 days after December 31, 2024, and is incorporated herein by reference.

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

The information required by this item will be set forth under the captions "Transactions with Related Persons and Indemnification" and "Information Regarding the Board and Corporate Governance" in the Company's definitive Proxy Statement for its 2025 Annual Stockholder Meeting, to be filed with the SEC within 120 days after December 31, 2024, and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this item will be set forth under the caption "Principal Accountant Fees and Services" in the Company's definitive Proxy Statement for its 2025 Annual Stockholder Meeting, to be filed with the SEC within 120 days after December 31, 2024, and is incorporated herein by reference.

PART IV

Item 15. Exhibit and Financial Statement Schedules.

a) We have filed the following documents as part of this Annual Report:

1. Financial Statements

The financial statements are included in Item 8. "Financial Statements and Supplementary Data."

2. Financial Statement Schedules

All schedules are omitted as information required is inapplicable or the information is presented in the financial statements and the related notes.

3. Exhibits

The following is a list of exhibits filed with this Annual Report incorporated herein by reference (numbered in accordance with Item 601 of Regulation S-K):

Exhibit Number	Exhibit Description	Form	File No.	Exhibit	Filing Date
2.1#	Asset Purchase Agreement, dated October 4, 2024 by and among Spruce Biosciences, Inc. and AVX (ABC), LLC	Filed herewith			
3.1	Amended and Restated Certificate of Incorporation	8-K	001-39594	3.1	October 14, 2020
3.2	Amended and Restated Bylaws	8-K	001-39594	3.2	October 14, 2020
4.1	Form of Common Stock Certificate	S-1/A	333-248924	4.1	October 5, 2020
4.2	Amended and Restated Investors' Rights Agreement, by and among the registrant and certain of its stockholders, dated February 19, 2020	S-1	333-248924	4.2	September 18, 2020
4.3	Form of Warrant to Purchase Common Stock issued to Silicon Valley Bank, dated September 23, 2019	S-1	333-248924	4.3	September 18, 2020
4.4	Description of Common Stock of the registrant	10-K	001-39594	4.4	March 22, 2021
4.5	Form of 2023 Pre-Funded Warrant to Purchase Common Stock	8-K	001-39594	4.1	February 9, 2023
4.6	Form of Common Stock Purchase Warrant	8-K	001-39594	4.2	February 9, 2023
4.7	Form of 2025 Pre-Funded Warrant to Purchase Common Stock	Filed herewith			
10.1+	Spruce Biosciences, Inc. Amended and Restated 2016 Equity Incentive Plan	S-1	333-248924	10.1	September 18, 2020
10.2+	Forms of Grant Notice, Stock Option Agreement and Notice of Exercise under the Spruce Biosciences, Inc. Amended and Restated 2016 Equity Incentive Plan	S-1	333-248924	10.2	September 18, 2020
10.3+	Spruce Biosciences, Inc. 2020 Equity Incentive Plan	S-1/A	333-248924	10.3	October 5, 2020

10.4+	Forms of Grant Notice, Stock Option Agreement and Notice of Exercise under the Spruce Biosciences, Inc. 2020 Equity Incentive Plan	S-1	333-248924	10.4	September 18, 2020
10.5+	Forms of Restricted Stock Unit Grant Notice and Award Agreement under the Spruce Biosciences, Inc. 2020 Equity Incentive Plan	10-K	001-39594	10.5	March 16, 2023
10.6+	Spruce Biosciences, Inc. 2020 Employee Stock Purchase Plan	S-1/A	333-248924	10.5	October 5, 2020
10.7+	Spruce Biosciences, Inc. 2020 Employee Stock Purchase Plan Offering Document	10-K	001-39594	10.6	March 22, 2021
10.8+	Form of Stock Option Grant Notice, Option Agreement and Notice of Exercise for Inducement Grant Outside of the Spruce Biosciences, Inc. 2020 Equity Incentive Plan	8-K	001-39594	10.2	January 5, 2022
10.9+	Spruce Biosciences, Inc. 2020 Non-Employee Director Compensation Policy, as amended on April 6, 2022	10-Q	001-39594	10.7	May 11, 2022
10.10+	Form of Indemnification Agreement by and between the registrant and its directors and executive officers	S-1	333-248924	10.7	September 18, 2020
10.11+	Spruce Biosciences, Inc. Severance and Change in Control Plan	S-1	333-248924	10.9	September 18, 2020
10.12+¥	Offer Letter, by and between the registrant and Samir Gharib, dated April 8, 2020	S-1	333-248924	10.16	September 18, 2020
10.13+	Letter Agreement, by and between the registrant and Michael Grey, dated March 24, 2017	S-1	333-248924	10.18	September 18, 2020
10.14+	Letter Agreement, by and between the registrant and Camilla V. Simpson, dated October 11, 2017	S-1	333-248924	10.19	September 18, 2020
10.15+	Letter Agreement, by and between the registrant and Daniel Spiegelman, dated August 31, 2020	S-1	333-248924	10.20	September 18, 2020
10.16+	Offer Letter, by and between the registrant and Javier Szwarcberg, M.D., MPH, dated December 29, 2021	8-K	001-39594	10.1	January 5, 2022
10.17+	Amendment to Offer Letter, by and between the registrant and Javier Szwarcberg, M.D., MPH, dated April 6, 2022	8-K	001-39594	10.1	April 8, 2022
10.18#	License Agreement, by and between the registrant and Eli Lilly and Company, dated May 2, 2016	S-1	333-248924	10.22	September 18, 2020
10.19	Loan and Security Agreement, by and between the registrant and Silicon Valley Bank, dated September 23, 2019	S-1	333-248924	10.23	September 18, 2020
10.20	First Amendment to Loan and Security Agreement, by and between the registrant and Silicon Valley Bank dated March 19, 2021	10-K	001-39594	10.19	March 22, 2021
10.21#	Second Amendment to Loan and Security Agreement, by and between the registrant and Silicon Valley Bank dated May 10, 2022	10-Q	001-39594	10.8	May 11, 2022
10.22	Open Market Sale Agreement℠, by and between the registrant and Jefferies LLC, dated February 25, 2022	10-K	001-39594	10.22	March 14, 2022
10.23	Lease Agreement, by and between the registrant and 611 Gateway Center LP, dated December 1, 2022	8-K	001-39594	10.1	December 2, 2022

10.24#	Collaboration and License Agreement, by and between the registrant and Kaken Pharmaceutical Co., LTD., dated January 5, 2023	10-K	001-39594	10.27	March 16, 2023
10.25	Securities Purchase Agreement, dated February 8, 2023, by and among Spruce Biosciences, Inc. and the Purchasers	8-K	001-39594	10.1	February 8, 2023
10.26#	Antibody License Agreement, dated December 20, 2024, by and between Spruce Biosciences, Inc. and Twist Bioscience Corporation		Filed herewith		
10.27#	Exclusive License Agreement, dated October 22, 2019, by and between BioMarin Pharmaceutical Inc. and Allievex Corp.		Filed herewith		
10.28#	Collaboration and License Agreement, dated January 15, 2025, by and between Spruce Biosciences, Inc. and HBM Alpha Therapeutics, Inc.		Filed herewith		
19.1	Insider Trading Policy		Filed herewith		
23.1	Consent of BDO USA, P.C., independent registered public accounting firm		Filed herewith		
24.1	Power of Attorney (see signature pages)				
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		Filed herewith		
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		Filed herewith		
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		Filed herewith		
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		Filed herewith		
97	Incentive Compensation Recoupment Policy	10-K	001-39594	97	March 18, 2024
101.INS	Inline XBRL Instance Document				
101.SCH	Inline XBRL Taxonomy Extension Schema with Embedded Linkbase Document				
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)				

+ Indicates management contract or compensatory plan

Pursuant to Item 601(b)(10) of Regulation S-K, certain portions of this exhibit have been omitted by means of marking such portions with asterisks because the registrant has determined that the information is the type that the registrant customarily and actually treats as private or confidential and is not material.

¥ Schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The registrant undertakes to furnish supplemental copies of any of the omitted schedules upon request by the SEC.

† The information in Exhibits 32.1 and 32.2 shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any

filing under the Securities Act or the Exchange Act (including this Annual Report), unless the Registrant specifically incorporates the foregoing information into those documents by reference.

Item 16. Form 10-K Summary.

Not applicable.

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.

SPRUCE BIOSCIENCES, INC.

April 15, 2025

By: */s/ Javier Szwarcberg, M.D., MPH*
Javier Szwarcberg, M.D., MPH
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Javier Szwarcberg, M.D., MPH and Samir Gharib and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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/ Javier Szwarcberg, M.D., MPH Javier Szwarcberg, M.D., MPH	Chief Executive Officer and Director (Principal Executive Officer)	April 15, 2025
/s/ *Samir Gharib* Samir Gharib	President and Chief Financial Officer (Principal Financial and Accounting Officer)	April 15, 2025
/s/ *Michael Grey* Michael Grey	Executive Chairman	April 15, 2025
/s/ *Tiba Aynechi, Ph.D.* Tiba Aynechi, Ph.D.	Director	April 15, 2025
/s/ *Percival Barretto-Ko* Percival Barretto-Ko	Director	April 15, 2025
/s/ *Bali Muralidhar, M.D, Ph.D.* Bali Muralidhar, M.D, Ph.D.	Director	April 15, 2025
/s/ *Camilla V. Simpson, M.Sc.* Camilla V. Simpson, M.Sc.	Director	April 15, 2025
/s/ *Daniel Spiegelman* Daniel Spiegelman	Director	April 15, 2025
/s/ *Kirk Ways, M.D, Ph.D.* Kirk Ways, M.D, Ph.D.	Director	April 15, 2025