Table of Contents

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, 2020

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	**81-2154263**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
2001 Junipero Serra Boulevard, Suite 640 Daly City, California	**94014**
(Address of principal executive offices)	**(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 Global Select 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. ☐

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

The Registrant did not have an aggregate market value for the common equity held by non-affiliates of the Registrant on the last business day of its most recently completed second fiscal quarter because there was no public market for the Registrant's common equity as of such date.

The number of shares of Registrant's Common Stock outstanding as of March 19, 2021 was 23,301,872.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive Proxy Statement for its 2021 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 in Part III, Items 10-14 of this Annual Report on Form 10-K.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this 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 anticipated timing, costs and conduct of our clinical trials for our only product candidate, tildacerfont; the timing and likelihood of regulatory filings and approvals for tildacerfont; our ability to commercialize tildacerfont, if approved; the pricing and reimbursement of tildacerfont, if approved; the potential benefits of strategic collaborations and our ability to enter into strategic arrangements; the timing and likelihood of success, plans and objectives of management for future operations; future results of anticipated product development efforts; 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, or 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 BUSINESSES

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. We expect these losses to increase as we continue our clinical development of, and seek regulatory approvals for, tildacerfont and any future product candidates.
- We will need substantial additional financing to develop tildacerfont and any future product candidates and implement our operating plans. If we fail to obtain additional financing, we may be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- We currently depend entirely on the success of tildacerfont, which is our only product candidate. If we are unable to advance tildacerfont in clinical development, obtain regulatory approval, and ultimately commercialize tildacerfont, 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 tildacerfont, which could prevent or delay regulatory approval and commercialization.
- 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.
- The U.S. Food and Drug Administration, or FDA, and comparable foreign regulatory authorities may require us to initiate one or more additional clinical trials for tildacerfont in adult patients with classic congenital adrenal hyperplasia, or CAH, including a Phase 3 clinical trial or trials. The estimated timing or scope of any such future clinical trials is not currently ascertainable. Even if regulatory approvals are obtained, we may never be able to successfully commercialize tildacerfont.
- 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 tildacerfont and any future product candidates.
- Our business has been and could continue to be adversely affected by the evolving and ongoing COVID-19 global pandemic in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. The COVID-19 pandemic could adversely affect our operations, as well as the business or operations of our manufacturers, clinical research organizations, or CROs, or other third parties with whom we conduct business.
- Tildacerfont is, and any 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 tildacerfont and any future product candidates.
- If the market opportunities for tildacerfont and any future product candidates are smaller than we believe they are, our future revenue may be adversely affected, and our business may suffer.
- We may not be successful in our efforts to expand our pipeline by identifying additional indications and formulations for which to investigate tildacerfont in the future. We may expend our limited resources to pursue a particular indication or formulation for tildacerfont and fail to capitalize on product candidates, indications, or formulations that may be more profitable or for which there is a greater likelihood of success.
- 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 tildacerfont and any future product candidates, we may not be able to generate product revenues.

- 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 tildacerfont.
- If we are unable to obtain and maintain sufficient intellectual property protection for 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 tildacerfont, if approved, and any future product candidates, and other proprietary technologies if approved, may be adversely affected.
- Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.
- We previously identified and remediated a material weakness in our internal control over financial reporting and may identify material weaknesses in the future or otherwise fail to maintain proper and effective internal controls, which may impair our ability to produce accurate financial statements on a timely basis.

PART I

Item 1. Business

Overview

We are a late-stage biopharmaceutical company focused on developing and commercializing novel therapies for rare endocrine disorders with significant unmet medical need. We are initially developing our wholly-owned product candidate, tildacerfont, as the potential first non-steroidal therapy to offer markedly improved disease control and reduce steroid burden for patients suffering from CAH. Classic CAH is a serious and life-threatening disease with no known novel therapies approved in approximately 50 years. In a 12-week Phase 2a proof-of-concept clinical trial, tildacerfont-treated adult patients suffering from classic CAH who had poor disease control despite being on standard of care therapy achieved approximately 80% reductions in hormones that are key indicators of poor disease control. Furthermore, 171 subjects across seven clinical trials to date have been administered tildacerfont with no drug-related serious adverse events, or SAEs, reported.

We have initiated CAHmelia-203, a placebo-controlled, double-blind Phase 2b clinical trial in adult patients with classic CAH with poor disease control and anticipate topline results in the first half of 2022. We have also initiated CAHmelia-204, a second Phase 2b clinical trial in adult patients with classic CAH with good disease control focused on glucocorticoid reduction and anticipate topline results in the second half of 2022. Based on post-hoc analyses of our clinical data to date, we have chosen to target two distinct groups of classic CAH patients with either good disease control or poor disease control. These two groups, which together make up the entire classic CAH patient population, have differing disease challenges centered on excessive adrenal androgen levels or excessive glucocorticoid usage, both of which have the potential to be addressed by treatment with tildacerfont, if approved. We believe our strategy to study CAH patients in these two enriched sub-populations may enable us to observe clinically meaningful outcomes. Additionally, we believe these two clinical trials will provide sufficient patient exposures for our registrational safety database, which are designed to potentially support registration in the United States and Europe. Assuming positive results in CAHmelia-204, we plan to meet with the FDA and comparable foreign regulatory authorities to discuss registration.

In addition, we plan to investigate tildacerfont for the treatment of classic CAH in children as young as two years of age, and plan to initiate the clinical development program for tildacerfont in the pediatric classic CAH population in the second half of 2021. We have received feedback from the FDA and European Medicines Agency, or EMA, on our planned Phase 2 clinical trial of tildacerfont in children with classic CAH. We have also submitted a pediatric investigational plan, or PIP, to the Pediatric Committee of the EMA regarding a registrational program in children with classic CAH. Beyond classic CAH, we believe tildacerfont has potential utility in a range of diseases where the underlying biology supports a need to reduce excess secretion of or hyperresponsiveness to adrenocorticotropic hormone, or ACTH. We are committed to leveraging our deep scientific knowledge of the biology of rare endocrine disorders, the unique benefits of tildacerfont, and our commercial expertise to dramatically transform the lives of individuals living with these devastating disorders.

Classic CAH is an autosomal recessive disease, driven by a mutation in the gene that encodes an enzyme necessary for the synthesis of key adrenal hormones. In classic CAH patients, the body is not able to produce cortisol, leading to serious health consequences. In the absence of cortisol, patients can face adrenal crisis and death rapidly as a result of any stressing event, such as infection. Physicians administer replacement steroid hormones to reduce the risk of adrenal crises and death; however, replacement alone is not sufficient to address all of the consequences associated with classic CAH.

The absence of cortisol alters the normal feedback cycle of the hypothalamic-pituitary-adrenal, or HPA, axis, and leads to excess secretion of ACTH, hyperplasia of the adrenal gland, and consequently high levels of endogenous androgen production. As a result, classic CAH patients suffer from premature puberty, impaired fertility, hirsutism, acne, the development of adrenal rest tumors, and an impaired quality of life, and additionally for females, virilized genitalia and menstrual irregularities. Currently, the only way to downregulate the production of excess androgens in classic CAH patients is to administer even higher doses of glucocorticoids, known as supraphysiologic glucocorticoid dosing. These elevated dose levels present specific side effects, including increased

risks of developing diabetes, cardiovascular disease, stunted growth, osteoporosis, thin skin, gastrointestinal disorders, and decreased lifespan.

Due to the severity of the disease, most developed countries have established newborn screening programs to test for classic CAH at birth. Infants diagnosed with classic CAH are generally initiated on glucocorticoid therapy at the time of diagnosis and lifelong disease management with steroids is required, with pediatric patients generally transitioning into the care of adult endocrinologists between the ages of 18 and 21. Due to the complexity of management of classic CAH, in the United States, patients are generally managed within specialty endocrinology clinics, and in the European Union, or EU, most countries have a small number of centers of excellence addressing the population. We estimate the total classic CAH populations are approximately 20,000 to 30,000 people in the United States and approximately 50,000 people in the EU, and, according to the National Organization for Rare Disorders, the estimated incidence of classic CAH in the United States and Europe is between one in 10,000 and one in 15,000 live births. In addition, we estimate based on industry reports that the global market opportunity in patients with classic CAH is at least approximately $3.0 billion.

Tildacerfont is a potent and highly selective, non-steroidal, oral antagonist of the CRF1 receptor, which is the receptor for corticotropin-releasing factor, or CRF, a hormone that is secreted by the hypothalamus. The CRF1 receptor is abundantly expressed in the pituitary gland where it is the primary regulator of the HPA axis. By blocking the CRF1 receptor, tildacerfont has the potential to address the uncontrolled cortisol feedback regulatory pathway in CAH, and in turn reduce the production of ACTH in the pituitary, limiting the amount of androgen produced downstream from the adrenal gland. We believe that by controlling excess adrenal androgens through an independent mechanism, tildacerfont could reduce the unwanted clinical symptoms associated with high androgen exposure. Tildacerfont use could also enable treating physicians to lower the supraphysiologic glucocorticoid doses given to classic CAH patients to near physiologic levels, thus reducing or avoiding the long-term and serious side effects associated with the chronic use of high dose glucocorticoids.

Tildacerfont has been evaluated in 171 patients across seven clinical trials in which it has been generally well tolerated. No drug-related SAEs have been reported related to tildacerfont treatment. To date, we have completed two Phase 2 clinical trials in patients with classic CAH, comprising of a two-week proof-of-mechanism dose ranging clinical trial, and a 12-week proof-of-concept clinical trial, in which we observed that tildacerfont led to the decrease in the levels of a series of hormones associated with adrenal hyperplasia and androgen synthesis, both of which are key indicators of poor disease control. In our 12-week clinical trial, among patients with highly elevated hormones and androgens at baseline, 60% achieved normalization of ACTH, one subject at week two prior to discontinuation and two subjects during month three, and 40% achieved normalization of androstenedione, or A4, during month three. A4 is an androgen steroid routinely used as a biomarker of androgen synthesis by the adrenal gland.

Through our clinical trials completed to date, we have conducted post-hoc analyses of two distinct groups of classic CAH patients, both on stable standard-of-care glucocorticoids: those who have poor disease control, as evidenced by highly elevated hormones and androgens at baseline; and those who have good disease control, as evidenced by hormones and androgens that are close to or within the normal range at baseline. In patients with poor disease control, the dose of glucocorticoids being administered was insufficient on its own to suppress adrenal hyperplasia and androgen synthesis. Patients with poor disease control may be intolerant to higher glucocorticoid doses or unwilling to accept the negative consequences resulting from chronic use of high doses of glucocorticoids. In patients with poor disease control, the addition of tildacerfont provided a potential non-steroidal solution to control excess androgen synthesis. Patients receiving tildacerfont showed reduced levels of disease-driving hormones and androgens by a mean of approximately 80%, resulting in levels close to those found in healthy adults without any changes to the glucocorticoid dosing in these patients.

We observed that classic CAH patients in our clinical trials with good disease control upon trial enrollment were receiving glucocorticoid doses approximately 44% higher than those patients with poor disease control. Dosing of tildacerfont in patients with good disease control was well tolerated and did not lead to further suppression of adrenal function or androgen synthesis. In these patients, tildacerfont may be able to allow a significant reduction in glucocorticoid dosing while continuing to maintain normal levels of androgens. Based on the strength of our clinical results to date, we believe tildacerfont has the potential to offer improved clinical outcomes for both poor disease control and good disease control classic CAH patients.

We have initiated CAHmelia-203, a double-blind, placebo-controlled Phase 2b clinical trial in adult patients with classic CAH who have poor disease control despite stable glucocorticoid dosing. The goals of this clinical trial are to: (i) assess the ability of three dose levels of tildacerfont to reduce the levels of disease associated hormones and androgens over a period of 12 weeks; (ii) assess the impact of dose-titration of tildacerfont to further improve these hormone and androgen levels over 24 weeks; (iii) assess clinical outcomes that result from hormone reductions over 70 weeks; and (iv) assess the long-term safety of tildacerfont over 70 weeks. We have also initiated CAHmelia-204, a second Phase 2b clinical trial in adult patients with classic CAH with good disease control focused on glucocorticoid reduction. The goals of this clinical trial are to: (i) evaluate the ability of tildacerfont to allow clinically meaningful reductions in glucocorticoid dosing over periods of 24 and 76 weeks while maintaining good disease control; (ii) assess the combined impact of tildacerfont administration and glucocorticoid reduction on improving clinical outcomes over 24 and 76 weeks; and (iii) assess the long-term safety of tildacerfont over 76 weeks. Based on analyses of our clinical data to date, we have chosen to target two distinct groups of classic CAH patients with either good disease control or poor disease control. These two groups, which together make up the entire classic CAH patient population, have differing disease challenges centered on excessive adrenal androgen levels or excessive glucocorticoid usage, both of which have the potential to be addressed by treatment with tildacerfont, if approved. We believe our strategy to study CAH patients in these two enriched sub-populations may enable us to observe clinically meaningful outcomes. Additionally, we believe these two clinical trials will provide sufficient patient exposures for our registrational safety database. Assuming positive results in CAHmelia-204, we plan to meet with the FDA and comparable foreign regulatory authorities to discuss registration. We also plan to investigate tildacerfont for the treatment of classic CAH in children as young as two years of age, and plan to initiate a clinical development program for tildacerfont in the pediatric classic CAH population in the second half of 2021.

We own worldwide development and commercialization rights for tildacerfont. We intend to build a highly specialized commercial organization to support the commercialization of tildacerfont, if approved, in the United States and Europe. Given a relatively small number of endocrinologists and specialists treat a large proportion of the patients with classic CAH, we believe this market can be effectively addressed with a modest-sized targeted commercial sales force, alongside various high-touch patient initiatives. If tildacerfont is approved for additional indications, we plan to leverage our rare disease commercial infrastructure and expertise to efficiently address those patient populations. We may also either build a commercial infrastructure or opportunistically seek strategic collaborations to benefit from the resources of biopharmaceutical companies specialized in either relevant disease areas or geographies.

We have developed and continue to expand our extensive patent portfolio for tildacerfont, covering composition of matter, method of synthesis, formulation, and use. We have also been granted orphan drug designation for tildacerfont for the treatment of CAH both in the United States and the EU. We have assembled a highly experienced team with broad capabilities in drug discovery, development, and commercialization. In aggregate, our team has contributed to the development and commercial launch of 40 products, including within the fields of endocrinology and rare diseases. Richard King, our Chief Executive Officer, previously served as Chief Operating Officer at Adamas Pharmaceuticals, Inc. and President and Chief Executive Officer of AcelRx Pharmaceuticals, Inc. Prior to that, Mr. King served as President and Chief Operating Officer of Tercica, Inc., a company focused on developing and commercializing therapeutics for rare endocrine disorders, until its acquisition by Ipsen, S.A. Samir Gharib, our Chief Financial Officer, previously served as Chief Financial Officer at Stemedica Cell Technologies. Rosh Dias, M.D., M.R.C.P., our Chief Medical Officer, previously served as Chief Medical Officer of Indivior PLC, and prior to that in clinical development and medical affairs roles with Amgen Inc., Onyx Pharmaceuticals, Inc., and Novartis International AG.

Our Development Plan for Tildacerfont

We are investigating tildacerfont in orphan indications where the underlying disease biology supports a need to reduce excess secretion of or hyperresponsiveness to ACTH. We are currently in late-stage clinical development for tildacerfont in adult patients with classic CAH. We have initiated the CAHmelia-203 trial in adult patients with classic CAH with poor disease control and anticipate topline results in the first half of 2022. We have also initiated the CAHmelia-204 trial in adult patients with classic CAH with good disease control focused on glucocorticoid reduction and anticipate topline results in the second half of 2022. Based on analyses of our clinical data to date, we have chosen to target two distinct groups of classic CAH patients with either good disease control or poor disease control. These two groups, which together make up the entire classic CAH patient population, have differing disease

challenges centered on excessive adrenal androgen levels or excessive glucocorticoid usage, both of which have the potential to be addressed by treatment with tildacerfont, if approved. We believe our strategy to study CAH patients in these two enriched sub-populations may enable us to observe clinically meaningful outcomes. Additionally, we believe these two clinical trials will provide sufficient patient exposures for our registrational safety database. Assuming positive results in CAHmelia-204, we plan to meet with the FDA and comparable foreign regulatory authorities to discuss registration.

We also plan to investigate tildacerfont for the treatment of classic CAH in children as young as two years of age, and plan to initiate the clinical development program for tildacerfont in the pediatric classic CAH population in the second half of 2021. By leveraging our existing Phase 1 program, which includes safety, tolerability, and pharmacokinetics of tildacerfont, in addition to dose modelling to adapt the information from adults to children, we plan to initiate a Phase 2 pediatric clinical trial. We have received feedback from the FDA and EMA on our planned Phase 2 pediatric clinical trial.

Polycystic ovary syndrome, or PCOS, is a hormonal disorder common among females of reproductive age affecting nearly five million females in the United States and approximately 115 million females worldwide. PCOS is characterized by elevated levels of androgens, cysts in the ovaries, and irregular periods. We have identified a subpopulation of patients where elevated levels of adrenal androgens are the cause of disease. We believe that tildacerfont may present a novel mechanism to reduce ACTH and provide a therapeutic option for females with this rare form of PCOS, representing 3-5% of females with PCOS (estimated to be 150,000 to 200,000 patients in the United States). We plan to file an investigational new drug application, or IND, to study tildacerfont in this patient population in the first half of 2021 and are pursuing orphan drug designation in this patient population. By leveraging our existing Phase 1 program, which includes safety, tolerability, and pharmacokinetics of tildacerfont, subject to the clearance of our planned IND, we plan to initiate a Phase 2 proof-of-concept clinical trial in the second half of 2021.

The following table summarizes our development plan for tildacerfont:

Product Candidate	Indication	Status	Key Anticipated Milestone(s)
Tildacerfont	Adult Classic Congenital Adrenal Hyperplasia	■ Initiated Phase 2b clinical trial (CAHmelia-203) to evaluate androgen reduction and clinical consequences in adult patients with classic CAH ■ Initiated Phase 2b clinical trial (CAHmelia-204) to evaluate glucocorticoid reduction and clinical consequences in adult patients with classic CAH	■ 1H 2022: CAHmelia-203 topline results ■ 2H 2022: CAHmelia-204 topline results
	Pediatric Classic Congenital Adrenal Hyperplasia	■ Received FDA and EMA feedback on planned Phase 2 clinical trial in children	■ 2H 2021: Initiate Phase 2 clinical trial
	Polycystic Ovary Syndrome	■ Developing clinical development plan in a subpopulation of females with a rare form of PCOS; planning Phase 2 proof-of-concept clinical trial	■ 1H 2021: File IND ■ 2H 2021: Initiate Phase 2 proof-of-concept clinical trial*

* Subject to clearance of the IND.

Our Strategy

- **Complete clinical development for tildacerfont and seek regulatory approval for the treatment of adults with classic CAH.** Our completed Phase 2 clinical trials of tildacerfont in classic CAH patients have demonstrated the potential of tildacerfont to lower ACTH and levels of key steroid precursors for androgen synthesis. We have initiated CAHmelia-203, a placebo-controlled, double blind Phase 2b clinical trial in adult patients with classic CAH with poor disease control and anticipate topline results in the first half of 2022. We have also initiated CAHmelia-204, a second Phase 2b clinical trial in adult patients with classic CAH with good disease control focused on glucocorticoid reduction and anticipate topline results in the second half of 2022. Based on analyses of our clinical data to date, we have chosen to target two distinct groups of classic CAH patients with either good disease control or poor disease control. These two groups, which together make up the entire classic CAH patient population, have differing disease challenges centered on excessive adrenal androgen levels or excessive glucocorticoid usage, both of which have the potential to be addressed by treatment with tildacerfont, if approved. We believe our strategy to study CAH patients in these two enriched sub-populations may enable us to observe clinically meaningful outcomes. Additionally, we believe two clinical trials will provide sufficient patient exposures for our registrational safety database. Assuming positive results in CAHmelia-204, we plan to meet with the FDA and comparable foreign regulatory authorities to discuss registration.

- **Advance tildacerfont through clinical development and seek regulatory approval for the treatment of children with classic CAH.** There is an urgent need to bring androgen-lowering and glucocorticoid-reduction therapy to pediatric classic CAH patients to avoid premature puberty, which together with the adverse effects of glucocorticoids, can prevent a child from growing to their full height. We are developing a pediatric development plan to assess the safety and efficacy of tildacerfont in patients as young as two years of age. We plan to initiate a pediatric development program in classic CAH in the second half of 2021. We have received feedback from the FDA and EMA on our planned Phase 2 clinical trial of tildacerfont in children with classic CAH.
- **Maximize the commercial potential of tildacerfont in classic CAH.** We intend to build a highly specialized commercial organization to support the commercialization of tildacerfont, if approved, in the United States and Europe. Given a relatively small number of endocrinologists and specialists treat a large proportion of the patients with classic CAH, we believe this market can be effectively addressed with a modest-sized targeted commercial sales force, alongside various high-touch patient initiatives. If tildacerfont is approved for additional indications, we plan to leverage our rare disorder commercial infrastructure and expertise to efficiently address those patient populations. We may also opportunistically either build a commercial infrastructure or seek strategic collaborations to benefit from the resources of biopharmaceutical companies specialized in either relevant disease areas or geographies.
- **Explore the potential of tildacerfont to bring therapeutic benefit to patients with other rare endocrine disorders.** We believe that tildacerfont has the potential to bring therapeutic benefit to patients suffering from rare endocrine disorders where the underlying disease biology supports a need to reduce excess secretion of or hyperresponsiveness to ACTH. Based on this biological rationale, we believe tildacerfont may have utility in controlling elevated levels of adrenal androgens in a subpopulation of females with a rare form of PCOS. We believe these patients may *potentially* benefit from treatment with tildacerfont by reducing their ACTH level and related adrenal androgen production. We plan to file an IND to study tildacerfont in this patient population in the first half of 2021. By leveraging our existing Phase 1 program, which includes safety, tolerability, and pharmacokinetics of tildacerfont, subject to the clearance of our planned IND, we believe we will be able to initiate a Phase 2 proof-of-concept clinical trial in the second half of 2021 and are planning to pursue orphan drug designation in this patient population in the United States. We will also continue to explore the utility of tildacerfont in other rare endocrine disorders, such as the severe form of non-classic CAH in which there is a strong scientific and clinical rationale.
- **Evaluate strategic opportunities to expand our product candidate portfolio.** We intend to seek to in-license or acquire development-stage product candidates in rare endocrine disorders that have the potential to complement our existing portfolio. We believe that there are many opportunities to leverage our deep endocrine expertise to develop new treatments for rare endocrine disorders with significant unmet medical needs.

Role of the Endocrine System and the HPA Axis

The endocrine system regulates most of the body's physiological activities through the actions of hormones, which are chemical and biochemical messengers secreted from different organs that influence growth, gastrointestinal function, maturation and development, reproduction, stress, metabolism, and nearly all aspects of homeostasis. The endocrine system includes, among other glands and organs, the pituitary gland, hypothalamus, pancreas, adrenal gland, thyroid and parathyroid, ovaries and testes, as well as specialized enteroendocrine cells. Hormonal secretion is complex and the body employs several mechanisms to exert positive and negative feedback control to maintain homeostasis.

The HPA axis is a critical component of the endocrine system and the body's response to stress. In a functioning HPA axis, CRF is synthesized and secreted from the hypothalamus in the brain. This stimulates the secretion of ACTH, through activation of the CRF1 receptor at the pituitary gland, which in turn stimulates the production of several hormones in the adrenal cortex: corticosteroids, which gauge the body's response to illness or injury; mineralocorticoids, which regulate salt and water levels; and androgens, which are male sex hormones. Cortisol, a glucocorticoid steroid, exerts a negative feedback response at the hypothalamus and pituitary, which decreases secretion of CRF and ACTH, respectively, to maintain an appropriate balance of all three hormones.

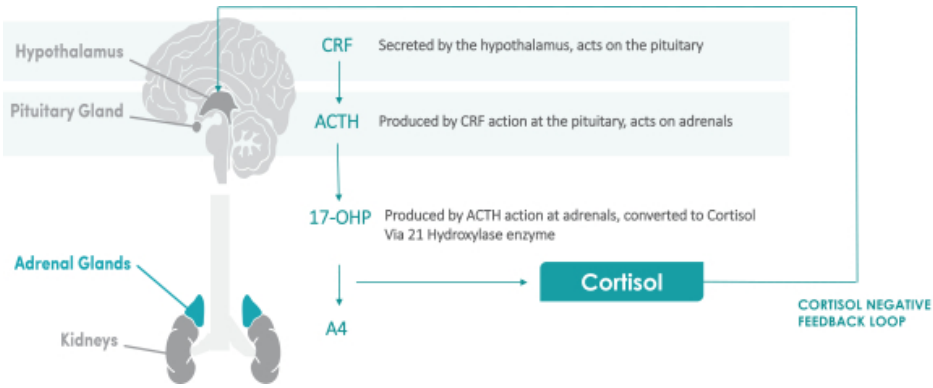

Figure 1. Normal HPA Axis function.

Classic CAH Disease Overview

Classic 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.

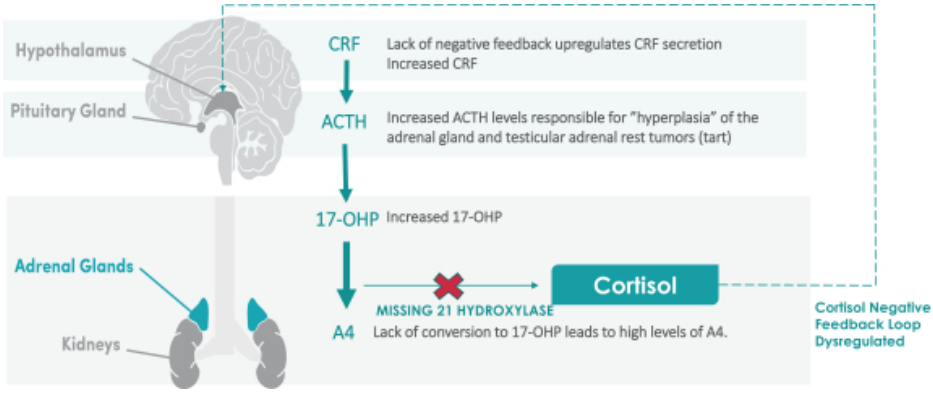

Figure 2. The dysregulation of the HPA axis in classic CAH.

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 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 15,000 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, or TARTs, benign tumors that can lead to pain and impaired fertility.

Numerous studies have documented diminished quality of life in patients with CAH related both to the disease and its treatment with glucocorticoids. For example, CAH patients commonly experience fatigue, sleep disturbances, concentration problems, and challenges with social interactions.

Patients with classic CAH face increased risk of mortality, with one study documenting an average reduced lifespan of 6.5 years. The causes of death were adrenal crisis (42%), cardiovascular disease (32%), cancer (16%), and suicide (10%).

Consequences of Lack of Cortisol and Aldosterone

A lack of functional 21-hydroxylase enzyme results in the inability to produce sufficient corticosteroids, such as cortisol, and mineralocorticoids, such as aldosterone. Cortisol functions as the body's main stress hormone. Biochemically, it regulates glucose metabolism, inflammation and blood pressure. On a behavioral level, it controls mood, motivation, fear, and sleep/wake cycles. Aldosterone regulates the electrolyte balance between sodium and potassium in the body. Low levels of aldosterone result in hyponatremia, low blood pressure and volume, dizziness, and lightheadedness. Restoration of the function of both cortisol and aldosterone is the primary goal of current therapies for classic CAH.

Consequences of the Accumulation of the Androgen Precursor 17-OHP

A consequence of the absence of 21-hydroxylase is the accumulation of 17-hydroxyprogesterone, or 17-OHP, a precursor molecule to androgens and cortisol. Without 21-hydroxylase to convert 17-OHP into cortisol, increased levels of 17-OHP are shunted to an alternative hormone resulting in increased synthesis of the testosterone precursor, A4, and related increases in the levels of other androgens in the body, resulting in virilization that

complicates fertility and sexual maturation in both females and males. The following figure depicts steroid treatment intervention in patients with classic CAH.

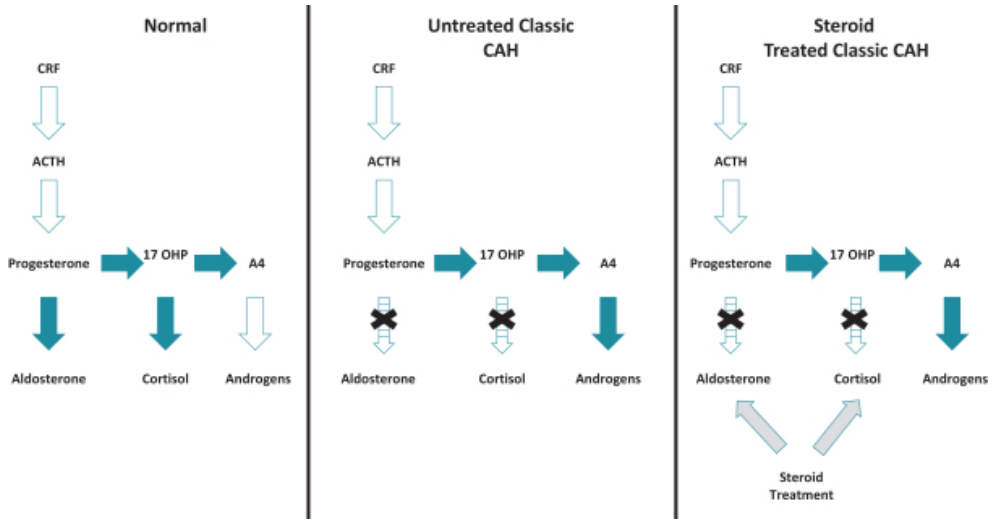

Figure 3. Depiction of steroid treatment intervention in patients with classic CAH.

Inadequate Regulation of Steroid Synthesis Leading to Androgen Excess

Cortisol serves as a negative regulator of the HPA axis, regulating its own production. Increasing levels of cortisol downregulate the synthesis of CRF in the hypothalamus and ACTH in the pituitary to ultimately reduce the production of cortisol precursor molecules, such as 17-OHP. In classic CAH patients, deficiencies in cortisol levels stimulate this feedback mechanism and results in excess production of CRF and ACTH. CRF produced in the hypothalamus binds to the CRF1 receptor in the pituitary gland to stimulate the production of ACTH. In turn, ACTH overproduction drives both adrenal hyperplasia, or enlargement of the adrenal glands, and overproduction of steroid molecules such as 17-OHP and A4, leading to increased androgen production. This serves to further exacerbate the excessive levels of androgens in these patients.

Current Treatment Paradigm and its Limitations

The mainstay of classic CAH therapy for over 50 years has been lifelong treatment with glucocorticoids such as hydrocortisone, prednisone, prednisolone, methylprednisolone, or dexamethasone. These treatments do not cure the disease, but they serve a two-fold purpose in disease management. Firstly, physiologic levels of glucocorticoids replace the missing cortisol in order to prevent adrenal crisis. Secondly, supraphysiologic levels of glucocorticoids reduce excess androgens through the negative feedback loop alleviating additional hyperandrogenic symptoms.

The level of glucocorticoid necessary to achieve therapeutic benefit is specific to each patient, requires adjustment to individual patient circumstances, and may change over the patient's lifetime, thereby creating multiple challenges for effective treatment. Chronic use of glucocorticoids requires careful management, because of the well-known serious side effects of these drugs, which include growth inhibition in children, high blood pressure, diabetes, psychological effects, skin thinning, and increased risks of infections.

Clinical management of classic CAH is a difficult balance between supplying sufficient levels of glucocorticoids to compensate for deficiencies in cortisol levels while minimizing side effects resulting in a narrow therapeutic window. In an analysis of classic CAH patients treated in the United States and the United Kingdom, or UK, only one-third of those dosed with glucocorticoids achieved optimal control of their androgen levels. While treatment with supraphysiologic glucocorticoids can help restore the regulation of CRF and ACTH production leading to reductions in excess 17-OHP and A4 synthesis, in order to restore a more appropriate balance, physicians

must identify the desired glucocorticoid dose for each patient. This is challenging, because the amount of cortisol needed to modulate 17-OHP and A4 levels is much higher than that required to functionally replace the missing cortisol.

From birth to adulthood, the aim of glucocorticoid treatment is to identify the right balance based on both the patient's physical maturation as well as gender. At birth, the aim of treatment is to provide an adequate level of steroids to prevent an adrenal crisis. Throughout childhood, treatment becomes more complex with both a need to maintain adequate steroid levels but also ensure androgen levels are as close to normal to prevent precocious puberty while not stunting growth and to prevent premature closure of bone growth plates as a result of treatment with supraphysiologic steroids. The aim of treatment for adolescents and adults is to provide the body with the ability to maintain a normal energy level, normal growth, and fertility while minimizing clinically overt signs of excess glucocorticoids or excess androgens. In adults, the balancing act may be different between males and females. Females experience more outward signs of excess androgens than males, so females are more attentive to androgen control through supraphysiologic glucocorticoids while males may be more attentive to the adverse outcomes associated with supraphysiologic glucocorticoid replacement.

This makes glucocorticoid therapy challenging, since treatment with high levels of glucocorticoids leads to, among other consequences, obesity, short stature, the loss of bone mineral density, drug-induced Cushing's disease, which is a condition that occurs from exposure to high cortisol levels for a long period of time, metabolic disorders, increased cardiovascular and infection risk, and early mortality. The following figure depicts the need to balance the negative consequences that result from poor control of androgen levels with those associated with high levels of glucocorticoids.

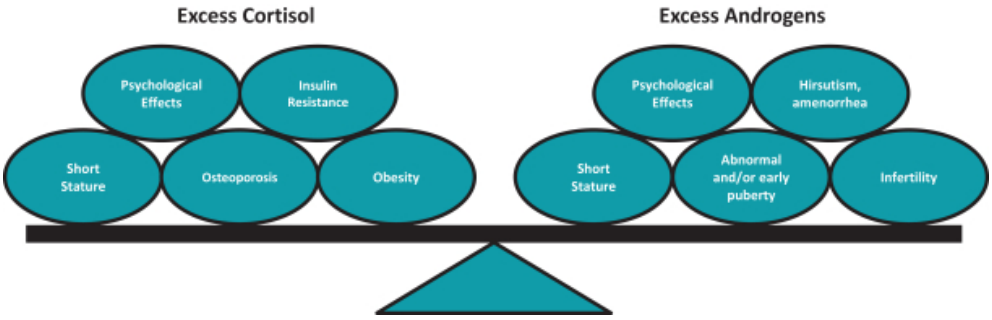

Figure 4. The challenge in treating CAH is balancing therapy to provide optimal control of androgens while avoiding excess cortisol levels.

A novel approach to suppress androgen synthesis would be to directly inhibit the ability of CRF to stimulate ACTH synthesis using a CRF1 receptor antagonist. This approach has the potential to dissociate physiologic cortisol replacement with glucocorticoids from cortisol's regulatory role as a negative-regulator of ACTH to both prevent the hyperplasia of the adrenal gland and reduce the ensuing excess androgen synthesis. In effect, this is an independent mechanism to block excessive ACTH production. We believe that an effective CRF1receptor antagonist will enable physicians to reduce the dose of glucocorticoids administered to patients in a way that will address their cortisol replacement needs and simultaneously avoid excessive androgen production.

Our Solution, Tildacerfont

Tildacerfont is a potent and highly selective, non-steroidal, oral, small-molecule antagonist of the CRF1 receptor, a regulator of the production of ACTH. The CRF1 receptor binds CRF, a potent mediator of endocrine, autonomic, behavioral, and immune responses to stress. Activation of the CRF1 receptor in the pituitary gland has been shown to increase the secretion of ACTH, which in turn drives the production of cortisol and androgens in the adrenal gland. By blocking the CRF1 receptor, tildacerfont can address the uncontrolled cortisol feedback regulatory pathway in CAH, and in turn reduce the production of ACTH in the pituitary, limiting the amount of androgen produced downstream from the adrenal gland. Tildacerfont has been assessed in 171 patients across seven clinical

trials, in which it has been well tolerated with no drug-related SAEs. In preclinical studies, we showed that blocking the binding of CRF to this receptor decreased ACTH production and the production of hormones and androgens such as 17-OHP and A4 and that tildacerfont was over 1,000-fold selective for the CRF1 receptor versus any other receptor tested. Based on preclinical data, receptor occupancy of at least 90% was predicted to be achieved at a dose of less than 400mg.

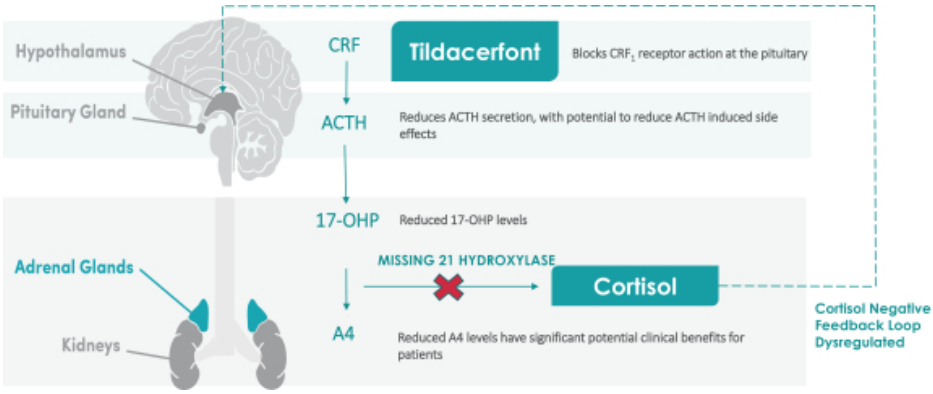

Figure 5. Tildacerfont blocks CRF1 receptors at the anterior pituitary gland to decrease secretion of ACTH, hormones, such as 17-OHP, and androgens, such as A4.

Tildacerfont has been investigated in five completed Phase 1 clinical trials in healthy adult volunteers, in single doses up to 800mg as well as in multiple doses ranging from 50mg to 200mg once daily, for 14 days. In all of these clinical trials, tildacerfont was generally well tolerated. A total of 145 healthy volunteers have received at least one dose of tildacerfont in completed studies. No drug-related SAEs during tildacerfont treatment were observed in these clinical trials and the most frequent non-procedural adverse events experienced by greater than 5% of the healthy volunteer population were headache and cough.

Completed Clinical Trials in Classic CAH Patients

We conducted two Phase 2a clinical trials of tildacerfont in adult patients with classic CAH on stable glucocorticoid therapy. Clinical trial SPR001-201 was an open-label, dose-ranging clinical trial in 24 patients. These patients received a series of doses of tildacerfont for two weeks each in addition to their standard daily glucocorticoid dose. Two patients participated in two cohorts in SPR001-201. Clinical trial SPR001-202 was a 12-week clinical trial of 11 patients treated with a fixed dose of 400mg tildacerfont once daily. Nine of the 11 SPR001-202 patients also participated in SPR001-201. A total of 26 unique classic CAH patients have been treated to date with tildacerfont. The results from the clinical trials to date suggest that tildacerfont may reduce elevated androgens and may also allow for reduction of supraphysiologic glucocorticoid doses.

Previous observations had identified that tildacerfont interacts with CYP3A4, a liver enzyme that is responsible for the metabolism of a number of drugs. When a drug inhibits or induces CYP3A4, it can impact the body's ability to metabolize other drugs. In SPR001-201, we observed that tildacerfont led to an approximately two-fold increase in the levels of dexamethasone, a glucocorticoid that is primarily metabolized through CYP3A4. In order to eliminate any potentially confounding drug-drug interactions from our clinical trial, we subsequently

removed patients who were being treated with dexamethasone from our efficacy analyses. No drug-drug interactions were observed with other glucocorticoids and we made no other modifications.

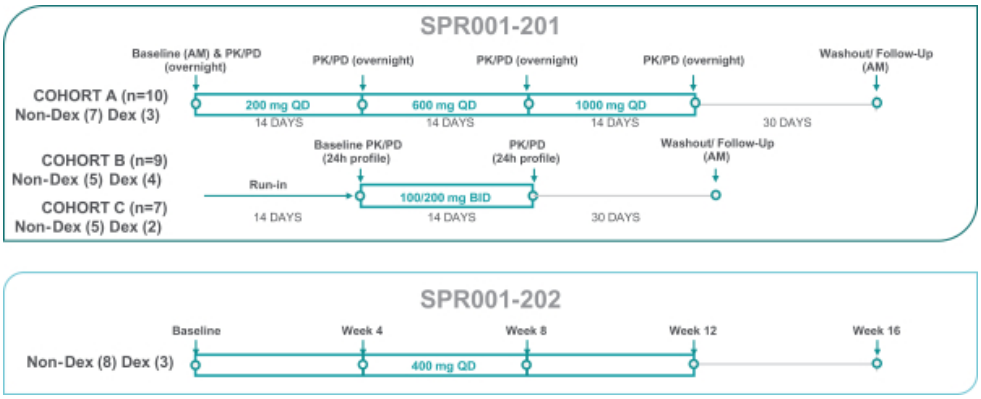

Figure 6. Dosing regimen in Phase 2 SPR001-201 and SPR001-202.

SPR001-201 Results

SPR001-201 was our first clinical trial in adults with classic CAH and was a proof-of-concept, dose-escalating Phase 2a clinical trial in patients who were on a stable glucocorticoid dosing regimen but still had levels of 17-OHP that were four-fold or greater above the 200 ng/dL upper limit of normal, or ULN. Patients enrolled in three sequential cohorts, and during the clinical trial, could not change their underlying glucocorticoid regimen to avoid confounding the effect of varying glucocorticoid levels on disease-driving hormones. The clinical trial assessed the safety and pharmacokinetics of tildacerfont across a range of doses from 200mg to 1,000mg once daily and 100mg and 200mg twice daily. Pharmacodynamic activity was assessed using ACTH, 17-OHP, and A4 overnight with the baseline and key assessment at 8:00 a.m. This overnight period was selected as it represents the time period during which excess production of ACTH and hormones and androgens peak. The goal of this clinical trial was to assess whether tildacerfont could blunt the magnitude of this rise in the hormones.

The enrollment screening criteria for SPR001-201 ensured that 17-OHP was elevated in all but one patient at baseline (8:00 a.m. on day one) enrolled in this clinical trial; however, the levels of ACTH and A4 were more variable. In a post-hoc analysis, we identified two homogenous patient groups using ACTH and A4 and classified these patients as either those with “poor disease control” or “good disease control”. In our clinical trial, patients with poor disease control had highly elevated ACTH, 17-OHP, and A4 levels, generally greater than twice the ULN and, more commonly, greater than four times the ULN. These patients with poor disease control were on a stable mean daily supraphysiologic dose of approximately 25mg of hydrocortisone, or a dose of another glucocorticoid equivalent to 25mg of hydrocortisone. Patients with good disease control had elevated 17-OHP levels but had ACTH and A4 generally less than twice the ULN and more commonly, within the normal bounds for ACTH and A4. These patients were on doses equivalent to a mean daily supraphysiologic dose 36mg of hydrocortisone, which was a 44% higher total daily dose than patients with poor disease control. These findings suggest that patients in the poor disease control patient group may have been receiving inadequate glucocorticoid doses to provide adequate control of their disease, possibly due to an inability to tolerate higher doses of glucocorticoids or unwillingness to accept the adverse outcomes attributed to chronic dosing of supraphysiologic glucocorticoids. Given the clear differences in baseline hormone profiles and glucocorticoid dosing, we decided to analyze the effect of tildacerfont on hormones in these two groups independently. We believe that by identifying these two homogeneous patient groups, and designing our development program around the two groups, we are uniquely positioned to address the two major areas of unmet medical need for these patients.

Table 1 summarizes the key demographic and baseline characteristics across the two patient groups. The demographics across both patient groups were similar. The age distribution trended to older subjects with an average age of 44 years, as compared to an age range of 19 years to 67 years, with an average body mass index, or BMI, of

approximately 31, signifying an obese population on average. The daily glucocorticoid dose and baseline hormones were different between the two patient groups.

	Good Disease Control (N=6)	Poor Disease Control (N=11)
Demographics		
Age (yrs), mean (SD)	44 (16.6)	45 (17.0)
Sex, Female, n (%)	5 (83%)	6 (55%)
Race, White n (%)	6 (100%)	10 (91%)
BMI (kg/m2), mean (SD)	31.3 (5.77)	30.0 (5.9)
Baseline Glucocorticoid dose		
Dose (mg) in Hydrocortisone equivalents	36.3 (8.02)	24.5 (8.6)
Baseline Hormones (8:00 a.m.)		
ACTH (pg/mL), geometric mean (CV%)	30.9 (273.1%)	397.0 (88.5%)
17-OHP (ng/dl), geometric mean (CV%)	1531.6 (489%)	6688.6 (113%)
A4 (ng/dL), geometric mean (CV%)	97.6 (338%)	333.1 (171%)

Table 1. Demographics and baseline hormones in non-dexamethasone patients (SPR001-201).

While the exposure levels, as a function of dose, generally demonstrated dose linearity, no clear dose-response was observed in ACTH, 17-OHP, and A4 reductions. The lowest evaluated dose of 200mg once daily resulted in hormone changes that were comparable to those observed at higher doses (Figures 7-9). Also, overall dosing twice daily did not result in greater hormone reductions compared to once daily dosing. This finding corresponds with the initial predicted receptor occupancy data based on preclinical experiments demonstrating at least 90% receptor occupancy at doses of tildacerfont up to 400mg.

Figures 7-9 below summarize the changes in hormones across the overnight period. We conducted a post-hoc analysis which divided the subjects in this study into two groups, based on their hormone and androgen levels at baseline: poor disease control and good disease control. In the poor disease control group, there were 11 patients at doses equal to 200mg, six of whom received 200mg once per day in Cohort A and five of whom received 100mg twice per day in Cohort C, and 12 patients at doses greater than 200mg, six of whom received 600mg once per day and the same six of whom received 1,000mg once per day. In the good disease control group, there were six patients, one patient at 200mg once per day in Cohort A and five patients at doses greater than 200mg, each receiving 200mg twice per day in Cohort B.

Patients in the poor disease control group had baseline levels of ACTH, 17-OHP, and A4 that were substantially above the target goal for these hormones (ACTH target of 63.3 pg/mL, 17-OHP target of 1200 ng/dL and A4 target of 152 ng/dL for males and 262 ng/dL for females). Subsequent to receiving tildacerfont for 14 days, the mean levels of all three hormones were generally reduced throughout the overnight period from 10:00 p.m. to 8:00 a.m. These reductions were observed despite no changes in glucocorticoid dosing. We believe that the reductions in the poor disease control group demonstrated proof of concept and supported further studies to assess the ability of tildacerfont to reduce hormones.

Patients in the good disease control group had mean baseline levels of ACTH and A4 that were already below the target goal for these hormones. Treatment with tildacerfont did not lead to clinically meaningful reduction of these levels, suggesting that administering tildacerfont in good disease control patients has a low risk of excessive adrenal suppression. We believe the observed changes in these hormones are reflective of typical day-to-day

variation in these patients. Treatment of patients with good disease control who had elevated levels of 17-OHP led to a modest decrease in 17-OHP.

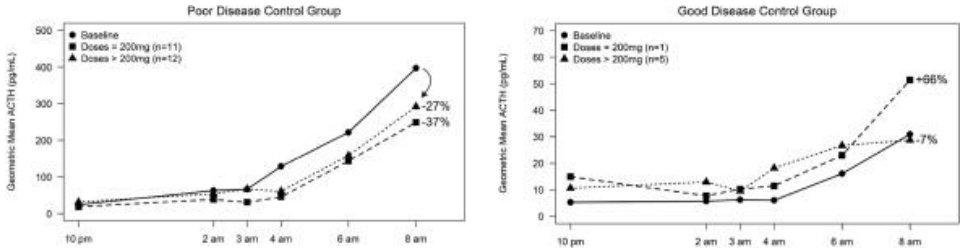

Figure 7. Change from baseline in ACTH (pg/mL) in poor and good disease control patients during the overnight period (SPR001-201).

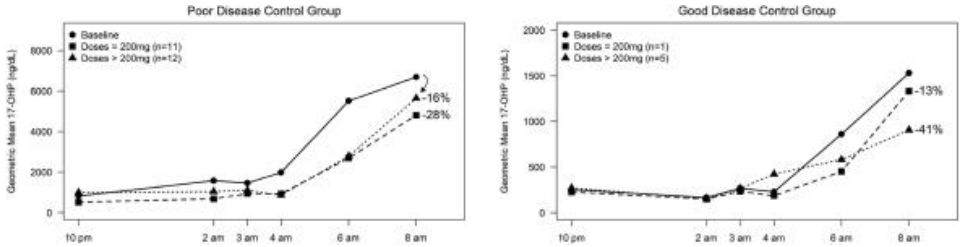

Figure 8. Change from baseline in 17-OHP (ng/dL) in poor and good disease control patients during the overnight period (SPR001-201).

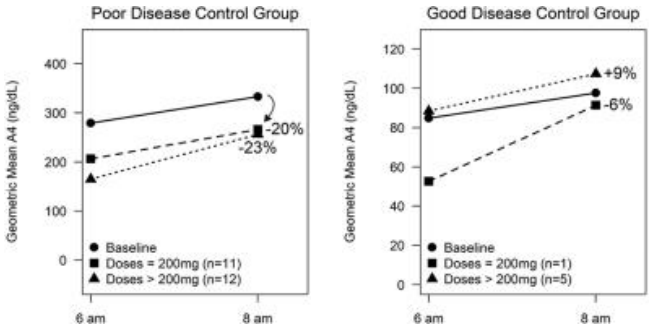

Figure 9. Change from baseline in A4 (ng/dL) in poor and good disease control patients (SPR001-201).

Of note, one classic CAH patient enrolled in this clinical trial, who had a pre-existing testicular mass classified as TART, saw a 25% decrease in the size of his tumor following six weeks of dosing with tildacerfont through two dose escalations in Cohort A. TARTs are directly driven by excess ACTH and the empiric standard of care to reduce TARTs is high dose dexamethasone. This tumor shrinkage is consistent with the mechanism of action of tildacerfont, reduction of excess ACTH, and provides the first known evidence of a non-steroidal, non-surgical reduction in a TART.

Tildacerfont was well tolerated in SPR001-201 at doses up to 1,000mg once daily. No drug-related SAEs were reported. The most common adverse event was headache (n=3). The majority of events were grade one in nature. A female subject (age 48; 200mg twice daily) experienced a grade three hot flush that resolved on its own within 30 minutes in the first week of treatment. One event of special interest was observed at the highest dose of 1,000mg

once daily. After 14 days of treatment at 1,000mg once daily, this patient experienced a grade one liver-related adverse event, as determined by the investigator. This patient had elevated levels of alanine transaminase, or ALT, between five and nine times ULN, elevations in aspartate aminotransferase, or AST, less than five times ULN, and no increases in bilirubin. The event resolved on its own without additional medical intervention. No cases of liver enzyme elevations above three times the ULN were observed in any patient receiving total daily doses of 600mg, which is approximately three times the proposed therapeutic dose, and below.

SPR001-202 Results

SPR001-202, our open-label, 12-week Phase 2a clinical trial, assessed the ability of a daily dose of 400mg of tildacerfont to lower disease-driving hormones such as ACTH, 17-OHP, and A4 over a 12-week dosing period. SPR001-202 was an extension clinical trial of SPR001-201, where the enrollment criteria was either prior participation in SPR001-201 or treatment-naïve patients meeting the 17-OHP criterion in SPR001-201. Disease-driving hormones were assessed at approximately 8:00 a.m. on each day corresponding to the peak excess hormone production. This clinical trial was conducted to evaluate the safety and tolerability of long-term treatment with tildacerfont and to assess the magnitude of hormone reductions after 12 weeks of treatment.

As with SPR001-201, dexamethasone subjects (n=3) were excluded from pharmacodynamic activity summaries but included in safety summaries. The table below summarizes the key demographic and baseline hormones in the non-dexamethasone patients.

	Good Disease Control (N=3)	Poor Disease Control (N=5)
Demographics		
Age (yrs), mean (SD)	48.0 (17.69)	42.4 (15.63)
Sex, Female, n (%)	3 (100%)	2 (40%)
Race, White n (%)	3 (100%)	4 (80%)
BMI (kg/m2), mean (SD)	35.5 (6.10)	27.8 (5.56)
Baseline Glucocorticoid dose		
Dose (mg) in Hydrocortisone equivalents	36.7 (11.6)	24.5 (11.5)
Baseline hormones		
ACTH (pg/mL), geometric mean (CV%)	12.2 (584.1%)	536.6 (108.5%)
17-OHP (ng/dl), geometric mean (CV%)	314.1 (1068.6%)	15323.3 (46.9%)
A4 (ng/dL), geometric mean (CV%)	28.8 (216.1%)	1001.1 (48.4%)

Table 2. Demographics and baseline hormones in good and poor disease control patients (SPR001-202).

Like with the SPR001-201 clinical trial, in the SPR001-202 clinical trial, we conducted a post-hoc analysis which divided the subjects in this study into a poor disease control group and a good disease control, based on their hormone and androgen levels at baseline: poor disease control and good disease control. We observed that tildacerfont-treated patients who were in the poor disease control group had mean maximum reductions in ACTH, 17-OHP, and A4 of approximately 80% compared to baseline at 8:00 a.m., bringing the levels of these key hormones to near normal levels that are used as targets for standard glucocorticoid therapy. In addition, 60% of patients achieved normalization of ACTH levels, one subject at week two prior to discontinuation from the clinical trial and two subjects during month three, and 40% achieved normalization of A4 levels during month three. We are not aware of normalization of these highly elevated hormones in classic CAH patients with any other investigational product candidate without increases to daily steroid doses.

As reflected in the figures below, we observed reductions in these hormones as early as the two-week time point and the reductions increased throughout the 12-week dosing period of the clinical trial. Last observation carried forward is applied for patients missing assessments during the 12-week period in the time course figures.

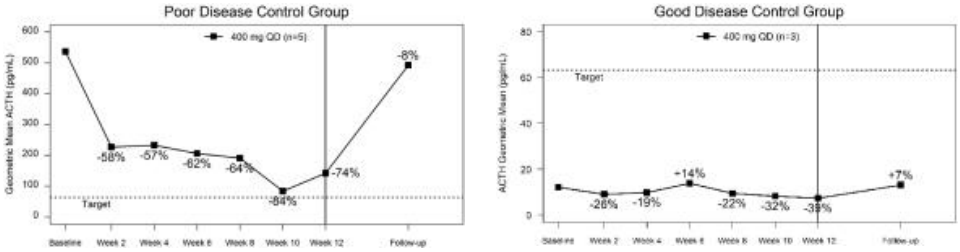

Figure 10. Change from baseline in ACTH (pg/mL) in poor and good disease control patients (SPR001-202).

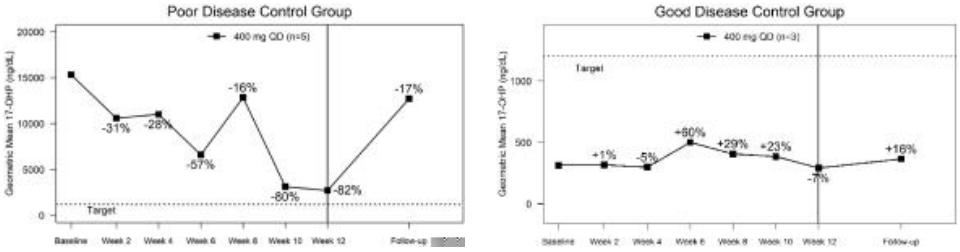

Figure 11. Change from baseline in 17-OHP (ng/dL) in poor and good disease control patients (SPR001-202).

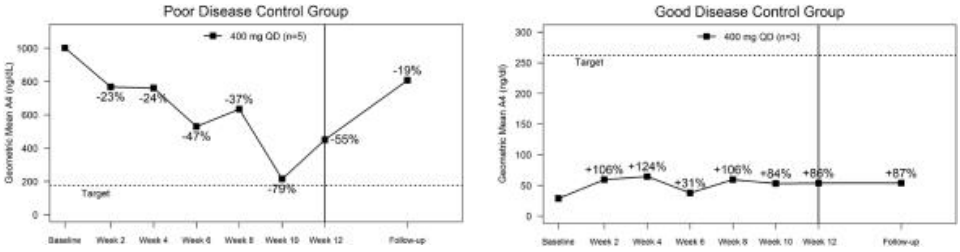

Figure 12. Change from baseline in A4 (ng/dL) in poor and good disease control patients (SPR001-202).

Upon completion of tildacerfont dosing at week 12, in poor disease control patients, levels of these disease-driving hormones increased, approaching their pre-trial baseline levels at follow-up, week 16. The results from this clinical trial are consistent with the ability of tildacerfont to inhibit CRF signaling, leading to reduction of adrenal stimulation by ACTH and the production of androgen precursors. Treatment with tildacerfont in this clinical trial led to this adrenal hormone and androgen reduction without requiring any change in the dose of glucocorticoids.

The best response for each patient in the non-dexamethasone poor disease control group in month three is summarized below. The majority of patients achieved robust reductions. One patient discontinued prior to month

three and is not included in this figure. This patient had reductions of 99%, 82% and 68% for ACTH, 17-OHP and A4, respectively, prior to discontinuation.

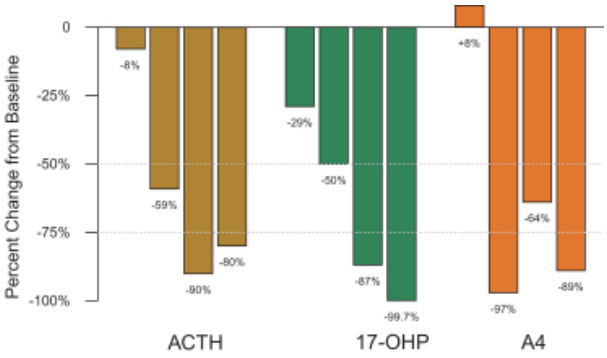

Figure 13. Change from baseline in hormones in poor disease control patients in month three (SPR001-202) at the individual patient level for subjects completing 12 weeks of treatment.

Patients who were in good disease control upon entry to SPR001-202 had mean levels of ACTH, 17-OHP and A4 that were well below the target goal. Administration of tildacerfont to these patients did not lead to significant changes in these levels. We believe that this finding is important because it supports that there may be a limit as to how much tildacerfont can suppress adrenal function, which could reduce the risk that excess dosing with tildacerfont could lead to excessive levels of suppression. This is consistent with the results we observed in SPR001-201.

Tildacerfont was well tolerated in SPR001-202. The most common adverse events were upper respiratory tract infection (n=2) and elevated A1c (n=2) and all four events deemed not related to tildacerfont treatment. The majority of events were grade one in nature. One subject discontinued study drug due to itching without a rash experienced between weeks two and four of treatment.

Patients in poor disease control were receiving supraphysiologic glucocorticoid doses equivalent to approximately 25mg hydrocortisone daily. Based on the levels of ACTH, 17-OHP, and A4 at baseline, these glucocorticoid doses were insufficient to adequately suppress androgen synthesis. However, the addition of tildacerfont lowered the levels of these hormones by approximately 80%, bringing them close to normal levels. In contrast, patients who were in good disease control upon enrollment in the clinical trial were receiving supraphysiologic glucocorticoid doses equivalent to 36mg of hydrocortisone daily. Because the baseline levels of ACTH and A4 were all well below the target goal, we believe that these patients may have been receiving glucocorticoid doses that were higher than would be necessary with the addition of tildacerfont. Furthermore, we believe that treatment of these patients with tildacerfont could enable these patients to reduce their glucocorticoid doses. Over time, we believe that tildacerfont may enable both groups of patients to achieve potentially normal or markedly improved levels of androgen synthesis with minimized levels of glucocorticoid replacement.

Late-Stage Clinical Trials in Classic CAH

We have two ongoing late-stage clinical trials in patients with classic CAH. We recently initiated CAHmelia-203, a randomized, double-blind, placebo-controlled, dose-ranging Phase 2b clinical trial to evaluate the safety and efficacy of tildacerfont in adults with classic CAH who are exhibiting high levels of adrenal hormones while on stable glucocorticoid dosing. This clinical trial will enroll approximately 72 patients who have levels of A4 that are at least 1.5-fold higher than the ULN and also ACTH levels that are at least twice as high as the ULN. For the first six weeks, patients will receive blinded placebo to assess their adherence to their existing glucocorticoid therapy. Patients who continue to meet all eligibility criteria at the end of this period will enter a three-part treatment period. During the placebo-controlled treatment period, patients will be randomized in a blinded manner to receive placebo, 50mg, 100mg, or 200mg tildacerfont once daily. Dosing in the placebo-controlled treatment period will continue for

12 weeks. The primary endpoint of the clinical trial will be the percentage change in A4 from baseline at week zero to week 12 with secondary endpoints including the mean percentage change in ACTH and 17-OHP; and the proportion of patients with levels of ACTH and A4 within the normal range, or levels of 17-OHP less than four times above normal. In the open-label extension period, all patients will receive tildacerfont following a proposed dose-escalation protocol based on hormone response in which the dosage can be increased up to 200mg daily. Following the 12-week dose-escalation period, all patients will continue receiving tildacerfont with the potential to increase the dose up to 200mg daily for an additional 46 weeks. Patients who achieve good disease control while on supraphysiologic glucocorticoid treatment will have the opportunity to taper down their glucocorticoid dosing in the open-label extension period according to a pre-specified algorithm in the protocol. Additional endpoints for this clinical trial include the percentage change in ACTH, 17-OHP, and A4 from baseline through week 70 as well as the proportion of patients with normalized levels of ACTH, A4, or levels of 17-OHP less than four times above normal. Other endpoints include the absolute change in glucocorticoids required to achieve good disease control, TARTs in men, clinical outcomes, and patient and clinician reported outcomes.

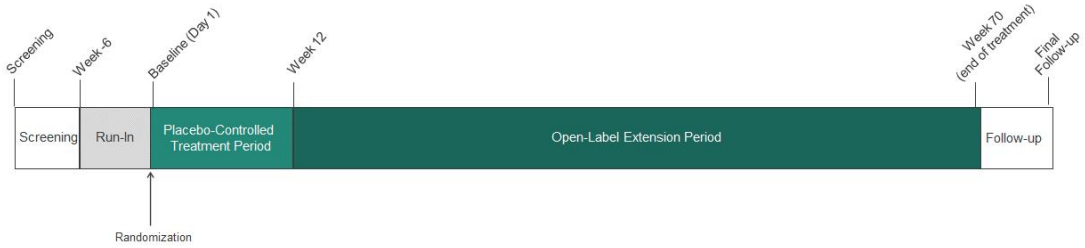

Figure 14. Design of trial CAHmelia-203

We also initiated CAHmelia-204, a randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of tildacerfont in reducing supraphysiologic glucocorticoid usage in approximately 90 adults with classic CAH in good disease control. This clinical trial is designed in two parts. In the first part of the clinical trial, patients will be randomized to receive 200mg tildacerfont once daily or placebo for 24 weeks. During the second part of the clinical trial, all patients will receive open-label tildacerfont for 52 weeks. Prior to initiation of the 24-week blinded treatment portion of the clinical trial, glucocorticoid dosing of all patients will be standardized to sponsor-provided hydrocortisone dosed three times per day or prednisolone dosed two times per day for a minimum of six weeks for patients requiring a conversion from their current therapy. During the tildacerfont treatment period, tapering of glucocorticoids will commence according to a pre-specified algorithm and continue to the lowest level possible (replacement levels only), as long as patients remain well controlled based on standard biomarkers and clinical assessments.

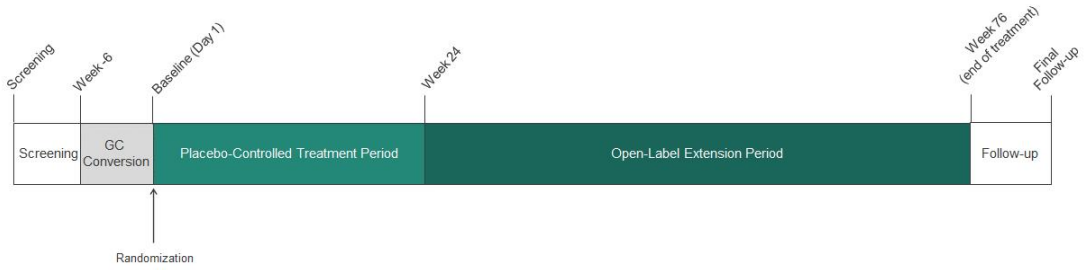

Figure 15. Design of trial CAHmelia-204

The primary endpoint of this clinical trial will be the absolute change in glucocorticoid dose at week 24. Exploratory endpoints include changes from baseline over 24 weeks and 76 weeks in levels of ACTH, 17-OHP, A4 and other disease-driving hormones of adrenal hyperplasia and androgen overproduction. Effects of tildacerfont on metabolism, cardiac function, body weight, fat mass, BMI, blood pressure, body composition, bone turnover, and bone density will be assessed as well as patient-reported measures of quality of life.

Based on analyses of our clinical data to date, we have chosen to target two distinct groups of classic CAH patients with either good disease control or poor disease control. These two groups, which together make up the entire classic CAH patient population, have differing disease challenges centered on excessive adrenal androgen levels or excessive glucocorticoid usage, both of which have the potential to be addressed by treatment with tildacerfont, if approved. We believe our strategy to study CAH patients in these two enriched sub-populations may enable us to observe clinically meaningful outcomes. Additionally, we believe these two clinical trials will provide sufficient patient exposures for our registrational safety database. Assuming positive results in CAHmelia-204, we plan to meet with the FDA and comparable foreign regulatory authorities to discuss registration.

Pediatric Trials of Tildacerfont

We plan to investigate tildacerfont for the treatment of classic CAH in children as young as two years of age, and plan to initiate the clinical development program for tildacerfont in the pediatric classic CAH population in the second half of 2021. At birth, newborns with classic CAH are immediately faced with a risk of adrenal crisis, which produces symptoms that include vomiting, severe dehydration, low blood pressure, and life-threatening shock. Replacement glucocorticoid therapy, initiated immediately after diagnosis, remains the customary treatment for children with classic CAH. Glucocorticoid therapy is administered to avoid precocious puberty. The growth suppressing effects of glucocorticoids, however, combined with the early bone growth closure from elevated levels of adrenal androgens, limits the height potential of children impacted by classic CAH. Many patients with classic CAH complete growth prematurely and are ultimately short as adults. We believe tildacerfont has the potential to reduce both the levels of adrenal androgens and the need for excess glucocorticoids, which may enable management of classic CAH at doses of glucocorticoids near physiologic replacement levels, with potential to enable more normal growth progression through childhood and adolescence. By leveraging our existing Phase 1 program, which includes safety, tolerability, and pharmacokinetics of tildacerfont, in addition to dose modelling to adapt the information from adults to children, we believe we will be able to initiate a Phase 2 pediatric clinical trial. We have received feedback from the FDA and EMA on our planned Phase 2 pediatric clinical trial. We estimate that children represent approximately 20% of the total classic CAH patient population.

Potential Role of Tildacerfont in the Treatment of Polycystic Ovary Syndrome

PCOS is a hormonal disorder common among females of reproductive age affecting nearly five million females in the United States and approximately 115 million females worldwide. PCOS is characterized by elevated levels of androgens, cysts in the ovaries, and irregular periods. Females with PCOS present with additional symptoms, including hirsutism, alopecia, acne, infertility, weight gain, fatigue, depression and mood changes. The underlying causes of PCOS are unknown. However, excess insulin secretion and low-grade inflammation, which stimulate the polycystic ovaries, have been linked to androgen excess. The source of this androgen excess may be ovarian, adrenal, both adrenal and ovarian, or from other sources. Adrenal androgen excess in PCOS appears to occur independently of ovarian androgen excess, suggesting it may represent an intrinsic, and possible primary source of abnormal synthesis of androgens. Adrenal androgen excess in PCOS does not result from enzymatic deficiencies, rather it represents an altered adrenal responsivity to ACTH. We believe that, in women whose PCOS is caused by elevated adrenal androgens, representing approximately 3-5% of females with PCOS (estimated to be 150,000 to 200,000 patients in the United States), tildacerfont may provide a therapeutic option to treat the underlying cause of disease through reduction of ACTH and overall ACTH hyperresponsiveness in this population. We plan to file an IND to study tildacerfont in this patient population in the first half of 2021 and are planning to pursue orphan drug designation in this patient population. By leveraging our existing Phase 1 program, which includes safety, tolerability, and pharmacokinetics of tildacerfont, subject to the clearance of our planned IND, we believe we will be able to initiate a Phase 2 proof-of-concept clinical trial in the second half of 2021.

Potential Role of Tildacerfont in the Treatment of Non-Classic CAH

The non-classic form of CAH, or non-classic CAH, also called late-onset CAH, occurs in approximately one in 1,000 of the general population. In females, non-classic CAH is characterized by a generally less severe dysregulation of cortisol production and clinically manifests with a variety of late-onset virilizing symptoms. Females may experience irregular periods, hirsutism, deep voice, and infertility. Some males and females may experience early onset puberty and rapid growth in childhood but short stature in adulthood. Other symptoms of non-classic CAH include low bone density, severe acne, obesity, and elevated lipids. Patients with non-classic CAH typically do not require glucocorticoids to replace deficiencies in cortisol levels. However, they possess high levels of adrenal androgens caused by the inability of their endogenous levels of cortisol to properly regulate ACTH production and adrenal stimulation. Although, genetic mutations have been associated with about 30% to 40% of residual 21-hydroxylase enzymatic activity, approximately 5% of patients presenting with non-classic CAH may have a mutation in one copy of the 21-hydroxylase gene, that results in clinical phenotype that is indistinguishable from classic CAH. We believe that tildacerfont has the potential to bring non-steroidal therapeutic benefit to these non-classic CAH patients with the severe form of disease.

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 tildacerfont, if approved, in the United States and Europe. Given a relatively small number of endocrinologists and specialists treat a large proportion of patients with classic CAH, we believe this market can be effectively addressed with a modest-sized targeted commercial sales force, alongside various high-touch patient initiatives. If tildacerfont is approved for additional indications, we plan to leverage our rare disease commercial infrastructure and expertise to efficiently address those patient populations. We may also either build a commercial infrastructure or opportunistically seek strategic collaborations to benefit from the resources of biopharmaceutical companies specialized in either relevant disease areas or geographies.

License Agreement with Eli Lilly and Company

In May 2016, we entered into a license agreement, or the License Agreement, with Eli Lilly and Company, or Lilly. Pursuant to the terms of the License Agreement, Lilly granted us an exclusive, worldwide, royalty bearing, sublicensable license under certain technology, patent rights, know-how, and proprietary materials, which we refer to collectively as the Lilly IP, and such patents, the Lilly Licensed Patents, relating to the CRF1 receptor antagonist compounds either listed in the License Agreement or covered by patent rights controlled by Lilly, which we refer to collectively as 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, which we refer to collectively as the Lilly Licensed Products, for all pharmaceutical uses, including all diagnostic, therapeutic, and prophylactic uses, for human or animal administration, which we refer to as the Field. Lilly retained rights under the Lilly IP and the Lilly Licensed Patents for internal research purposes.

Under the 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 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 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 sub-teens, or 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 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 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.

Intellectual Property

We have developed and continue to expand our patent portfolio for tildacerfont. We have licensed from Lilly 31 patents in the United States and other countries throughout the world covering composition of matter of tildacerfont, which are expected to expire in 2027, absent any patent term adjustments or extensions. We also have pending applications from the same family in El Salvador, Venezuela, and Pakistan covering tildacerfont, which, if issued, would also be expected to expire in 2027, absent any patent term adjustments or extensions. Additionally, we have licensed patents in the United States and other countries from Lilly covering methods of making tildacerfont, which are 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, and one of these applications has been issued. The issued patent is expected to expire around 2038. The remaining patent applications, if issued, would be expected to expire between 2038 and 2041, absent any patent term adjustments or extensions. We have also filed an international patent application and applications in Argentina and Taiwan directed to combination therapies as well as further uses of tildacerfont. Any patents that would issue from these applications would be expected to expire no later than 2040, absent any patent term adjustments or extensions. 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.

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 Agreement, Lilly granted intellectual property rights to know-how that are important to our business. The License Agreement imposes various development, regulatory, and commercial diligence obligations, payment of milestones and/or royalties, and other obligations.

In addition, we have been granted Orphan Drug Designation for tildacerfont for the treatment of patients with CAH in the United States and the EU, providing the opportunity to receive seven years of market exclusivity in the United States, which can be extended to seven and a half years if clinical trials are conducted in accordance with an agreed-upon pediatric investigational plan, and ten years of market exclusivity in the EU, which can be extended to 12 years in the EU if clinical trials are conducted in accordance with an agreed-upon PIP.

Upon approval in the United States, as tildacerfont has not previously been approved in the United States for any indication, tildacerfont may be eligible for five years of new chemical entity exclusivity, which would run currently with its seven years of orphan drug exclusivity if we obtain orphan drug exclusivity for its approved uses. Further, upon approval in the EU, as tildacerfont has not previously been approved in the EU for any indication,

tildacerfont may be eligible for eight years of data exclusivity, as well as two years of market exclusivity. In the EU, an additional one year of exclusivity may be obtained if tildacerfont is approved for a new indication that provides a significant clinical benefit.

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.

In addition to patent protection around tildacerfont, we have also licensed from Lilly patents in the United States and other countries throughout the world directed to composition of matter around other CRF1 antagonists.

Manufacturing

We rely on contract manufacturing organizations, or CMOs, to produce tildacerfont in accordance with the FDA's current Good Manufacturing Practices, or 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. Tildacerfont is manufactured using common chemical engineering and synthetic processes from readily available raw materials. We have entered into manufacturing, development, and clinical supply agreements with our CMOs that provide for the procurement of active pharmaceutical ingredient, or API, and drug product in connection with our planned and future clinical trials. These agreements contain no minimum purchase commitments or other purchase obligations. To date, the CMOs have met our manufacturing requirements, and we expect them to be capable of providing sufficient quantities of API and our drug product to meet estimated full-scale commercial needs. We plan to enter into commercial manufacturing and supply agreements with our CMOs prior to commercialization of tildacerfont, if approved, in the United States and Europe. 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 tildacerfont at commercial scale. Based upon a range of prices of currently marketed therapies indicated for orphan diseases, we believe that our cost of goods for tildacerfont will be highly competitive.

Competition

The commercialization of new drugs is competitive, and we may face worldwide competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, and ultimately generic companies. Our competitors may develop or market therapies that are more effective, safer, or less costly than any that we are commercializing, or may obtain regulatory or reimbursement approval for their therapies more rapidly than we may obtain approval for ours.

We are aware of three other companies actively developing treatments for patients with classic CAH. Neurocrine Biosciences, Inc., or Neurocrine, is developing a CRF1 receptor antagonist and has completed a two-week Phase 2 clinical trial in adults with classic CAH. Neurocrine has initiated a Phase 2 clinical trial in children between the ages of 14 and 17 years of age diagnosed with classic CAH and a registrational trial for adult patients with classic CAH. Neurocrine has initiated a registrational program in pediatric classic CAH in 2021. BridgeBio Pharma, Inc. plans to evaluate an AAV5 gene therapy product candidate to treat classic CAH in a Phase 1/2 proof of concept study in 2021. In addition, Crinetics Pharmaceuticals, Inc. has initiated a Phase 1 study in 2021 to evaluate to ability of an oral ACTH antagonist to suppress ACTH-stimulated secretion in healthy volunteers.

In addition, while tildacerfont ultimately seeks to significantly reduce steroid use for patients with classic CAH, patients will continue use of their steroid regimen. As high doses of corticosteroids are the current standard of care for the treatment of classic CAH, in the United States alone, there are more than two dozen companies

manufacturing steroid-based products. One such company is Diurnal Group PLC, or Diurnal, which is developing an exogenous cortisol treatment with a modified release intended to more closely match the physiological release profile of cortisol but recently announced a failed Phase 3 clinical trial and placed its U.S. development activities on hold. Diurnal submitted a Marketing Authorization Application, or MAA, to the EMA in December of 2019.

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. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or FDCA, and implementing regulations. Drugs 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 drug 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, or 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 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, or 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, or NDA, for a new drug;
- a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug 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 drug'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 NDA;
- satisfactory completion of an FDA advisory committee review, if applicable; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Before testing any compounds with potential therapeutic value in humans, the drug 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 drug 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 drug candidate at any time before or during clinical trials due to safety concerns or non-compliance.

Clinical trials involve the administration of the drug candidate 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.

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.

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

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

After the NDA submission is accepted for filing, the FDA reviews the NDA 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, 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, 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 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 NDA, 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 NDA 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 of the NDA 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, or REMS, is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA 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.

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. 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.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and 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 for 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, or ANDA, or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, 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 innovator 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.

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.

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) and teaching hospitals, certain ownership and investment interests held by physicians and their immediate family members. Beginning in

2022, applicable manufacturers also will be required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year.

We may also be subject to 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, or 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 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, or 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 influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other Member States allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs 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 Affordable Care Act's provisions of importance to the pharmaceutical industry, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and a cap on the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, including individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There have been executive, judicial and Congressional challenges to certain aspects of the Affordable Care Act. For example, the Tax Cuts and Jobs Act of 2017, or the Tax Act, was enacted, which includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the Affordable Care Act are invalid as well. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The U.S. Supreme Court is currently reviewing this case, although it is unknown when a decision will be made. Although the U.S. Supreme Court has not yet ruled on the constitutionality of the Affordable Care Act, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden 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 through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic, unless additional Congressional action is taken. In addition, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

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 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. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. Several final rules have been recently promulgated that seek to implement several of the Trump administration's proposals. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives.

We anticipate that these new laws will result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. 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. Further, it is possible that additional government action is taken in response to the COVID-19 pandemic.

Data Privacy and Security

We may also be subject to federal, state, and foreign data privacy and security laws and regulations. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations (e.g., Section 5 of the FTC Act), govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. HIPAA, as amended by HITECH, and its implementing regulations, impose requirements relating to the privacy, security and transmission of individually identifiable health information on certain health care providers, health plans and health care clearinghouses, known as covered entities, and their business associates that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities as well as their covered subcontractors. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Further, entities that 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 may be subject to criminal penalties.

Even when HIPAA does not apply, according to the FTC, violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5 of the FTC Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

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. By way of example, California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling certain personal data of consumers or households. The California Consumer Privacy Act, or the CCPA, requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA became effective on January 1, 2020, and the California Attorney General may bring enforcement actions for violations beginning July 1, 2020. The CCPA has been amended from time to time, and it remains unclear what, if any, further modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

We also are or will become subject to privacy laws in the jurisdictions in which we are established or in which we sell or market our products or run clinical trials. For example, in the European Economic Area, or EEA, we are subject to Regulation (EU) 2016/679, the GDPR, in relation to our collection, control, processing, and other use of personal data (i.e. data relating to an identified or identifiable living individual). We process personal data in relation to participants in our clinical trials in the EEA including the health and medical information of these participants. The GDPR is directly applicable in each EU and EEA Member State, and, by operation of the so-called UK GDPR, on which see more below, continues to apply in substantially equivalent form in the context of the United Kingdom-related establishments and processing operations, and may therefore apply in the context of our United Kingdom-related processing operations. The GDPR provides that EEA member states may make their own further laws and regulations to introduce specific requirements related to the processing of 'special categories of personal data,' including personal data related to health, biometric data used for unique identification purposes and genetic information; as well as personal data related to criminal offences or convictions – in the United Kingdom, the United Kingdom Data Protection Act 2018 complements the UK GDPR in this regard. Such laws may introduce further conditions, including limitations which could limit our ability to collect, use and share personal data, and/or otherwise lead to greater divergence on the law that applies to the processing of such data types across the EEA and/or United Kingdom, compliance with which, as and where applicable, may increase our costs and could increase our overall compliance risk. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and implement policies as part of its mandated privacy governance framework. It also requires data controllers to be transparent and disclose to data subjects (in a concise, intelligible and easily accessible form) how their personal information is to be used, imposes limitations on retention of personal data; defines for the first time pseudonymized (i.e., key-coded) data; introduces mandatory data breach notification requirements; and sets higher standards for data controllers to demonstrate that they have obtained valid consent for certain data processing activities. A particular issue presented by certain European data protection laws, including the GDPR, is that they generally restrict transfers of personal data from Europe, including the EEA, United Kingdom and Switzerland, to the United States and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal data.

Recent legal developments in the EU have created complexity and uncertainty regarding such transfers of personal data from the EEA to the United States, e.g. on July 16, 2020 in a case known colloquially as "Schrems II," the Court of Justice of the European Union, or the CJEU, invalidated the EU-US Privacy Shield Framework, or the Privacy Shield, under which personal data could be transferred from the EEA to U.S. entities who had self-certified under the Privacy Shield scheme. Following this decision, the United Kingdom government has similarly invalidated use of the EU U.S. Privacy Shield as a mechanism for lawful personal data transfers from the United Kingdom to the United States under the so-called UK GDPR, and the Swiss Federal Data Protection and Information Commissioner announced that the Swiss-U.S. Privacy Shield does not provide adequate safeguards for the purposes of personal data transfers from Switzerland to the United States. The CJEU's decision in Schrems II also raised questions about whether one of the primary alternatives to the EU-U.S. Privacy Shield, namely, the European Commission's Standard Contractual Clauses, can lawfully be used for personal data transfers from Europe to the United States or other third countries that are not the subject of an adequacy decision of the European Commission. While the CJEU upheld the adequacy of the Standard Contractual Clauses in principle in Schrems II, it made clear that reliance on those Clauses alone may not necessarily be sufficient in all circumstances. Use of the Standard Contractual Clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular regarding applicable surveillance laws and relevant rights of individuals with respect to the transferred data. In the context of any given transfer, where the legal regime applicable in the destination country may or does conflict with the intended operation of the Standard Contractual Clauses and/or applicable European law, the decision in Schrems II and subsequent draft guidance from the European Data Protection Board, or EDPB, would require the parties to that transfer to implement certain supplementary technical, organizational and/or contractual measures to rely on the Standard Contractual Clauses as a compliant 'transfer mechanism.' However, the aforementioned draft guidance from the EDPB on such supplementary technical, organizational and/or contractual measures appears to conclude that no combination of such measures could be sufficient to allow effective reliance on the Standard Contractual Clauses in the context of transfers of personal data 'in the clear' to recipients in countries where the power granted to public authorities to access the transferred data goes beyond that which is 'necessary and proportionate in a democratic society' – which may, following the CJEU's conclusions in Schrems II on relevant powers of United States public authorities and commentary in that draft EDPB guidance, include the United States in certain circumstances (e.g., where Section 702 of the US Foreign Intelligence Surveillance Act applies). At present, there are few, if any, viable alternatives to

the EU-U.S. Privacy Shield and the Standard Contractual Clauses. As such, if we are unable to implement a valid solution for personal data transfers from Europe, including, for example, obtaining individuals' explicit consent to transfer their personal data from Europe to the United States or other countries, we will face increased exposure to regulatory actions, substantial fines and injunctions against processing personal data from Europe. Inability to import personal data from Europe, including the EEA, United Kingdom or Switzerland, may also: restrict our activities in Europe; limit our ability to collaborate with partners as well as other service providers, contractors and other companies subject to European data protection laws; and/or require us to increase our data processing capabilities in Europe at significant expense or otherwise cause us to change the geographical location or segregation of our relevant systems and operations – any or all of which could adversely affect our financial results. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of delivering our services and operating our business. The type of challenges we face in Europe will likely also arise in other jurisdictions that adopt laws similar in construction to the GDPR or regulatory frameworks of equivalent complexity.

We are subject to the supervision of local data protection authorities in those EU jurisdictions where we are established or otherwise subject to the GDPR, and we maintain an office in Switzerland, which has its own set of stringent privacy and data protection laws and regulations. Fines for certain breaches of the GDPR are significant: up to the greater of €20 million or 4% of total global annual turnover. Further, the United Kingdom's vote in favor of exiting the European Union, often referred to as Brexit, and ongoing developments in the United Kingdom have created uncertainty with regard to data protection regulation in the United Kingdom. Following the United Kingdom's withdrawal from the European Union on January 31, 2020, pursuant to the transitional arrangements agreed to between the United Kingdom and European Union, the GDPR continued to have effect in United Kingdom law, and continued to do so until December 31, 2020 as if the United Kingdom remained a Member State of the European Union for such purposes. Following December 31, 2020, and the expiry of those transitional arrangements, the data protection obligations of the GDPR continue to apply to United Kingdom-related processing of personal data in substantially unvaried form under the so-called "UK GDPR" (i.e., the GDPR as it continues to form part of law in the United Kingdom by virtue of section 3 of the European Union (Withdrawal) Act 2018, as amended (including by the various Data Protection, Privacy and Electronic Communications (Amendments etc) (EU Exit) Regulations)). However, going forward, there will be increasing scope for divergence in application, interpretation and enforcement of the data protection law as between the United Kingdom and EEA. Furthermore, the relationship between the United Kingdom and the EEA in relation to certain aspects of data protection law remains somewhat uncertain. For example, it is unclear whether transfers of personal data from the EEA to the United Kingdom will be permitted to take place on the basis of a future adequacy decision of the European Commission, or whether a "transfer mechanism," such as the Standard Contractual Clauses, will be required. For the meantime, under the post-Brexit Trade and Cooperation Agreement between the European Union and the United Kingdom, it has been agreed that transfers of personal data to the United Kingdom from European Union Member States will not be treated as "restricted transfers" to a non-EEA country for a period of up to four months from January 1, 2021, plus a potential further two months extension, or the extended adequacy assessment period. This will also apply to transfers to the United Kingdom from EEA Member States, assuming those Member States accede to the relevant provision of the Trade and Cooperation Agreement. Although the current maximum duration of the extended adequacy assessment period is six months it may end sooner, for example, in the event that the European Commission adopts an adequacy decision in respect of the United Kingdom, or the United Kingdom amends the UK GDPR and/or makes certain changes regarding data transfers under the UK GDPR/ Data Protection Act 2018 without the consent of the European Union (unless those amendments or decisions are made simply to keep relevant United Kingdom laws aligned with the European Union's data protection regime). If the European Commission does not adopt an 'adequacy decision' in respect of the United Kingdom prior to the expiry of the extended adequacy assessment period, from that point onwards the United Kingdom will be an "inadequate third country" under the GDPR and transfers of data from the EEA to the United Kingdom will require a "transfer mechanism," such as the Standard Contractual Clauses.

Additionally, as noted above, the United Kingdom has transposed the GDPR into United Kingdom domestic law by way of the UK GDPR with effect from January 2021, which could expose us to two parallel regimes, each of which potentially authorizes similar fines and other potentially divergent enforcement actions for certain violations. Also, following the expiry of the post-Brexit transitional arrangements, the United Kingdom Information Commissioner's Office is not able to be our "lead supervisory authority" in respect of any "cross border processing"

for the purposes of the GDPR. For so long as we are unable to, and/or do not, designate a lead supervisory authority in an EEA member state, with effect from January 1, 2021, we are not able to benefit from the GDPR's "one stop shop" mechanism. Amongst other things, this would mean that, in the event of a violation of the GDPR affecting data subjects across the United Kingdom and the EEA, we could be investigated by, and ultimately fined by the United Kingdom Information Commissioner's Office and the supervisory authority in each and every EEA member state where data subjects have been affected by such violation.

For more information on the potential impact of the GDPR, and associated EEA data protection laws, on our business, see the section titled "Risk Factors—Failure to comply with data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business."

The U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act of 1977, or FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the 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. In the EU, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under the EU regulatory systems, we must submit a marketing authorization application either under the so-called centralized or national authorization procedures.

Centralized procedure. The centralized procedure provides for the grant of a single marketing authorization, which is issued by the European Commission based on the opinion of the Committee for Medicinal Products for Human Use, or the CHMP, of the EMA and that is valid in all EU Member States, as well as Iceland, Liechtenstein and Norway. 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 constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the Centralized Procedure 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, when the authorization of a medicinal product is 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.

- *National authorization procedures*. There are also two other possible routes to authorize medicinal products in several EU countries, 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.

In the EEA, upon receiving marketing authorization, new chemical entities 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. 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. 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.

The EMA grants orphan drug designation to promote the development of products that may offer therapeutic benefits for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the EU. In addition, orphan drug designation can be granted if the drug is intended for a life threatening, seriously debilitating or serious and chronic condition in the EU and without incentives it is unlikely that sales of the drug in the EU would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the EU of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation provides opportunities for free protocol assistance, fee reductions for access to the centralized regulatory procedures and ten years of market exclusivity following drug approval, which can be extended to 12 years if trials are conducted in accordance with an agreed-upon pediatric investigational plan. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

For other countries outside of the EU, such as 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. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

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

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, 2020, we had 17 employees, including 11 in research and development and six 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. In response to the COVID-19 pandemic, we implemented significant changes that we determined were in the best interest of our employees, as well as the communities in which we operate, and which comply with government regulations. This includes allowing our employees to work from home.

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 2001 Junipero Serra Boulevard, Suite 640, Daly City, CA 94014. 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, 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 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 on Form 10-K, 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.

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 only product candidate, tildacerfont. 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 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 tildacerfont is not successfully developed and approved in the United States or Europe, we may never generate any revenue. For the year ended December 31, 2020, we reported a net loss of $29.5 million. As of December 31, 2020, we had an accumulated deficit of $60.8 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 tildacerfont and any future product candidates. 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 tildacerfont and any future 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, tildacerfont and any future product candidates. We will require significant additional amounts in order to prepare for commercialization, and, if approved, to launch and commercialize tildacerfont.

As of December 31, 2020, we had cash and cash equivalents of $157.2 million. In October 2020, we consummated our initial public offering, or 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. We believe, based on our current operating plan, that our cash and cash equivalents will be sufficient to fund our operations for at least the next 12 months.

However, 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. For example, as a result of the COVID-19 pandemic, we have amended our clinical trial protocols to enable remote visits to mitigate any potential impacts. As a result of this home health component, the overall costs of our Phase 2b clinical trials have increased and may continue to increase in the future.

We will require additional capital for the further development and commercialization of tildacerfont and any 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. As a result of the COVID-19 pandemic and actions taken to slow its spread, 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 tildacerfont 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 tildacerfont 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 currently depend entirely on the success of tildacerfont, which is our only product candidate. If we are unable to advance tildacerfont in clinical development, obtain regulatory approval, and ultimately commercialize tildacerfont, or experience significant delays in doing so, our business will be materially harmed.

We currently only have one product candidate, tildacerfont, and our business and future success depends entirely on our ability to develop, obtain regulatory approval for, and then successfully commercialize, tildacerfont, which is currently in clinical development for adult patients with classic CAH. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development that may be able to better sustain failure of a lead product candidate. We have initiated CAHmelia-203, a placebo-controlled, double-blind Phase 2b clinical trial in adult patients with classic CAH with poor disease control and anticipate topline results in the first half of 2022. We have also initiated CAHmelia-204, a second Phase 2b clinical trial in adult patients with classic CAH with good disease control focused on glucocorticoid reduction and anticipate topline results in the second half of 2022.

Assuming positive results in CAHmelia-204, we plan to meet with the FDA and comparable foreign regulatory authorities to discuss registration. While we believe these two clinical trials will provide sufficient patient exposures for our registrational safety database, the FDA and comparable foreign regulatory authorities may not agree and may require us to enroll additional patients or initiate one or more additional clinical trials, including a Phase 3 clinical trial or trials. If the FDA or comparable foreign regulatory authorities require us to conduct one or more clinical trials, including a Phase 3 clinical trial or trials, the design, duration, and scope of such clinical trials will be decided upon after further discussions with the FDA or comparable foreign regulatory authorities, and at this time are not ascertainable. As a result, we are unable to predict with certainty the estimated timing or scope of any future clinical trials of tildacerfont we may be required to conduct.

In addition, we have received feedback from the FDA and European Medicines Agency, or EMA, on our planned Phase 2 clinical trial of tildacerfont in children with classic CAH in order to initiate the clinical development program for tildacerfont in the pediatric classic CAH population in the second half of 2021. The COVID-19 pandemic continues to evolve and any impacts on these projected milestones for both the adult and pediatric classic CAH programs are highly uncertain and cannot be predicted with confidence.

The success of tildacerfont will depend on several factors, including the following:

- successful enrollment in our ongoing and planned clinical trials and completion of such clinical trials with favorable results;
- acceptance by the FDA and EMA of data from our ongoing Phase 2b clinical trials in adult patients with classic CAH;
- demonstrating safety and efficacy to the satisfaction of applicable regulatory authorities;
- the outcome, timing, and cost of meeting regulatory requirements established by the FDA, EMA, and other comparable foreign regulatory authorities;
- receipt of marketing approvals from applicable regulatory authorities, including one or more 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 tildacerfont;
- 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 tildacerfont.

Even if regulatory approvals are obtained, we may never be able to successfully commercialize tildacerfont. 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.

Our clinical trials may fail to adequately demonstrate the safety and efficacy of tildacerfont, 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 rare endocrine disorders for which there is limited clinical experience, and our two ongoing Phase 2b clinical trials use novel endpoints that do not have regulatory precedent in classic CAH due to the lack of clinical trials in classic CAH, which add complexity to the conduct and analysis of data from our clinical trials and may delay or prevent regulatory approval. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of tildacerfont in other indications.

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 tildacerfont and any future product candidates.

Preclinical and clinical testing is expensive and 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 tildacerfont may not be predictive of the results of later-stage clinical trials. However, 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, tildacerfont has not yet been evaluated in pediatric patients with classic CAH, and the results may not be similar to the results observed in clinical trials of adult patients. In addition, we intend to use doses in our two Phase 2b clinical trials 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 may face significant setbacks as we conduct our two Phase 2b clinical trials in adult patients with classic CAH, which may delay or prevent regulatory approval of tildacerfont.

Further, if patients drop out of our clinical trials, miss scheduled doses or follow-up visits, or otherwise fail to follow clinical trial protocols, whether as a result of the COVID-19 pandemic, actions taken to slow the spread of COVID-19 or otherwise, 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 tildacerfont and any 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, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial, the design of the clinical trial, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

In particular, each indication for which we are evaluating tildacerfont is a rare endocrine disorder with limited patient populations from which to draw participants in clinical trials. For example, we estimate the total classic CAH populations are approximately 20,000 to 30,000 people in the United States and approximately 50,000 people in the European Union, or EU. We will be required to identify and enroll a sufficient number of patients with the disorder under investigation for our clinical trials of tildacerfont. 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 endocrine 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.

Our clinical trials have been, and may in the future be, affected by the COVID-19 pandemic. For example, the COVID-19 pandemic may impact patient enrollment in our two ongoing Phase 2b clinical trials. In particular, some sites may pause enrollment to focus on, and direct resources to, COVID-19, while at other sites, patients may choose not to enroll or continue participating in the clinical trial as a result of the pandemic. In addition, patient visits to endocrinologists in the United States have slowed as a result of the COVID-19 pandemic. Further, according to the Centers for Disease Control and Prevention, people who have serious chronic medical conditions, including those such as classic CAH, are at higher risk of getting very sick from COVID-19. As a result, current or potential patients in our ongoing and planned clinical trials may choose to not enroll, not participate in follow-

up clinical visits, or drop out of the trial as a precaution against contracting COVID-19. Further, some patients may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services.

We are unable to predict with confidence the likelihood or duration of such patient enrollment delays and difficulties, whether related to COVID-19 or otherwise. If patient enrollment is delayed for an extended period of time, our Phase 2b clinical trials 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.

Before we can initiate clinical trials for tildacerfont 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 tildacerfont or any future product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of tildacerfont 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 CROs and other third parties for regulatory submissions for tildacerfont 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, or IRBs, or Ethics Committees, or ECs;
- IRBs or ECs refusing to approve, suspending or terminating the clinical trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the clinical trial;
- changes to clinical trial protocols;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- sites deviating from clinical trial protocol or dropping out of a clinical trial;
- manufacturing sufficient quantities of tildacerfont or any 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 tildacerfont and any future product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- 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 tildacerfont 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, or cGMP, regulations or other applicable requirements, or infections or cross-contaminations of tildacerfont 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, or 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 the COVID-19 pandemic on our ongoing and planned clinical trials.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting, or completing our planned and ongoing 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 IRBs 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 tildacerfont or any future product candidates, the commercial prospect of tildacerfont or any 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 tildacerfont or any 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 tildacerfont and our competitors may be able to bring products to market before we do, and the commercial viability of tildacerfont could be significantly reduced. Any of these occurrences may harm our business, financial condition, and prospects significantly.

Tildacerfont is, and any 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 tildacerfont and any future product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing, and distribution of tildacerfont is 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 tildacerfont and any 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 tildacerfont and any future product candidates in the United States until we receive approval of an NDA from the FDA. We have not previously submitted an NDA 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 tildacerfont 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 tildacerfont and any future product candidates either prior to or post-approval, or may object to elements of our clinical development program.

Tildacerfont and any 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 tildacerfont and any 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 of tildacerfont and any future product candidates may not be sufficient to satisfy the FDA or comparable foreign regulatory authorities to support the submission of an NDA 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 two ongoing Phase 2b clinical trials 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 tildacerfont or any future product candidates and could substantially increase the costs of commercializing tildacerfont or any future product candidates. The demand for 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 any 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 or foreign marketing application for tildacerfont and any 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, or REMS, 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.

Our business has been and could continue to be adversely affected by the evolving and ongoing COVID-19 global pandemic in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. The COVID-19 pandemic could adversely affect our operations, as well as the business or operations of our manufacturers, CROs, or other third parties with whom we conduct business.

Our business has been and could continue to be adversely affected by the evolving COVID-19 pandemic, which was declared by the World Health Organization as a global pandemic. As COVID-19 continues to spread, we may experience ongoing disruptions that could severely impact our business and clinical trials, including:

- delays or difficulties in enrolling patients in our clinical trials;

- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site; investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruption in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 outbreak which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;
- interruptions or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- risk that participants enrolled in our clinical trials will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- refusal of the FDA to accept data from clinical trials in affected geographies; and
- increased costs relating to mitigating the impact of COVID-19 on any of the foregoing factors.

These and other disruptions in our operations and the global economy could negatively impact our business, operating results and financial condition.

Our clinical trials have been, and may in the future be, affected by the COVID-19 pandemic. For example, the COVID-19 pandemic may impact patient enrollment in our two ongoing Phase 2b clinical trials. In particular, some sites may pause enrollment to focus on, and direct resources to, COVID-19, while at other sites, patients may choose not to enroll or continue participating in the clinical trial as a result of the pandemic. In addition, patient visits to endocrinologists in the United States have slowed as a result of the COVID-19 pandemic. Further, according to the Centers for Disease Control and Prevention, people who have serious chronic medical conditions, including those such as classic CAH, are at higher risk of getting very sick from COVID-19. As a result, current or potential patients in our ongoing and planned clinical trials may choose to not enroll, not participate in follow-up clinical visits, or drop out of the trial as a precaution against contracting COVID-19. Further, some patients may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupts healthcare services.

If patient enrollment is delayed for an extended period of time, our ongoing and planned clinical trials could be delayed or otherwise adversely affected. Similarly, our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, may be adversely impacted.

In addition, ongoing or planned clinical trials may also be impacted by interruptions or delays in the operations of the FDA and comparable foreign regulatory agencies. For example, we and our CROs have also made certain adjustments to the operation of our trials in an effort to ensure the monitoring and safety of patients and minimize risks to trial integrity during the pandemic in accordance with the guidance issued by the FDA, and may need to make further adjustments in the future. For example, we have amended our clinical trial protocols to enable remote visits to mitigate any potential impacts as a result of the COVID-19 pandemic. As a result of this home health component, the overall costs of our Phase 2b clinical trials have increased and may continue to increase in the future. Many of these adjustments are new and untested, may not be effective, may affect the integrity of data collected, and may have unforeseen effects on the progress and completion of our clinical trials and the findings from such clinical trials.

In addition, we may encounter a shortage in supplies of, or in delays in shipping, our study drug or other components of the clinical trial vital for successful conduct of the trial. For example, in our two ongoing Phase 2b clinical trials, patients will continue to use their steroid regimen for the duration of the clinical trial. In particular, we have experienced a shortage of supply of hydrocortisone as a result of the COVID-19 pandemic, which if continued indefinitely, could adversely affect the timing and ultimately success of our clinical trials. Further, the successful conduct of our clinical trials depends on retrieving laboratory data from patients. Any failure by the laboratories with which we work to send us such data could impair the progress of such clinical trials. These events could delay our clinical trials, increase the cost of completing our clinical trials, and negatively impact the integrity, reliability, or robustness of the data from our clinical trials.

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 COVID-19 or other infectious diseases could impact personnel at our CROs or third-party manufacturing facilities upon which we rely, or the availability or cost of materials, which could disrupt the supply chain for tildacerfont. To the extent our suppliers and service providers are unable to comply with their obligations under our agreements with them or they are otherwise unable to deliver or are delayed in delivering goods and services to us due to the COVID-19 pandemic, our ability to continue meeting clinical supply demand for tildacerfont or otherwise advancing development of tildacerfont may become impaired.

The spread of COVID-19 and actions taken to reduce its spread may also materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, there could be a significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity and financial position. In addition, the trading prices for other companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms.

COVID-19 and actions taken to reduce its spread continue to evolve. The extent to which COVID-19 may impede the development of tildacerfont, reduce the productivity of our employees, disrupt our supply chains, delay our clinical trials, reduce our access to capital or limit our business development activities, will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this “Risk Factors” section.

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, topline, and preliminary 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. 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.

Further, others, including regulatory agencies, 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 approval for, and commercialize, tildacerfont and any future product candidates may be harmed, which could harm our business, operating results, prospects, or financial condition.

If the market opportunities for tildacerfont and any 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 tildacerfont 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 of tildacerfont on treatments for rare endocrine disorders with relatively small patient populations. For example, we believe that tildacerfont has the potential to bring therapeutic benefit to patients suffering from endocrine disorders where the underlying disease biology supports a need to reduce excess secretion of or hyperresponsiveness to ACTH, including, but not limited to, a severe form of non-classic CAH in adults and a subpopulation of females with a rare form of PCOS with primary adrenal androgen excess, representing 3-5% of females with PCOS (estimated to be 150,000 to 200,000 patients in the United States). Given the relatively small number of patients who have the disorders that we are targeting and intend to target with tildacerfont, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare endocrine 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, while classic CAH is usually detected at birth through required newborn screening programs in most developed countries, new 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 classic CAH may be limited or may not be amenable to treatment with tildacerfont, if approved. Further, even if we obtain significant market share for tildacerfont in classic CAH, 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 endocrine disorder.

We may not be successful in our efforts to expand our pipeline by identifying additional indications and formulations for which to investigate tildacerfont in the future. We may expend our limited resources to pursue a particular indication or formulation for tildacerfont and fail to capitalize on product candidates, indications, or formulations that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we are focused on specific indications and formulations for tildacerfont. As a result, we may fail to generate additional clinical development opportunities for tildacerfont for a number of reasons, including, tildacerfont may in certain indications, on further study, be shown to have harmful side effects, limited to no efficacy, or other characteristics that suggest it is unlikely to receive marketing approval and achieve market acceptance in such additional indications.

We plan to conduct several clinical trials for tildacerfont in parallel over the next several years, including multiple clinical trials in adult and pediatric patients with classic CAH and in a subpopulation of females with a rare form of PCOS. As a result, we may forgo or delay pursuit of opportunities with other indications that could have had greater commercial potential or likelihood of success. However, we may focus on or pursue one or more of our target indications over other potential indications and such development efforts may not be successful, which would cause us to delay the clinical development and approval of tildacerfont. Furthermore, research programs to identify additional indications for tildacerfont require substantial technical, financial, and human resources. We may also pursue additional formulations for tildacerfont, including transitioning from a tablet formulation to a granulate formulation. However, we may not successfully develop these additional formulations for chemistry-related, stability-related, or other reasons. Our resource allocation decisions may cause us to fail to capitalize on viable

commercial products or profitable market opportunities. Our spending on current and future research and development programs for specific indications may not yield any commercially viable products.

Additionally, we may pursue additional in-licenses or acquisitions of development-stage assets or programs, which entails additional risk to us. Identifying, selecting and acquiring promising product candidates requires substantial technical, financial, and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a particular product candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit.

For example, if we are unable to identify programs that ultimately result in approved products, we may spend material amounts of our capital and other resources evaluating, acquiring and developing products that ultimately do not provide a return on our investment.

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, 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 tildacerfont is also subject to approval.

We expect to submit a Marketing Authorization Application, or MAA, to the EMA for approval of tildacerfont in the EU for the treatment of classic CAH. As with the FDA, obtaining approval of an MAA from the EMA is a similarly lengthy and expensive process and the EMA has its own procedures for approval for 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 tildacerfont 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 tildacerfont 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 tildacerfont and any 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 tildacerfont 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 tildacerfont, if approved, in the United States and Europe.

The establishment and development of our own sales force or the establishment of a contract sales force to market tildacerfont 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 of tildacerfont. To the extent we rely on third parties to commercialize tildacerfont, 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 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 tildacerfont or any future product candidates.

Use of tildacerfont or any 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 tildacerfont and any 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 tildacerfont and any future product candidates could cause us or regulatory authorities to interrupt, delay 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 171 patients across seven 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, or ALT, between five and nine times the upper limit of normal, or ULN, elevations in aspartate aminotransferase, or AST, less than five times the ULN, and no increases in bilirubin. The event resolved on its own without additional medical intervention. No cases of liver enzyme elevations above three times the ULN were observed in any patient receiving total daily doses of 600mg, which is approximately three times the proposed therapeutic dose for adults with classic CAH, and below. 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. The 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, only adults have been treated with tildacerfont, and the safety profile in pediatric patients is unknown and may be different than that observed in previous clinical trials. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects.

Additionally, if tildacerfont and any 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 change their approvals of such product;
- 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, or to sued and held liable for harm caused to subjects or patients;
- 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 tildacerfont and any future product candidates, if approved, and could significantly harm our business, results of operations, and prospects.

If we receive regulatory approval for tildacerfont and any 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.

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 also requires 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 or modify any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- 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 tildacerfont and any 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, or the DOJ, the Office of Inspector General of the U.S. Department of Health and Human Services, or 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 bodies. 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 FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval for tildacerfont and any future product candidates. 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 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 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 agency 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 may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical 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.

Separately, in response to the global COVID-19 pandemic, in March 2020 the FDA announced its intention to postpone most foreign inspections of manufacturing facilities and products and routine surveillance inspections of domestic manufacturing facilities. In July 2020, the FDA restarted routine pre-announced surveillance inspections of domestic manufacturing facilities on a risk-based basis. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to 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 tildacerfont and any future product candidates, tildacerfont and any future product candidates may not gain market acceptance among physicians, patients, healthcare payors and others in the medical community.

Tildacerfont and any future product candidates may not be commercially successful. The commercial success of tildacerfont or any 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 tildacerfont or any 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 tildacerfont and any 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. In addition, even if tildacerfont and any 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 tildacerfont and any future product candidate is approved for marketing, and we are found to have improperly promoted off-label uses, or if physicians prescribe or use tildacerfont and any future product candidates off-label, we may become subject to prohibitions on the sale or marketing of tildacerfont and any 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, such as tildacerfont, if approved. 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. However, if we receive marketing approval for tildacerfont and any 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 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 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 to have engaged in the promotion of tildacerfont or any 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 tildacerfont and any future product candidates, which could make it difficult for us to sell tildacerfont and any future product candidates profitably.

Successful sales of tildacerfont and any 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 governmental healthcare programs, such as Medicare and Medicaid, 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 of tildacerfont on treatments for rare endocrine disorders with 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. Assuming 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 tildacerfont or any 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 tildacerfont or any 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 tildacerfont and any 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 tildacerfont and any future product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

We intend to seek approval to market tildacerfont in the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for 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.

Recently enacted legislation, future legislation and healthcare reform measures may increase the difficulty and cost for us to obtain marketing approval for and commercialize tildacerfont and any 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 and improve the quality of healthcare.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or 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, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

There have been extensive judicial and Congressional challenges to certain aspects of the Affordable Care Act. By way of example, legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act, or the Tax Act, included a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The United States Supreme Court is currently reviewing this case, although it is unknown when a decision will be made. Although the Supreme Court has not yet ruled on the constitutionality of the Affordable Care Act, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden 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 through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic, unless additional Congressional action is taken. In addition, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

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 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 Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to drug pricing

that attempted to implement several of the Trump administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, implementing a portion of the importation executive order. Further, on November 20, 2020, the U.S. Department of Health & Human Services, or HHS, finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, the Centers for Medicare & Medicaid Services, or CMS, issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives.

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. 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 tildacerfont, 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 the Affordable Care Act, these new laws, and other healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. In addition, it is possible that additional governmental action will be taken in response to the COVID-19 pandemic. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from third-party payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize tildacerfont, if approved.

A variety of risks associated with marketing tildacerfont and any future product candidates internationally could materially adversely affect our business.

We plan to seek regulatory approval for tildacerfont and any future product candidates internationally and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, 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, or 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 may seek to in-license or acquire development-stage product candidates in endocrine disorders that have the potential to complement our existing portfolio. 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. 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.

If we fail to develop tildacerfont for additional indications, our commercial opportunity may be limited.

One of our strategies is to pursue clinical development of tildacerfont in additional endocrine disorders, including, but not limited to, pediatric classic CAH and a subpopulation of females with a rare form of PCOS. The endocrine disorders we are targeting are all rare disorders and, as a result, the market size for the treatment of patients with such disorders is limited. In addition, CRF1 receptor antagonism may not be an appropriate or effective mechanism in indications where disease biology supports a need to reduce ACTH. Due to these factors, our ability to grow revenue may be dependent on our ability to successfully develop and commercialize tildacerfont for the treatment of additional indications. Developing, obtaining regulatory approval and commercializing tildacerfont for additional indications will require substantial additional funding and is prone to the risks of failure inherent in drug development. We may not be able to successfully advance any of these indications through the development process. Even if we receive regulatory approval to market tildacerfont for the treatment of any of these additional indications, any such additional indications may not be successfully commercialized, widely accepted in the

marketplace, or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize tildacerfont for these additional indications, our commercial opportunity may be limited.

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. Although we believe that we hold a leading position in our focus on rare endocrine disorders, 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 tildacerfont. We believe the key competitive factors that will affect the development and commercial success of tildacerfont are efficacy, safety and tolerability profile, reliability, convenience of dosing, price and reimbursement.

Although classic CAH is part of the newborn screening program in most developed countries, there are no known novel therapies that have been approved in approximately 50 years. We are aware of three other companies actively developing treatments for patients with classic CAH. Neurocrine Biosciences, Inc., or Neurocrine, is developing a CRF1 receptor antagonist and has completed a two-week Phase 2 clinical trial in adults with classic CAH. Neurocrine has initiated a Phase 2 clinical trial in a pediatric classic CAH population and a registrational trial for adult patients with classic CAH. Neurocrine has initiated a registrational program in pediatric classic CAH in 2021. BridgeBio Pharma, Inc. plans to evaluate an AAV5 gene therapy product candidate to treat classic CAH in a Phase 1/2 proof of concept study in 2021. In addition, Crinetics Pharmaceuticals, Inc. has initiated a Phase 1 study in 2021 to evaluate the ability of an oral ACTH antagonist to suppress ACTH-stimulated secretion in healthy volunteers.

In addition, while tildacerfont ultimately seeks to significantly reduce steroid use for patients with classic CAH, patients will continue use of their steroid regimen. As corticosteroids are the current standard of care for the treatment of classic CAH, in the United States alone, there are more than two dozen companies manufacturing steroid-based products. One such company is Diurnal Group PLC, or Diurnal, which is developing an exogenous cortisol treatment with a modified release intended to more closely match the physiological release profile of cortisol but recently announced a failed Phase 3 clinical trial and placed its U.S. development activities on hold. Diurnal submitted a MAA to the EMA in December of 2019.

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 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 tildacerfont are likely to be efficacy, safety, and convenience.

Even though we have obtained orphan drug designation for tildacerfont for the treatment of CAH, we may not be able to obtain or maintain the benefits associated with orphan drug status, including market exclusivity.

Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 people in the United States, or a patient population of greater than 200,000 people in the

United States, but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the EMA Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the EU.

We have received orphan drug designation for tildacerfont for the treatment of patients with CAH in both the US and EU. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug may be entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug and same indication for that time period. The applicable period is seven years in the United States and ten years in the EU, which may be extended by six months and two years, respectively, in the case of product candidates that have complied with the respective regulatory agency's agreed upon pediatric investigation plan. The exclusivity period in the EU can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. In addition, even after a drug is granted orphan exclusivity and approved, the FDA and the EMA can subsequently approve a different drug for the same condition or the same drug for a different condition, which may subject the orphan-exclusive product to off-label competition. As well, before the expiration of the orphan exclusivity period, the FDA or EMA may grant approval to a competitor if it concludes that a subsequent application for the same drug for the same indication is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the EU, the EMA may deny marketing approval for a product candidate if it determines such product candidate is structurally similar to an approved product for the same indication. In addition, if an orphan designated product receives marketing approval for an indication broader than or different from what is designated, such product may not be entitled to orphan exclusivity. Even though the FDA has granted orphan drug designation to tildacerfont for the treatment of classic CAH, if we receive approval for tildacerfont for a modified or different indication, our current orphan designations may not provide us with exclusivity.

Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process. Also, regulatory approval for any product candidate may be withdrawn, and other product candidates may obtain approval before us and receive orphan drug exclusivity, which could block us from entering the market.

Even if we obtain orphan drug exclusivity for tildacerfont, that exclusivity may not effectively protect us from competition because different drugs can be approved for the same condition before the expiration of the orphan drug exclusivity period.

We are currently pursuing orphan drug designation for tildacerfont for the treatment of a subpopulation of females with a rare form of PCOS. The incidence and prevalence of this target patient population is based on our estimates and third-party data. If the market opportunity for this target population is larger than we estimate, we may be unable to receive orphan drug designation. Additionally, if orphan drug designation is granted, we may be unable to maintain any benefits associated with orphan drug designation, including market exclusivity.

Periodically, we make estimates regarding the incidence and prevalence of target patient populations based on various third-party sources and internally generated analysis. Our estimates may be inaccurate or based on imprecise data. As described above, under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 people in the United States, or a patient population of greater than 200,000 people in the United States, but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. If our incidence or prevalence estimates for the subpopulation of females with a rare form of PCOS are incorrect, we may be unable to receive orphan drug designation.

Even if the FDA grants orphan drug designation for tildacerfont for the treatment of a subpopulation of females with a rare form of PCOS, exclusive marketing rights in the United States may be limited if we seek FDA marketing approval for an indication broader than the orphan designated indication. Additionally, any product candidate that initially receives orphan drug status designation, may lose such designation if the FDA later

determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, others may obtain orphan drug status for products addressing the same diseases or conditions as products we are developing, thus limiting our ability to compete in the markets addressing such diseases or conditions for a significant period of time. As a result, our business and prospects could 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 tildacerfont 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 tildacerfont could delay the development and commercialization of tildacerfont in certain geographies for certain indications, which would harm our business prospects, financial condition, and results of operations.

Our failure to successfully in-license, acquire, develop, and market additional product candidates or approved products would impair our ability to grow our business.

Although a substantial amount of our efforts are focused on the clinical development, potential regulatory approval and commercialization of tildacerfont, a key element of our long-term strategy is to in-license, acquire, develop, market, and commercialize a portfolio of products to treat patients with endocrine disorders. Because we do not have the necessary internal research and development capabilities, unless we build such capabilities internally, we will be dependent upon pharmaceutical companies, academic scientists, and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify and select promising biopharmaceutical product candidates and products, negotiate licensing or acquisition agreements with their current owners, and finance these arrangements. The process of proposing, negotiating, and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing, sales, and other resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses, and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all. Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including preclinical or clinical testing and approval by the FDA, the EMA and other similar regulatory authorities. All product candidates are prone to risks of failure during biopharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, any approved products that we acquire may not be manufactured or sold profitably or achieve market acceptance.

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 and retain highly qualified managerial, scientific, and medical personnel. We are highly dependent on our management, scientific, and medical personnel. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, prospects, financial condition or results of operations.

We conduct our operations in Daly City, 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.

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

As of December 31, 2020, we had 17 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 tildacerfont 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.

In addition, we initiated enrollment in CAHmelia-203, our ongoing placebo-controlled, double-blind Phase 2b clinical trial in adult patients with classic CAH with poor disease control, and in CAHmelia-204, our second Phase 2b clinical trial in adult patients with classic CAH with good disease control focused on glucocorticoid reduction. Our future financial performance and our ability to commercialize tildacerfont 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 tildacerfont 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 tildacerfont 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, or the Loan Agreement, with Silicon Valley Bank, providing for a term loan, or the Term Loan. In April 2020, we entered into a deferral agreement with Silicon Valley Bank, or the Deferral Agreement, whereby we and Silicon Valley Bank agreed to extend the repayment dates of all monthly payments of principal due and the maturity date with respect to the Term Loan by six months. In March 2021, we entered into a First Amendment to Loan and Security Agreement, or the First Amendment, with Silicon Valley Bank. The First Amendment increased the aggregate principal amount of the Term Loan commitment by Silicon Valley Bank to up to $30.0 million. As of December 31, 2020, we had $4.5 million outstanding under the Loan Agreement. Following the First Amendment, the principal amount due under the Loan Agreement was $5.0 million as of the date of this Annual Report.

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 Silicon Valley Bank not to encumber our intellectual property assets without its prior written consent unless a security interest in the underlying intellectual property is necessary to have a security interest in the accounts and proceeds that are part of the assets securing the Term Loan, in which case our intellectual property shall automatically be included within the assets securing the Term Loan. As a result, if we default on any of our obligations under the Loan Agreement, Silicon Valley Bank 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, Silicon Valley Bank 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, Silicon Valley Bank 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 “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources—Loan Agreement” 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.

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 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 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, physicians 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. If we or our employees, independent contractors, consultants, commercial partners, or vendors violate these laws, we could face substantial penalties.

Our relationships with customers, physicians, 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, or 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, 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) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, such reporting obligations will include payments and other transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified nurse anesthetists, and certified nurse-midwives.

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 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 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 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 European Union General Data Protection Regulation, or 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, 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 healthcare programs, contractual damages, 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.

Our internal computer systems, or those used by our third-party collaborators or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security and back-up measures, our internal computer, server, and other information technology systems as well as those of our third-party collaborators, consultants, contractors, suppliers, and service providers, may be vulnerable to damage from physical or electronic break-ins, computer viruses, malware, ransomware, natural disasters, terrorism, war, telecommunication and electrical failure, denial of service, and other cyberattacks or disruptive incidents that could result in unauthorized access to, use or disclosure of, corruption of, or loss of sensitive, and/ or proprietary data, including personal information, including health-related information, and could subject us to significant liabilities and regulatory and enforcement actions, and reputational damage. 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. If we or our third-party collaborators, consultants, contractors, suppliers, or service providers were to suffer an attack or breach, for example, that resulted in the unauthorized access to or use or disclosure of personal or health information, we may have to notify consumers, partners, collaborators, government authorities, and the media, and may be subject to investigations, civil penalties, administrative and enforcement actions, and litigation, any of which could harm our business and reputation. Likewise, we rely on our third-party research institution collaborators and other third parties to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. The COVID-19 pandemic has generally increased the risk of cybersecurity intrusions. For example, there has been an increase in phishing and spam emails as well as social engineering attempts from “hackers” hoping to use the recent COVID-19 pandemic to their advantage. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate or unauthorized access to or disclosure or use

of confidential, proprietary, or other sensitive, personal, or health information, we could incur liability and suffer reputational harm, and the development and commercialization of tildacerfont could be delayed.

Failure to comply with data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and our partners may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. If we violate HIPAA, we may 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.

Even when HIPAA does not apply, according to the Federal Trade Commission, or the FTC, failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of the Federal Trade Commission Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

In addition, California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling certain personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA became effective January 1, 2020, and the California Attorney General may bring enforcement actions for violations beginning July 1, 2020. The CCPA has been amended from time to time, and it remains unclear what, if any, further modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

Foreign data protection laws, including the GDPR, which became effective in May 2018, may also apply to health-related and other personal data obtained outside of the United States. The GDPR is directly applicable in each EU and EEA Member State, and, by operation of the so-called UK GDPR, continues to apply in substantially equivalent form in the context of the United Kingdom-related establishments and processing operations. The GDPR provides that EEA member states may make their own further laws and regulations to introduce specific requirements related to the processing of 'special categories of personal data,' including personal data related to health, biometric data used for unique identification purposes and genetic information; as well as personal data related to criminal offences or convictions – in the United Kingdom, the United Kingdom Data Protection Act 2018 complements the UK GDPR in this regard. Such laws may introduce further conditions, including limitations which could limit our ability to collect, use and share personal data, and/or otherwise lead to greater divergence on the law that applies to the processing of such data types across the EEA and/or United Kingdom, compliance with which, as and where applicable, may increase our costs and could increase our overall compliance risk.

The GDPR has imposed stringent requirements for controllers and processors of personal data, including, for example, by extending the rights available to affected data subjects, materially expanding the definition of what is expressly noted to constitute personal data, introducing mandatory personal data breach notifications to Supervisory Authorities and affected individuals (in certain circumstances), setting limitations on retention of information, increasing requirements pertaining to special categories of personal data (such as health data, biometric data, genetic information), and requiring that prescriptive obligations must be met when we engage third-party processors to

process of personal data on our behalf. A particular issue presented by certain European data protection laws, including the GDPR, is that they generally restrict transfers of personal data from Europe, including the EEA, United Kingdom and Switzerland, to the United States and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal data. Recent legal developments in the EU have created complexity and uncertainty regarding transfers of personal data from the EEA to the United States, e.g. on July 16, 2020 in a case known colloquially as "Schrems II," the Court of Justice of the European Union, or CJEU, invalidated the EU-US Privacy Shield Framework, or Privacy Shield, under which personal data could be transferred from the EEA to U.S. entities who had self-certified under the Privacy Shield scheme. Following this decision, the United Kingdom government has similarly invalidated use of the EU U.S. Privacy Shield as a mechanism for lawful personal data transfers from the United Kingdom to the United States under the so-called UK GDPR, and the Swiss Federal Data Protection and Information Commissioner announced that the Swiss-U.S. Privacy Shield does not provide adequate safeguards for the purposes of personal data transfers from Switzerland to the United States. The CJEU's decision in Schrems II also raised questions about whether one of the primary alternatives to the EU-U.S. Privacy Shield, namely, the European Commission's Standard Contractual Clauses, can lawfully be used for personal data transfers from Europe to the United States or other third countries that are not the subject of an adequacy decision of the European Commission. While the CJEU upheld the adequacy of the Standard Contractual Clauses in principle in Schrems II, it made clear that reliance on those Clauses alone may not necessarily be sufficient in all circumstances. Use of the Standard Contractual Clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular regarding applicable surveillance laws and relevant rights of individuals with respect to the transferred data. In the context of any given transfer, where the legal regime applicable in the destination country may or does conflict with the intended operation of the Standard Contractual Clauses and/or applicable European law, the decision in Schrems II and subsequent draft guidance from the European Data Protection Board, or EDPB, would require the parties to that transfer to implement certain supplementary technical, organizational and/or contractual measures to rely on the Standard Contractual Clauses as a compliant 'transfer mechanism.' However, the aforementioned draft guidance from the EDPB on such supplementary technical, organizational and/or contractual measures appears to conclude that no combination of such measures could be sufficient to allow effective reliance on the Standard Contractual Clauses in the context of transfers of personal data 'in the clear' to recipients in countries where the power granted to public authorities to access the transferred data goes beyond that which is 'necessary and proportionate in a democratic society' – which may, following the CJEU's conclusions in Schrems II on relevant powers of United States public authorities and commentary in that draft EDPB guidance, include the United States in certain circumstances (e.g., where Section 702 of the US Foreign Intelligence Surveillance Act applies). At present, there are few, if any, viable alternatives to the EU-U.S. Privacy Shield and the Standard Contractual Clauses. As such, if we are unable to implement a valid solution for personal data transfers from Europe, including, for example, obtaining individuals' explicit consent to transfer their personal data from Europe to the United States or other countries, we will face increased exposure to regulatory actions, substantial fines and injunctions against processing personal data from Europe. Inability to import personal data from Europe, including the EEA, United Kingdom or Switzerland, may also: restrict our activities in Europe; limit our ability to collaborate with partners as well as other service providers, contractors and other companies subject to European data protection laws; and/or require us to increase our data processing capabilities in Europe at significant expense or otherwise cause us to change the geographical location or segregation of our relevant systems and operations – any or all of which could adversely affect our financial results. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of delivering our services and operating our business. The type of challenges we face in Europe will likely also arise in other jurisdictions that adopt laws similar in construction to the GDPR or regulatory frameworks of equivalent complexity.

The GDPR applies to any company established in the EEA as well as to those outside the EEA if they process personal data in relation to the offering of goods or services to individuals in the EEA and/or the monitoring of their behavior. The UK GDPR has an equivalent territorial scope in the context of the United Kingdom-related establishments and processing operations. Accordingly, we may be subject to the GDPR and/or UK GDPR in relation to our data processing activities that are carried out in relation to individuals in the EEA and/or United Kingdom. Under the GDPR, fines of up to €20 million or up to 4% of an undertaking's total worldwide annual turnover of the preceding financial year, whichever is higher, may be imposed. Further, following the withdrawal of the UK from the EU and the end of the transitional period, we will have to comply with the GDPR and separately the UK GDPR, each regime having the ability to fine up to the greater of €20 million/ £17 million or 4% of global

turnover. In addition to administrative fines, a wide variety of other potential enforcement powers are available to competent authorities in respect of potential and suspected violations of the GDPR, including extensive audit and inspection rights, and powers to order temporary or permanent bans on all or some processing of personal data carried out by noncompliant actors. Implementing mechanisms to endeavor to ensure compliance with the GDPR and relevant local legislation in EEA Member States and the UK may be onerous and may interrupt or delay our development activities, and adversely affect our business, financial condition, results of operations, and prospects. In addition to the foregoing, a breach of the GDPR or other applicable privacy and data protection laws and regulations could result in regulatory investigations, reputational damage, orders to cease/change our use of data, enforcement notices, or potential civil claims including class action-type litigation. While we have taken steps to comply with the GDPR where applicable, including by reviewing our security procedures, engaging data protection personnel, and entering into data processing agreements with relevant contractors, our efforts to achieve and remain in compliance may not be fully successful.

Compliance with U.S. and foreign privacy and security laws, rules and regulations could require us to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Each of these constantly evolving laws can be subject to varying interpretations. Failure to comply with U.S. and foreign data protection laws and regulations could result in government investigations and enforcement actions (which could include civil or criminal penalties), fines, private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, patients about whom we or our partners obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

The withdrawal of the UK from the EU may adversely impact our ability to obtain regulatory approvals of our product candidates in the EU, result in restrictions or imposition of taxes and duties for importing our product candidates into the EU, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the EU.

Following the result of a referendum in 2016, the UK left the EU on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the EU, the UK was subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules continued to apply. A trade and cooperation agreement, or the Trade and Cooperation Agreement, that outlines the future trading relationship between the United Kingdom and the European Union was agreed in December 2020.

Since a significant proportion of the regulatory framework in the UK applicable to our business and our product candidates is derived from EU directives and regulations, Brexit has had, and may continue to have, a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the UK or the EU. For example, Great Britain is no longer be covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA and, unless a specific agreement is entered into, a separate process for authorization of drug products, including tildacerfont and any future product candidates, will be required in Great Britain. It is currently unclear whether the Medicines & Healthcare products Regulatory Agency, or MHRA, in the UK is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our tildacerfont in the UK or the EU and restrict our ability to generate revenue and achieve and sustain profitability.

While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the UK and the EU there may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Further, should the UK diverge from the EU from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK or the EU for tildacerfont and any future product candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected

duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU.

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

We face an inherent risk of product liability as a result of the clinical testing of 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 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 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 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 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 $7.0 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, 2020, after reducing net operating losses, or NOLs, and tax credits for amounts not expected to be utilized, we had federal NOL carryforwards of approximately $58.6 million and state NOL carryforwards of approximately $58.4 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 $3.0 million and $0.6 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, or CARES Act, federal NOL carryforwards generated in tax years beginning after December 31, 2017 may be carried forward indefinitely but, in the case of tax years beginning after 2020, may only be used to offset 80% of our taxable income annually. Similar rules may apply under state tax laws. For example, on June 29, 2020, California enacted A.B. 85 which imposed limits on the usability of California state net operating losses and certain tax credits in tax years beginning after 2019 and before 2023. 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 an 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, 2020 concluded that an ownership change occurred in May 2016 and in August 2020. As a result of the ownership change, 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, 2020, we recorded a full valuation allowance on our net deferred tax assets.

Changes in tax laws or regulations that are applied adversely to us or our customers 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 enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, the CARES Act, modified certain provisions of the Tax Act. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the CARES

Act or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax 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 U.S. tax expense.

Risks Related to Our Reliance on Third Parties

We depend on intellectual property licensed from Lilly, 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. 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. See “Business—License Agreement with Eli Lilly and Company” for a description of our license agreement, which includes a description of the termination provision of this agreement.

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 tildacerfont.

We currently rely on, and intend to continue relying on, third-party CROs in connection with our clinical trials for 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, delayed, or terminated and we may not be able to complete development of, obtain regulatory approval for or successfully commercialize tildacerfont and any future product candidates. As a result, our financial results and the commercial prospects for 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 COVID-19 or other 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 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 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, or APIs, and the finished products of tildacerfont or the associated packaging and administration syringes used in our current product format and we may rely on single source suppliers for clinical supply of API and drug product of tildacerfont. We will need to identify and qualify a third-party manufacturer prior to commercialization of tildacerfont, and we intend to enter into agreements for commercial production with third-party suppliers. As tildacerfont is intended to treat rare endocrine disorders, we will only require a low-volume of raw materials and APIs, and in some cases with single-source suppliers and manufacturers. Our reliance on third-party suppliers and manufacturers, including single-source suppliers, could harm our ability to develop 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 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 tildacerfont and any future product candidates must be approved by the applicable regulatory authorities, including the FDA, pursuant to inspections that will be conducted after an NDA or comparable foreign regulatory marketing application is submitted. We currently do not control the manufacturing process of tildacerfont and are completely dependent on our contract manufacturing partners for compliance with the FDA's 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 strict regulatory requirements, they will not be able to secure or maintain FDA approval for the manufacturing facilities. In addition, we have no 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 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 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 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 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 COVID-19 or other 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.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for 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 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 tildacerfont, any future product candidates, and other proprietary technologies we develop. If we are unable to obtain or maintain patent protection with respect to 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 tildacerfont, 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 enforced in the patents that may be issued from the applications we currently or may in the future own or license from third parties. Further, if any patents 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 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, or 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;
- other parties may have designed around our claims or developed 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, 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 tildacerfont, 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;
- 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.

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 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 tildacerfont and any future product candidates but that are not covered by the claims of our patents;
- 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; 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 tildacerfont or any future product candidates will be considered patentable by the USPTO, courts in the United States, or by patent offices and 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 tildacerfont 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 tildacerfont and any future product candidates. Furthermore, even if they are unchallenged, our patents may not adequately protect our intellectual property, provide exclusivity for tildacerfont 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 tildacerfont or any future product candidates is threatened, it could dissuade companies from

collaborating with us to develop, or threaten our ability to commercialize, tildacerfont 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, or 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, 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 tildacerfont, our business may be materially harmed.

Depending upon the timing, duration, and specifics of any FDA marketing approval of tildacerfont, 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, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term, or 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, or SPC. If we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market tildacerfont 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. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or 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, 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 a license agreement with Lilly under which we are granted intellectual property rights that are important to our business and our only product candidate, tildacerfont. If we fail to comply with our obligations under the license agreement, or we are subject to a bankruptcy, the license agreement may be terminated, in which event we would not be able to develop, commercialize or market tildacerfont. See "Business—License Agreement with Eli Lilly and Company" for a description of our license agreement with Lilly.

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 tildacerfont, 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 licensor 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 licensor, or any future licensor fail to adequately protect this intellectual property, our ability to commercialize tildacerfont 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. These systems and processes may be negatively impacted by the current pandemic in various aspects. 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 tildacerfont.

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 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 federal 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.

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 tildacerfont, 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. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We may become 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 tildacerfont 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 tildacerfont. 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, tildacerfont 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 tildacerfont. 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 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 from third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and 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 application. 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 tildacerfont. 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 tildacerfont. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our activities related to tildacerfont 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. Nevertheless, we are not aware of any issued patents that will prevent us from marketing tildacerfont.

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 tildacerfont. 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 tildacerfont, 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 tildacerfont 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.

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 tildacerfont 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.

If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do either. Proving invalidity or unenforceability is difficult. For example, in the United States, proving invalidity before federal courts requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management’s time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity or enforceability of the patents in court. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid or unenforceable, we may incur substantial monetary damages, encounter significant delays in bringing tildacerfont to market and be precluded from developing, manufacturing or selling tildacerfont.

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, tildacerfont, and any future product candidates or the use of tildacerfont 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 tildacerfont 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 tildacerfont. 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.

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.

If a third party prevails in a patent infringement lawsuit against us, we may have to stop making and selling the infringing product, pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing a third party's patents, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure.

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 tildacerfont. 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 tildacerfont, 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.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees 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 tildacerfont, any future 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. 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, which could adversely affect our business. 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.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court, and we may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.

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 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. Similar mechanisms for challenging the validity and enforceability of a patent exist in foreign patent offices and courts and may result in the revocation, cancellation, or amendment of any foreign patents we or our licensors hold now or in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

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 tildacerfont and 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.

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.

We rely on trade secrets to protect our proprietary technologies, 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 tildacerfont 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 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 tildacerfont 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

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 may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely 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 since its trading began on October 9, 2020 to March 19, 2021 has ranged from a low of $15.38 to a high of $32.42. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report, these factors include:

- the commencement, enrollment or results of our ongoing and planned clinical trials of tildacerfont or any future clinical trials we may conduct of tildacerfont and any future product candidates, or changes in the development status of tildacerfont and any future product candidates;
- acceptance by the FDA and EMA of data from our two Phase 2b clinical trials or any future clinical trials we conduct;
- any delay in our regulatory filings for 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;
- 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 tildacerfont and any future product candidates;
- changes in laws or regulations applicable to 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 tildacerfont and any future product candidates, if approved;
- changes on 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 tildacerfont and any future product candidates;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of 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 classic CAH in adult and pediatric patients and a subpopulation of females with a rare form of PCOS, and other rare endocrine disorders that we may target;
- actual or anticipated variations in 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;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- issuances of debt or equity securities;
- sales of our common stock by us or our stockholders in the future;
- 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;
- general political, health, and economic conditions, including the COVID-19 pandemic; and
- other events or factors, 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. 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 type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results or financial condition.

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 Silicon Valley Bank, 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, or the Jumpstart Our Business Startups Acts of 2012. 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, not being required to have our internal control over financial reporting audited by our independent registered public accounting firm under Section 404 of the Sarbanes-Oxley Act or 2002, or the Sarbanes-Oxley Act, 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 $1.07 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 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.

We previously identified and remediated a material weakness in our internal control over financial reporting and may identify material weaknesses in the future or otherwise fail to maintain proper and effective internal controls, which may impair our ability to produce accurate financial statements on a timely basis.

During the preparation of our financial statements for the years ended December 31, 2018 and 2019, we identified a material weakness in internal control over financial reporting primarily related to a lack of timely review over the financial statement close process. During these periods, we did not have a sufficient complement of qualified personnel within the accounting function and had a lack of segregation of duties to adequately conduct review and analysis of certain routine transactions.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis. This material weakness could result in a misstatement

of account balances or disclosures that would result in a material misstatement to the annual or interim financial statements that would not be prevented or detected. To address our material weakness, we added a chief financial officer and controller, and we implemented new processes and controls, formalized documentation of policies and procedures, and recruited additional accounting personnel. We have fully remediated the material weakness as of the filing date of this Annual Report for the fiscal year ending December 31, 2020. Completion of remediation does not provide assurance that our remediation or other controls will continue operating effectively. Remediation costs consisted primarily of additional personnel expenses, which did not have a material impact to our financial statements.

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. Commencing with our fiscal year ending December 31, 2021, 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 our Form 10-K filing for that year, 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.

The measures we have taken to date, and actions we may take in the future, may not be sufficient to remediate the control deficiencies that led to our material weakness in our internal control over financial reporting or to prevent or avoid potential future material weaknesses. We may not have identified all material weaknesses. Moreover, our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Further, weaknesses in our disclosure controls and internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective controls or any difficulties encountered in their implementation or improvement could harm our operating results or cause us to fail to meet our reporting obligations and may result in a restatement of our financial statements for prior periods, which could cause the price of our common stock to decline. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

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, or the 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 March 19, 2021, there were 23,301,872 shares of our common stock outstanding. Of these shares, only the shares of common stock sold in the IPO by us, other than to our affiliates, are freely tradable without restriction in the public market.

The lock-up agreements pertaining to the IPO will expire on April 7, 2021. After the lock-up agreements expire, up to 16,405,123 shares of common stock will be eligible for sale in the public market, of which 11,924,778 shares are held by directors, executive officers, and other affiliates and will be subject to volume limitations under Rule 144 under the Securities Act of 1933, as amended, or the Securities Act. 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, the lock-up agreements, and Rule 144 and Rule 701 under the 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.

Further, the holders of 15,492,019 shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act, subject to the 180-day lock-up agreements described above. 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 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. If we sell 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 ESPP, the number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year 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.

General Risk Factors

Our failure to meet Nasdaq's continued listing requirements could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of Nasdaq, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with the listing requirements of Nasdaq.

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.

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 tildacerfont. Our ability to obtain clinical supplies of tildacerfont and any 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.

We could be subject to securities class action litigation.

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

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters are located at 2001 Junipero Serra Boulevard, Suite 640, Daly City, California 94014, where we occupy approximately 8,000 square feet of office space pursuant to a lease entered into in February 2020, which began on September 1, 2020 and is set to expire on November 30, 2025.

We believe our existing facility meets our current needs.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

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 Global Select Market under the symbol "SPRB" since October 9, 2020. Prior to that date, there was no public market for our common stock.

Holders of Common Stock

As of March 19, 2021, we had 23,301,872 shares of common stock outstanding held by 22 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.

Recent Sales of Unregistered Securities

Stock Option Grants

For the year ended December 31, 2020, we granted options to purchase 1,775,808 shares of our common stock to certain of our employees and directors with a weighted-average exercise price of $3.33 per share. The offer, sale and issuance of these options were deemed to be exempt from registration under the Securities Act in reliance on either Rule 701 in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701 or Section 4(a)(2) in that the issuance of securities was to accredited investors in a private placement transaction that did not involve a public offering.

Issuance of Common Stock upon Conversion of Redeemable Convertible Preferred Stock

On October 8, 2020, upon consummation of our IPO, all shares of our then-outstanding redeemable convertible preferred stock automatically converted into 15,492,019 shares of common stock. The common stock was issued pursuant to the exemption from the registration requirements of the Securities Act provided by Section 3(a)(9) or Section 4(2) of the Securities Act.

Issuance of Common Stock upon Exercise of Warrants

In September 2019, in connection with the first and second tranches under the Loan and Security Agreement with Silicon Valley Bank, we issued a warrant to purchase up to an aggregate of 49,609 shares of our common stock at $1.44 per share. The warrant was net-exercised for 46,358 shares of our common stock in November 2020.

Use of Proceeds

We commenced our IPO pursuant to the registration statement on Form S-1, as amended (File No. 333-48924), that was declared effective on October 8, 2020 and a registration statement on Form S-1 MEF (File No. 333-249397), which was effective on filing on October 8, 2020, and registered an aggregate of 6,900,000 shares of our common stock. We sold 6,900,000 shares of our common stock at a public offering price of $15.00 per share for aggregate gross proceeds of $103.5 million. On October 14, 2020, we completed our IPO. Cowen and Company, LLC, SVB Leerink LLC, Credit Suisse Securities (USA) LLC and RBC Capital Markets, LLC acted as joint book-running managers for the IPO.

The underwriting discounts and commissions for our IPO totaled approximately $7.2 million. We incurred additional costs of approximately $2.9 million in offering expenses, which when added to the underwriting discounts and commissions paid by us, amounts to total fees and costs of approximately $10.1 million. Thus, net offering proceeds to us, after deducting underwriting discounts, commissions and offering expenses, were $93.4 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

There has been no material change in the use of proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on October 9, 2020.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

Item 6. Selected Financial Data.

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 the 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 late-stage biopharmaceutical company focused on developing and commercializing novel therapies for rare endocrine disorders with significant unmet medical need. We are initially developing our wholly-owned product candidate, tildacerfont, as the potential first non-steroidal therapy to offer markedly improved disease control and reduce steroid burden for patients suffering from classic congenital adrenal hyperplasia, or CAH. Classic CAH is a serious and life-threatening disease with no known novel therapies approved in approximately 50 years. In a 12-week Phase 2a proof-of-concept clinical trial, tildacerfont-treated adult patients suffering from classic CAH who had poor disease control despite being on standard of care therapy achieved approximately 80% reductions in hormones that are key indicators of poor disease control. Furthermore, 171 subjects across seven clinical trials to date have been administered tildacerfont with no drug-related SAEs reported.

We have initiated CAHmelia-203, a placebo-controlled, double-blind Phase 2b clinical trial in adult patients with classic CAH with poor disease control and anticipate topline results in the first half of 2022. We have also initiated CAHmelia-204, a second Phase 2b clinical trial in adult patients with classic CAH with good disease control focused on glucocorticoid reduction and anticipate topline results in the second half of 2022. Based on post-hoc analyses of our clinical data to date, we have chosen to target two distinct groups of classic CAH patients with either good disease control or poor disease control. These two groups, which together make up the entire classic CAH patient population, have differing disease challenges centered on excessive adrenal androgen levels or excessive glucocorticoid usage, both of which have the potential to be addressed by treatment with tildacerfont, if approved. We believe our strategy to study CAH patients in these two enriched sub-populations may enable us to observe clinically meaningful outcomes. Additionally, we believe these two clinical trials will provide sufficient patient exposures for our registrational safety database. Assuming positive results in CAHmelia-204, we plan to meet with the FDA and comparable foreign regulatory authorities to discuss registration.

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 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. We intend to build a highly specialized commercial organization to support the commercialization of tildacerfont, if approved, in the United States and Europe. Given a relatively small number of endocrinologists and specialists treat a large proportion of patients with classic CAH, we believe this market can be effectively addressed with a modest-sized targeted commercial sales force, alongside various high-touch patient initiatives. If tildacerfont is approved for additional indications, we plan to leverage our rare disorder commercial infrastructure and expertise to efficiently address those patient populations. We may also either build a commercial infrastructure or opportunistically seek strategic collaborations to benefit from the resources of biopharmaceutical companies specialized in either relevant disease areas or geographies.

We rely, and expect to continue to rely, on third parties for the manufacture of tildacerfont for preclinical studies and clinical trials, as well as for commercial manufacture if tildacerfont obtains 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 year ended December 31, 2020, we incurred a net loss of $29.5 million and used $27.5 million of cash in operations. As of December 31, 2020, we had an accumulated deficit of $60.8 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.

In October 2020, we consummated our initial public offering, or 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. Since inception through December 31, 2020, we have raised aggregate gross financing proceeds of $224.0 million, including $103.5 million from our IPO in October 2020, $116.0 million from the sale of our redeemable convertible preferred stock and $4.5 million from the issuance of debt. As of December 31, 2020, we had cash and cash equivalents of $157.2 million. We believe, based on our current operating plan, that our cash and cash equivalents will be sufficient to fund our operations for at least the next 12 months. We have based this projection on assumptions that may be inaccurate and as a result, we may utilize our capital resources sooner than we expect. We expect our expenses will increase significantly in connection with our ongoing activities, as we:

- advance tildacerfont through our ongoing Phase 2b clinical trials in adult patients with classic CAH;
- pursue regulatory approvals of tildacerfont in adult patients with classic CAH;
- advance clinical development of tildacerfont in additional indications, including pediatric classic CAH and a subpopulation of females with a rare form of polycystic ovary syndrome, or PCOS;
- build a highly specialized commercial organization to support the commercialization of tildacerfont, if approved, in the United States and Europe;
- build a commercial infrastructure or opportunistically seek strategic collaborations to benefit from the resources of biopharmaceutical companies specialized in either relevant disease areas or geographies, if tildacerfont is approved for additional indications;
- identify additional indications and formulations for which to investigate tildacerfont in the future and expand our pipeline of product candidates;
- implement operational, financial, and management information systems;
- hire additional personnel;
- operate as a public company; and
- obtain, maintain, expand, and protect our intellectual property portfolio.

Our business has been and could continue to be adversely affected by the evolving COVID-19 pandemic. For example, the COVID-19 pandemic has resulted in and could result in delays to our clinical trials for numerous reasons including additional delays or difficulties in enrolling patients, diversion of healthcare resources away from the conduct of clinical trials, interruption or delays in the operations of the FDA or other regulatory authorities, and delays in clinical sites receiving the supplies and materials to conduct our clinical trials. At this time, the extent to which the COVID-19 pandemic impacts our business will depend on future developments, which are highly uncertain and cannot be predicted.

Components of Results of Operations

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 CROs engaged to manage and conduct clinical trials;
  - preclinical studies—expenses associated with preclinical studies performed by vendors;
  - manufacturing—expenses associated with contract manufacturing; labeling, packaging, distribution of clinical trial supplies, and consulting;
  - other research and development—expenses associated with 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 to advance tildacerfont. These expenses will primarily consist of expenses for the administration of clinical trials as well as manufacturing costs for clinical material supply. We expect that significant additional spending will be required to progress tildacerfont through clinical development and regulatory approval.

Research and development expenses are recognized as they are incurred. If deposits are required by external vendors, a portion of the deposit is included as a prepaid expense until sufficient progress has occurred to amortize the deposit to expense in the statement of operations.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs (including salaries, bonuses, benefits, and stock-based compensation expense) for personnel in executive, finance, and other administrative functions. General and administrative expenses also include legal fees, professional fees paid for accounting, auditing, consulting, tax, and investor relations services, 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 U.S. Securities and Exchange Commission, or the SEC, and those of the Nasdaq Stock Market, Inc., or 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, as we advance tildacerfont through clinical development and 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 with Silicon Valley Bank.

Other Income, Net

Other income, net primarily consists of interest income earned on our cash and cash equivalents.

Results of Operations

Comparisons of the Year Ended December 31, 2020 and 2019

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

	Year Ended December 31,		
	2020	2019	Change
Operating expenses:			
Research and development	$ 23,854	$ 10,817	$ 13,037
General and administrative	5,562	2,290	3,272
Total operating expenses	29,416	13,107	16,309
Loss from operations	(29,416)	(13,107)	(16,309)
Interest expense	(323)	(65)	(258)
Other income, net	200	84	116
Net loss	$ (29,539)	$ (13,088)	$ (16,451)

Research and Development Expenses

Research and development expenses were $23.9 million for the year ended December 31, 2020, compared to $10.8 million for the year ended December 31, 2019. The overall increase in research and development expenses was primarily related to an increase in clinical development, manufacturing, preclinical studies and personnel costs, associated with our progressing clinical development. The following table sets forth the primary external and internal research and development expenses for the periods presented below (in thousands).

	Year Ended December 31,		
	2020	2019	Change
External expenses:			
Clinical development	$ 12,747	$ 4,323	$ 8,424
Manufacturing	4,132	1,940	2,192
Preclinical studies	1,744	707	1,037
Other research and development	685	412	273
Internal expenses:			
Personnel	4,376	3,301	1,075
Allocated overhead	170	134	36
Total research and development expenses	$ 23,854	$ 10,817	$ 13,037

General and Administrative Expenses

General and administrative expenses were $5.6 million for the year ended December 31, 2020, compared to $2.3 million for the year ended December 31, 2019. The overall increase in general and administrative expenses was primarily driven by an increase of $1.6 million in professional and consultant service fees related to becoming and operating as a public company, an increase of $1.0 million in personnel-related expenses, and an increase of $0.5 million in administrative expenses primarily related to an increase in directors' and officers' liability insurance premiums.

Interest Expense

Interest expense was $0.3 million for the year ended December 31, 2020, compared to $0.1 million for the year ended December 31, 2019. The increase was due to interest expense incurred in 2020 on the Term Loan with Silicon Valley Bank, which we entered into in September 2019.

Other Income, Net

Other income, net was $0.2 million for the year ended December 31, 2020, compared to $0.1 million for the year ended December 31, 2019. The increase was primarily due to interest income on higher cash and cash equivalents balances in 2020.

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, 2020, we had an accumulated deficit of $60.8 million. As of December 31, 2020, we had cash and cash equivalents of $157.2 million. In October 2020, we consummated our 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. We believe, based on our current operating plan, that our cash and cash equivalents will be sufficient to fund our operations for at least the next 12 months.

Loan Agreement

In September 2019, we entered into the Loan Agreement with Silicon Valley Bank providing for the Term Loan. Pursuant to the Loan Agreement, we requested $2.5 million from the first tranche in connection with the entry into the Loan Agreement, which is currently outstanding, and we drew the second tranche of $2.0 million in December 2019.

In April 2020, we and Silicon Valley Bank entered into the Deferral Agreement whereby we and Silicon Valley Bank agreed to extend the repayment dates of all monthly payments of principal due and the maturity date with respect to the Term Loan by six months. In March 2021, we entered into First Amendment with Silicon Valley Bank. The First Amendment increased the aggregate principal amount of the Term Loan commitment by Silicon Valley Bank to up to $30.0 million. Up to $20.0 million is available under the first tranche of the Term Loan, or the First Tranche, $5.0 million of which was advanced immediately to repay the outstanding obligations under the Term Loan prior to the First Amendment with the remainder of the First Tranche commitments available through December 31, 2021, and up to $10.0 million is available under the second tranche, or the Second Tranche, subject to the completion of certain clinical and financial milestones which Second Tranche commitment is available through December 31, 2022. Pursuant to the First Amendment, the Term Loan will mature on January 1, 2026. As of March 22, 2021, we have $5.0 million outstanding under the Term Loan.

The Loan Agreement, as amended by the Deferral Agreement and the First Amendment, provides for monthly cash interest-only payments following the funding date of each respective tranche and continuing thereafter through December 31, 2022 to the extent that the Company does not borrow any part of the Second Tranche or December 31, 2023 if the Company has borrowed some or all of the Second Tranche. Outstanding principal balances under the Term Loan, as amended by the First Amendment, bear interest at a floating per annum rate equal to (A) if the Company does not borrow under the Second Tranche, the greater of (x) 1% above the prime rate or (y) 4.25%; or (B) if the Company does borrow under the Second Tranche, the greater of (x) 3% above the prime rate or (y) 6.25%.

Following the interest-only period, the outstanding Term Loan balance will be payable in (i) 37 consecutive monthly payments (or 25 if the Company borrows under the Second Tranche) 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 amendment interest-only period, over the repayment period, plus (ii) monthly payments of accrued but unpaid interest. The final payment due on the maturity date shall include all outstanding principal and all accrued unpaid interest and an End of Term Payment totaling (x) 6% of the original funded principal amount of the First Tranche if the Company does not borrow under the Second Tranche, or (y) 9.5% of the total original funded principal amount under the First and Second Tranche if the Company does borrow under the Second Tranche.

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 end of term payment, a prepayment fee between 1% and 3% of the principal amount of the first and second tranches, and any bank expenses become due and payable.

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, Silicon Valley Bank 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, Silicon Valley Bank 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.

In connection with the first and second tranches under the Loan Agreement prior to the First Amendment, we issued a warrant to purchase up to an aggregate of 49,609 shares of common stock at $1.44 per share. We 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 also as a debt discount, which is amortized to interest expense using the effective interest method over the term of the Term Loan. The warrant was net-exercised for 46,358 shares of our common stock in November 2020.

Funding Requirements

To date, we have not generated any revenue. We do not expect to generate any meaningful revenue unless and until we obtain regulatory approval and commercialize tildacerfont 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 research and development activities related to developing tildacerfont, as tildacerfont continues to advance into later stages of development for the treatment of classic CAH in adult patients, as we conduct clinical trials of tildacerfont in pediatric classic CAH and a rare form of PCOS, as we seek regulatory approvals for tildacerfont, and incur expenses associated with hiring additional personnel to support our research and development efforts. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, the successful development of tildacerfont is highly uncertain, and we may never succeed in achieving regulatory approval for tildacerfont in classic CAH in adult patients or other indications. In addition, we expect to incur additional costs associated with operating as a public company.

We may seek to raise capital through equity or debt financings, collaborative agreements 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 tildacerfont;
- 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 tildacerfont;
- our plan to expand our research and development activities;
- the costs associated with manufacturing tildacerfont and establishing commercial supplies and sales, marketing, and distribution capabilities;
- the costs associated with securing and establishing 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 tildacerfont 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 the COVID-19 pandemic.

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 the COVID-19 pandemic and actions taken to slow its spread, 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 tildacerfont or other research and development initiatives. We also could be required to seek collaborators for tildacerfont 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 tildacerfont 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.

Summary Statement 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,	
	2020	2019
Net cash used in operating activities	$ (27,519)	$ (12,617)
Net cash used in investing activities	(74)	(4)
Net cash provided by financing activities	181,035	12,433
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ 153,442	$ (188)

Cash Used in Operating Activities

For the year ended December 31, 2020, net cash used in operating activities was $27.5 million, which consisted of a net loss of $29.5 million, partially offset by and a net change of $1.2 million in our net operating assets and liabilities and by $0.9 million in non-cash charges. The net change in our operating assets and liabilities was primarily due to a net increase in accounts payable and accrued expenses of $3.7 million and a $0.3 million net increase in accrued compensation and noncurrent assets and liabilities, partially offset by a net increase in prepaid expenses and other current assets of $2.9 million. The non-cash charges of $0.9 million consisted of stock-based compensation expense, non-cash lease expense, and depreciation and amortization expense.

For the year ended December 31, 2019, net cash used in operating activities was $12.6 million, which consisted of a net loss of $13.1 million, partially offset by a net change of $0.3 million in our net operating assets and liabilities and $0.2 million in non-cash charges. The net change in our operating assets and liabilities was primarily due to a net increase in accrued compensation of $0.6 million, partially offset by a net decrease in accounts payable and accrued expenses of $0.2 million and a net increase in prepaid expenses of $0.1 million. The non-cash charges of $0.2 million primarily consisted of stock-based compensation expense and depreciation expense.

Cash Used in Investing Activities

For the year ended December 31, 2020 and 2019, cash used in investing activities was less than $0.1 million and related to the purchase of property and equipment.

Cash Provided by Financing Activities

For the year ended December 31, 2020, cash provided by financing activities was $181.0 million, consisting primarily of net proceeds from the issuance of common stock in connection with our IPO and the issuance and sale of Series B redeemable convertible preferred stock.

For the year ended December 31, 2019, cash provided by financing activities was $12.4 million, consisting primarily of net proceeds of $7.9 million from the issuance and sale of Series A redeemable convertible preferred stock and net proceeds of $4.5 million from the issuance of a term loan.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations and commitments as of December 31, 2020 (in thousands):

	Payments Due by Period				
	Less than 1 Year	1 to 3 Years	4 to 5 Years	More than 5 years	Total
Operating lease obligations	$ 377	$ 942	$ 957	$ —	$ 2,276
Long-term debt obligations	2,571	1,929	—	—	4,500
Total	$ 2,948	$ 2,871	$ 957	$ —	$ 6,776

We enter into contracts in the normal course of business with third-party contract manufacturing organizations and CROs for clinical trials, non-clinical studies and testing, 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 the License Agreement under which we are obligated to make aggregate milestone payments upon the achievement of specified milestones as well as royalty payments. The payment obligations under the License Agreement are contingent upon future events, such as our achievement of specified milestones or generating product sales. As of December 31, 2020, we were unable to estimate the timing or likelihood of achieving these milestones or generating future product sales. See the section titled “License Agreement with Lilly and Company” above.

Off-Balance Sheet Arrangements

We did not have off-balance sheet arrangements during the periods presented, and we do not currently have any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Critical Accounting Policies, Significant Judgments and Use of Estimates

Our financial statements have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities and expenses, as well as the related disclosure of contingent assets and liabilities as of the date of the financial statements. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources.

Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management’s judgments and estimates.

While our significant accounting policies are described in the notes to our financial statements, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results.

Accrued Research and Development Expenses

We record accruals for estimated costs of preclinical, clinical, and manufacturing development, within accrued expenses which are significant components of research and development expenses. A substantial portion of our ongoing research and development activities is conducted by third-party service providers, including CROs. Our contracts with CROs generally include fees such as initiation fees, investigator grants, clinical safety, data management, laboratory expenses, project management, and pass-through expenses. 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. We accrue the costs

incurred under agreements with these third parties based on estimates of actual work completed in accordance with the respective agreements. We determine the estimated costs through discussions with internal personnel and external service providers as to the progress, or stage of completion or actual timeline (start-date and end-date) of the services and the agreed-upon fees to be paid for such services. 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.

If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust accrued expenses or prepaid expenses accordingly, which impact research and development expenses. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period.

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.

Stock-Based Compensation Expense

We account for stock-based compensation expense by measuring and recognizing compensation expense for all share-based awards made to employees and non-employees based on estimated grant-date fair values. We use the straight-line method to allocate compensation cost to reporting periods over the requisite service period, which is generally the vesting period. We recognize actual forfeitures by reducing the stock-based compensation expense in the same period as the forfeitures occur. We estimate the fair value of share-based awards to employees and non-employees using the Black-Scholes option-pricing valuation model. The Black-Scholes model requires the input of subjective assumptions, including fair value of common stock, expected term, expected volatility, risk-free interest rate, and expected dividend yield, which are described in greater detail below.

Estimating the fair value of equity-settled awards as of the grant date using the Black-Scholes option pricing model is affected by assumptions regarding several complex variables. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop. These inputs are as follows:

- Fair value of common stock— Prior to the IPO, the fair value of our common stock was determined by the Board of Directors since it was not publicly traded. The Board of Directors determined fair value of the common stock at the time of grant of the option by considering a number of objective and subjective factors including valuation reports prepared by third-party valuation firms, valuation of comparable companies, sales of redeemable convertible preferred stock to third parties, operating and financial performance, the lack of liquidity of capital stock, and general and industry specific economic outlook, amongst other factors. Following the IPO, the fair market value of our common stock is determined based on the closing price of our common stock on the Nasdaq Global Select Market.
- Expected term—The expected term represents the period that our options granted are expected to be outstanding and is determined using the simplified method for employees (based on the mid-point between the vesting date and the end of the contractual term) and is based on the remaining contractual term for non-employees. We have very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for our stock option grants.
- Expected volatility—Since we were a privately-held company until October 2020, we do not have sufficient historical data regarding the volatility of our common stock. Accordingly, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their market capitalization, stage of development, area of specialty, and stock-specific attributes. We will continue to apply this process until enough historical information regarding the volatility of our own stock price becomes available.

- Risk-free interest rate—The risk-free interest rate is based on the U.S. constant maturity rates with remaining terms similar to the expected term of the options.
- Expected dividend yield—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

For options granted to non-employee consultants, the fair value of these options is also measured using the Black-Scholes option-pricing model reflecting the same assumptions as applied to employee options in each of the reported periods, other than the expected term which is assumed to be the remaining contractual life of the option.

We will continue to use judgment in evaluating the expected volatility, expected terms, and interest rates utilized for our stock-based compensation expense calculations on a prospective basis.

JOBS Act

We are an "emerging growth company" as defined in the 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 $1.07 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, 2020 consisted of readily available checking and money market funds. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, a sudden change in market interest rates would not be expected to have a material impact on our financial condition and/or results of operations. We do not believe that our cash or cash equivalents have significant risk of default or illiquidity. 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. In addition, we maintain significant amounts of cash and cash equivalents at one financial institution that is in excess of federally insured limits.

Additionally, the interest rate for borrowings under the Loan Agreement is variable. A hypothetical 10% relative change in interest rates during any of the periods presented would not have had a material impact on our financial statements. We do not currently engage in hedging transactions to manage our exposure to interest rate risk.

Foreign Currency Exchange Risk

To date, foreign currency transaction gains and losses have not been material to our financial statements, and we have not had a formal hedging program with respect to foreign currency. Our expenses are generally denominated in U.S. dollars. Our operations may be subject to fluctuations in foreign currency exchange rates in the future. A hypothetical 10% change in exchange rates during any of the periods presented would not have had a material impact on our financial statements included elsewhere in this Annual Report.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our financial statements included elsewhere in this Annual Report.

Effects of Exchange Rate Fluctuations

We do not believe that exchange rate fluctuations had a significant impact on our results of operations for any periods presented herein.

Item 8. Financial Statements and Supplementary Data.

SPRUCE BIOSCIENCES, INC.
INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Stockholders and Board of Directors
Spruce Biosciences, Inc.
Daly City, California

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Spruce Biosciences, Inc. (the "Company") as of December 31, 2020 and 2019, the related statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for 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, 2020 and 2019, and the results of its operations and its cash flows for the years then ended**,** in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Principle

As discussed in Note 2 to the financial statements, the Company has changed its method of accounting for leases in 2020 due to the adoption of Accounting Standards Codification Topic 842, *Leases*.

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, LLP

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

San Jose, California
March 22, 2021

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

	December 31, 2020	December 31, 2019
ASSETS		
Current assets:		
Cash and cash equivalents	$ 157,150	$ 3,924
Prepaid expenses	2,971	215
Other current assets	276	513
Total current assets	160,397	4,652
Restricted cash	216	—
Right-of-use assets	1,793	—
Other assets	477	40
Total assets	$ 162,883	$ 4,692
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 3,628	$ 1,878
Term loan, current portion	2,554	1,252
Accrued expenses and other current liabilities	2,496	265
Accrued compensation and benefits	1,085	908
Total current liabilities	9,763	4,303
Term loan, net of current portion	1,922	3,193
Lease liability, net of current portion	1,653	—
Other liabilities	118	20
Total liabilities	13,456	7,516
Commitments and contingencies (Note 7)		
Series A redeemable convertible preferred stock, $0.0001 par value; 0 shares and 28,000,000 shares authorized, issued and outstanding as of December 31, 2020 and 2019, respectively; liquidation preference of $0 and $28,000 as of December 31, 2020 and 2019, respectively	—	27,813
Stockholders' equity (deficit):		
Preferred stock, $0.0001 par value; 10,000,000 shares and 0 shares authorized as of December 31, 2020 and 2019, respectively; 0 shares issued and outstanding as of December 31, 2020 and 2019	—	—
Common stock, $0.0001 par value; 200,000,000 shares and 41,000,000 shares authorized as of December 31, 2020 and 2019, respectively; 23,260,399 shares and 764,408 shares issued and outstanding as of December 31, 2020 and 2019, respectively	2	1
Additional paid-in capital	210,266	664
Accumulated deficit	(60,841)	(31,302)
Total stockholders' equity (deficit)	149,427	(30,637)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 162,883	$ 4,692

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

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

	Year Ended December 31,	
	2020	2019
Operating expenses:		
Research and development	$ 23,854	$ 10,817
General and administrative	5,562	2,290
Total operating expenses	29,416	13,107
Loss from operations	(29,416)	(13,107)
Interest expense	(323)	(65)
Other income, net	200	84
Net loss	$ (29,539)	$ (13,088)
Net loss per share, basic and diluted	$ (4.93)	$ (17.12)
Weighted-average shares of common stock outstanding, basic and diluted	5,991,213	764,408

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

SPRUCE BIOSCIENCES, INC.
STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share amounts)

	Redeemable Convertible Preferred Stock								
	Series A		Series B		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount			
Balance as of December 31, 2018	20,000,000	$ 19,872	—	$ —	764,408	$ 1	$ 411	$ (18,214)	$ (17,802)
Issuance of Series A redeemable convertible preferred stock, net of issuance costs of $60	8,000,000	7,941	—	—	—	—	—	—	—
Stock-based compensation	—	—	—	—	—	—	196	—	196
Issuance of warrant to purchase common stock	—	—	—	—	—	—	57	—	57
Net loss	—	—	—	—	—	—	—	(13,088)	(13,088)
Balance as of December 31, 2019	28,000,000	27,813	—	—	764,408	1	664	(31,302)	(30,637)
Issuance of Series B redeemable convertible preferred stock, net of issuance costs of $367	—	—	73,333,330	87,633	—	—	—	—	—
Conversion of redeemable convertible preferred stock into common stock upon initial public offering	(28,000,000)	(27,813)	(73,333,330)	(87,633)	15,492,019	1	115,445	—	115,446
Initial public offering of common stock, net of underwriting expenses and offering costs of $10,149	—	—	—	—	6,900,000	—	93,351	—	93,351
Exercise of common stock options	—	—	—	—	57,614	—	51	—	51
Exercise of common stock warrant	—	—	—	—	46,358	—	—	—	—
Stock-based compensation	—	—	—	—	—	—	755	—	755
Net loss	—	—	—	—	—	—	—	(29,539)	(29,539)
Balance as of December 31, 2020	—	$ —	—	$ —	23,260,399	$ 2	$ 210,266	$ (60,841)	$ 149,427

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

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

	Year Ended December 31,	
	2020	2019
Cash flows from operating activities		
Net loss	$ (29,539)	$ (13,088)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	755	196
Depreciation and amortization	36	12
Non-cash lease expense	66	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(2,883)	(67)
Accounts payable and accrued expenses	3,733	(226)
Accrued compensation and benefits	177	572
Other assets	(6)	(36)
Other liabilities	142	20
Net cash used in operating activities	(27,519)	(12,617)
Cash flows from investing activities		
Purchases of property and equipment	(74)	(4)
Net cash used in investing activities	(74)	(4)
Cash flows from financing activities		
Proceeds from issuance of Series A redeemable convertible preferred stock, net of issuance costs	—	7,941
Proceeds from issuance of Series B redeemable convertible preferred stock, net of issuance costs	87,633	—
Proceeds from initial public offering, net of underwriting discounts and commissions	96,255	—
Payment of issuance costs for initial public offering	(2,904)	—
Proceeds from exercise of common stock options	51	—
Proceeds from issuance of term loan, net of issuance costs of $8	—	4,492
Net cash provided by financing activities	181,035	12,433
Net increase (decrease) in cash, cash equivalents and restricted cash	153,442	(188)
Cash, cash equivalents, and restricted cash at beginning of period	3,924	4,112
Cash, cash equivalents, and restricted cash at end of period	$ 157,366	$ 3,924
Supplemental cash flow data:		
Cash paid for interest	$ 192	$ 20
Supplemental disclosure of non-cash investing and financing activities:		
Right-of-use assets recognized in exchange for lease liabilities	$ 1,858	$ —
Conversion of Series A redeemable convertible preferred stock to common stock upon initial public offering	$ 27,813	$ —
Conversion of Series B redeemable convertible preferred stock to common stock upon initial public offering	$ 87,633	$ —
Fair value of common stock warrant issued in connection with term loan	$ —	$ 57
Exercise of 46,358 shares of common stock related to a cashless exercise of common stock warrant issued in connection with term loan	$ —	$ —

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 rare endocrine disorders with significant unmet medical need. The Company is initially developing its wholly-owned product candidate, tildacerfont, as the potential first non-steroidal therapy to offer markedly improved disease control and reduce steroid burden for patients suffering from classic congenital adrenal hyperplasia (CAH) and a rare form of polycystic ovary syndrome (PCOS). The Company is located in Daly City, California and was incorporated in the state of Delaware in April 2016.

Reverse Stock Split

In October 2020, the Company filed an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of shares of the Company's common stock on a 1-for-6.541 basis (Reverse Stock Split). Adjustments corresponding to the Reverse Stock Split were made to the ratio at which the Company's redeemable convertible preferred stock converted into common stock in connection with the closing of the initial public offering (IPO). The par value of the common stock and number of shares authorized were not adjusted as a result of the Reverse Stock Split. All references to common stock, options to purchase common stock, warrants, share data, per share data, and related information contained in the financial statements and related footnotes have been retrospectively adjusted to reflect the effect of the Reverse Stock Split for all periods presented.

Initial Public Offering

In October 2020, the Company consummated its IPO and issued a total of 6,900,000 shares of common stock, which includes 900,000 shares issued pursuant to the exercise of the underwriters' option to purchase additional shares, at an offering price of $15.00 per share. In aggregate, the Company received net proceeds of $93.4 million, after deducting underwriting discounts and commissions and offering expenses. Upon the closing of the IPO, all outstanding shares of the Company's redeemable convertible preferred stock automatically converted into 15,492,019 shares of common stock.

Liquidity and Capital Resources

As of December 31, 2020, the Company had cash and cash equivalents of $157.2 million, which is sufficient to fund its planned operations for a period of at least twelve months following the issuance of the accompanying financial statements.

The Company has incurred significant losses and negative cash flows from operations. During the year ended December 31, 2020, the Company incurred a net loss of $29.5 million and used $27.5 million of cash in operations. As of December 31, 2020, the Company had an accumulated deficit of $60.8 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 redeemable convertible preferred stock, debt, and the IPO. In February 2020, the Company issued and sold 36,666,665 shares of Series B redeemable convertible preferred stock (Series B preferred stock) for approximately $43.6 million in net proceeds. In August 2020, the Company issued and sold an additional 36,666,665 shares of Series B preferred stock for approximately $44.0 million in net proceeds.

The Company anticipates that it will need to raise substantial additional financing in the future to fund its operations. In order to meet these additional cash requirements, the Company may seek to 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. 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.

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, valuation of common stock and stock-based compensation, valuation of warrants and income tax 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 and commercial success of the Company's product candidate, tildacerfont, ability to obtain regulatory approval of tildacerfont, 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 and untested manufacturing capabilities, and dependence on key individuals and sole source suppliers.

The Company's business has been and could continue to be adversely affected by the evolving COVID-19 pandemic. For example, the COVID-19 pandemic has resulted in and could result in delays to the Company's clinical trials for numerous reasons including additional delays or difficulties in enrolling patients, diversion of healthcare resources away from the conduct of clinical trials, interruption or delays in the operations of the FDA or other regulatory authorities, and delays in clinical sites receiving the supplies and materials to conduct our clinical trials. At this time, the extent to which the COVID-19 pandemic impacts the Company's business will depend on future developments, which are highly uncertain. The Company will continue to evaluate the impact that these events could have on its future operations, financial position, and results of operations and cash flows.

Segment Reporting

The Company operates and manages its business as one operating segment, which is the business of designing and developing novel therapies for rare endocrine disorders. The Company's chief executive officer, who is the chief operating decision maker, 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.

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 consist of amounts invested in money market funds.

Restricted Cash

The Company has cash in a collateral account related to a letter of credit issued on behalf of the Company for the security deposit on the non-cancelable operating lease for an office facility. The collateralized cash in connection with the letter of credit was classified as restricted cash on the balance sheet as of December 31, 2020 based on the terms of the lease agreement, which expires in 2025, unless extended.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the condensed statements of cash flows (in thousands):

	December 31,	
	2020	2019
Cash and cash equivalents	$ 157,150	$ 3,924
Restricted cash	216	—
Total cash, cash equivalents and restricted cash	$ 157,366	$ 3,924

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 estimated interest rates currently available to the Company for debt with similar terms.

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 sheet. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held.

Leases

The Company adopted Accounting Standards Update (ASU), No. 2016-02, Leases (Topic 842) effective January 1, 2020.

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 and excludes lease incentives. 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 minimum lease payments is recognized on a straight-line basis over the non-cancelable lease term. 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. The Company also elected the package of practical expedients under the transition guidance that will retain the historical lease classification and initial direct costs for any leases that exist prior to adoption of the new guidance and the practical expedient to not separate lease and non-lease components. Prior period amounts have not been adjusted and continue to be reported in accordance with the Company's historical accounting under previous lease guidance, Accounting Standards Codification (ASC) 840, Leases (Topic 840). See Note 4 to these financial statements for additional detail.

During 2019, leases were accounted for under ASC 840, Leases, and classified as operating leases. The Company's operating lease agreements include scheduled rent escalations over the lease term. During 2019, rent expense was charged ratably on a straight-line basis over the life of the lease from the date the Company obtains the legal right to use and control the leased space.

Redeemable Convertible Preferred Stock

The Company records redeemable convertible preferred stock at fair value on the dates of issuance, net of issuance costs. Upon the occurrence of certain events that are outside the Company's control, including a deemed liquidation event such as a merger, acquisition and sale of all or substantially all of the Company's assets, holders of the redeemable convertible preferred stock can cause redemption for cash. Therefore, redeemable convertible preferred stock is classified as temporary equity (mezzanine) on the balance sheet as events triggering the liquidation preferences are not solely within the Company's control. The carrying values of the redeemable convertible preferred stock are adjusted to their liquidation preferences if and when it becomes probable that such a liquidation event will occur. Upon the consummation of the IPO, all shares of redeemable convertible preferred stock outstanding were automatically converted into 15,492,019 shares of common stock.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses include, but are not limited to, 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.

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 services 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.

Patent Costs

Costs related to filing and pursuing patent applications are expensed as incurred, as recoverability of such expenditures is uncertain. These costs are included in general and administrative expenses and were immaterial for each of the periods presented.

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 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 must assess 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. As of December 31, 2020 and 2019, the Company maintains a full valuation allowance on its net deferred tax assets.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merits, as the largest amount of benefit that is more likely than not to be realized upon the 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.

Stock-Based Compensation

The Company has an equity incentive plan under which various types of equity-based awards including, but not limited to, incentive stock options, non-qualified stock options, and restricted stock awards, may be granted to employees, non-employee directors, and non-employee consultants.

For equity awards granted to employees and directors, the Company recognizes compensation expense based on the estimated grant-date fair values. The fair value of stock options is determined using the Black-Scholes option

pricing model. The Company recognizes compensation expense for stock option awards on a straight-line basis over the requisite service period of the award, generally four years. Forfeitures are recorded as they occur.

Stock-based compensation expense related to stock options granted to nonemployees is recognized based on the fair value of the stock options, determined using the Black-Scholes option pricing model, as they are earned. The awards generally vest over the period the Company expects to receive services from the nonemployee. Non-employee stock-based compensation expense was not material in any period presented.

The Company's determination of the fair value of stock options with time-based vesting on the date of grant utilizes the Black-Scholes option-pricing model and is impacted by its common stock price as well as other variables including, but not limited to, expected term that options will remain outstanding, expected common stock price volatility over the term of the option awards, risk-free interest rates and expected dividends. The fair value of a stock-based award is recognized over the period during which an optionee is required to provide services in exchange for the option award, known as the requisite service period (usually the vesting period) on a straight-line basis. Stock-based compensation expense is recognized based on the fair value determined on the date of grant and is reduced for forfeitures as they occur.

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, redeemable convertible preferred stock, stock options, employee stock purchase plan and common stock warrants are considered to be potentially dilutive securities. Basic and diluted net loss attributable to common stockholders per share is presented in conformity with the two-class method required for participating securities as the redeemable convertible preferred stock is considered a participating security because it participates in dividends with common stock. The holders of all series of redeemable convertible preferred stock do not have a contractual obligation to share in the Company's losses. As such, the net loss was attributed entirely to common stockholders. 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.

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.

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 Not Yet Adopted

In June 2016, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2016-13, Measurement of Credit Losses on Financial Instruments (Topic 326): *Measurement of Credit Losses on Financial Instruments*. ASU 2016-13 requires companies to measure credit losses utilizing a methodology that reflects expected credit losses and requires a consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU 2016-13 is effective for non-EGC's electing to use the extended transition period for complying with new or revised accounting standards for fiscal years beginning after December 15, 2019, and for EGC's for fiscal years beginning after December 15, 2022, with early adoption permitted. The Company expects to adopt this ASU on January 1, 2023. The Company is currently assessing the impact of adopting this standard, but based on a preliminary assessment, does not expect the adoption of this guidance to have a material impact on its financial statements.

In December 2019, the FASB issued ASU 2019-12, Income Taxes (Topic 740): *Simplifying the Accounting for Income Taxes*. The amendments in ASU 2019-12 are intended to simplify various aspects related to accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. ASU 2019-12 is effective for public business entities for fiscal years beginning after December 15, 2020 and the Company will adopt on January 1, 2021. The Company is currently assessing the impact of adopting this standard; however, it does not expect the adoption of this guidance to have a material impact on its financial statements.

Recently Adopted Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02, Leases. ASU 2016-02 requires a lessee to recognize right of use asset and lease liability for all leases with lease terms of more than 12 months, along with additional qualitative and quantitative disclosures. ASU 2016-02 is effective for the Company beginning January 1, 2022, with early adoption permitted. The Company elected the modified retrospective approach and adopted ASC 842 on January 1, 2020. The Company also elected the package of practical expedients under the transition guidance that will retain the historical lease classification and initial direct costs for any leases that exist prior to adoption of the new guidance and the practical expedient to not separate lease and non-lease components. As of the date of adoption, the Company did not have any leases subject to capitalization under ASC 842, and as such, there was no impact to the financial statements. Since adoption, the Company entered into a new lease and recorded a $1.9 million right-of-use asset and $1.9 million lease liability upon commencement of the lease in September 2020. See Note 5 for further disclosure.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820). This new guidance removes, modifies and adds to certain disclosure requirements on fair value measurements in Topic 820. This new guidance became effective for all entities for fiscal years beginning after December 15, 2019. Accordingly, the Company adopted ASU 2018-13 as of January 1, 2020. The adoption did not have any impact on the Company's financial statements as of and for the year ended December 31, 2020.

3. Fair Value Measurements

The carrying amounts of cash equivalents approximate their fair value based upon quoted market prices. Certain of the Company's financial instruments are not measured at fair value on a recurring basis but are recorded at amounts that approximate their fair value due to their liquid or short-term nature, such as cash, prepaid expenses, accounts payable and accrued expenses. The Company did not have any financial assets measured nor liabilities recorded at fair value on a recurring or non-recurring basis as of December 31, 2020 and 2019.

The estimated fair value of the term loan was $4.8 million as of December 31, 2020 and was based on estimated interest rates currently available to the Company for debt with similar terms, a Level 3 input.

4. Balance Sheet Components

Accrued Expenses and Other Current Liabilities

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

	December 31,	
	2020	2019
Accrued research and development expenses	$ 2,002	$ 265
Accrued general and administrative expenses	245	—
Lease liability, current portion	249	—
Total accrued expenses and other current liabilities	$ 2,496	$ 265

Accrued research and development expenses were primarily related to clinical trials, preclinical studies, and manufacturing.

5. Leases

The Company leases space under non-cancelable operating leases which require the Company to pay base rent, real estate taxes, insurance, general repairs, and maintenance. The Company does not have finance leases. As described in Note 2, the Company adopted ASC Topic 842 as of January 1, 2020.

In February 2020, the Company entered into a non-cancelable operating lease for office space with a commencement date of September 2020. The monthly payments escalate over the 63-month term with total gross commitments of $2.3 million. The lease includes an option to renew the lease term for an additional period of 60 months. The renewal option is not included in the lease term or minimum lease payments disclosures below as the Company is not reasonably certain to exercise the option. Lease incentives, which relate to rent abatement, were considered in the calculation of the lease liability and right-of-use asset. Lease expense for the year ended December 31, 2020 was $0.1 million.

In February 2019, the Company entered into a short-term lease for office space with a commencement date of March 2019. Total gross commitments over the 12-month term were $0.2 million. In February 2020, the Company extended the lease for an additional three months for a total of $42 thousand in additional commitments. The lease was terminated in May 2020.

Short-term lease expense for the year ended December 31, 2020 was $0.1 million. Rent expense for the year ended December 31, 2019 was $0.1 million and was recognized under prior Topic 840.

Lease right-of-use assets and liabilities are recognized at the commencement date based on the present value of the remaining minimum lease payments over the lease term, with certain adjustments as described in Note 2. As the leases do not provide an implicit rate, the Company uses a collateralized incremental borrowing rate based on the information available at the commencement date to determine the lease liability. As of December 31, 2020, the weighted-average remaining lease term for operating leases was 4.9 years and the weighted-average discount rate was 7.0%. Cash paid for amounts included in the measurement of lease liabilities was $37 thousand for the year ended December 31, 2020.

The Company recognizes monthly operating lease expense on a straight-line basis over the term of the lease. 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. Variable lease expense for the year ended December 31, 2020 was minimal.

Future minimum annual lease commitments under the Company's non-cancelable operating leases as of December 31, 2020 were as follows (in thousands):

	Amount
2021	$ 377
2022	464
2023	478
2024	493
2025	464
Total undiscounted future minimum lease payments	2,276
Less: present value discount	(374)
Total discounted future minimum lease payments	$ 1,902
Lease liability, current portion (included in "accrued expenses and other current liabilities" on the condensed balance sheet)	$ 249
Lease liability, net of current portion	1,653
Total operating lease liability	$ 1,902

6. Term Loan

In September 2019, the Company entered into a Loan and Security Agreement (the Loan Agreement) with Silicon Valley Bank (SVB) providing for a term loan (the Term Loan). In April 2020, the Company and SVB entered into an agreement (the Deferral Agreement) whereby the parties agreed to extend the Interest-Only Period (defined below), repayment dates of all monthly payments of principal due and the maturity date with respect to the Term Loan by six months. All other terms of the Term Loan remained unchanged. The Deferral Agreement was determined to be a debt modification, resulting in a prospective yield adjustment based on the revised terms.

Pursuant to the Loan Agreement, the Company had the ability to request up to $4.5 million of borrowings in two tranches of term loans. In September 2019, the Company requested $2.5 million from the first tranche (the First Tranche) in connection with the entry into the Loan Agreement. The Loan Agreement provided the option to request an additional $2.0 million (the Second Tranche), after the Company reached certain borrowing conditions as stipulated in the Loan Agreement. The Company satisfied these conditions and drew the Second Tranche of $2.0 million in December 2019. Pursuant to the Deferral Agreement, principal payments shall commence in January 2021 and the Term Loan will mature in September 2022.

Outstanding principal balances under the Term Loan bear interest at a floating per annum rate equal to the greatest of: (i) 1% below the prime rate, (ii) 4.25%, or (iii) 1% below the prime rate as of September 23, 2019. Under the Term Loan, as amended by the Deferral Agreement, the Company is required to make monthly payments of interest only commencing on the first day of the month following the funding date of each respective tranche and continuing thereafter through December 31, 2020 (the Interest-Only Period). Following the Interest-Only Period, the outstanding Term Loan balance will be payable in (i) 21 consecutive equal monthly payments of principal beginning on the first day of the calendar month 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 note balance, as of January 1, 2021, over the repayment period, plus (ii) monthly payments of accrued but unpaid interest. The final payment due on the maturity date shall include all outstanding principal and all accrued unpaid interest and an End of Term Payment totaling 6% of the combined principal amount of the First and Second Tranches, or $0.3 million. The End of Term Payment is being accrued through interest expense using the effective interest method. 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 End of Term Payment, a prepayment fee between 1% and 3% of the principal amount of the First and Second Tranches, and any bank expenses become due and payable.

In connection with the First and Second Tranches under 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.

The Company also incurred $8 thousand of debt issuance costs in connection with the Term Loan, which is being amortized using the effective interest method over the life of the Term Loan. The unamortized debt issuance costs and debt discount balance was $24 thousand as of December 31, 2020.

The Term Loan and unamortized discount and debt issuance costs balances as of December 31, 2020 are shown below (in thousands):

	December 31, 2020
Total Term Loan debt	$ 4,500
Less: unamortized discount and debt issuance costs	(24)
Total Term Loan, net	4,476
Less: Term Loan, current portion	(2,554)
Term loan, net of current portion	$ 1,922

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, 2020, management believes that the Company was in compliance with all financial covenants under the Loan Agreement and there had been no material adverse change.

As of December 31, 2020, future principal payments per year under the Term Loan were as follows (in thousands):

	Amount
2021	2,571
2022	1,929
Total	$ 4,500

The Company made interest payments on the Term Loan of $0.2 million during the year ended December 31, 2020.

As discussed in Note 14, the Loan Agreement was amended in March 2021.

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.

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 year ended December 31, 2020 and management is not aware of any pending or threatened litigation.

8. Capital Structure

Common Stock

As of December 31, 2020 and 2019, the Company was authorized to issue 200,000,000 and 41,000,000 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) and after any redeemable convertible preferred share dividends are fully paid. The holder of each share of common stock is entitled to one vote. As of December 31, 2020, no dividends were declared.

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

	December 31,	
	2020	2019
Series A redeemable convertible preferred stock	—	4,280,690
Stock options, issued and outstanding	2,278,771	859,322
Stock options, available for future issuance	2,637,076	4,598
Employee stock purchase plan, available for future issuance	220,640	—
Common stock warrant	—	49,609
Total shares reserved	5,136,487	5,194,219

Redeemable Convertible Preferred Stock

Immediately prior to the closing of the IPO, all outstanding shares of the Company's redeemable convertible preferred stock converted into 15,492,019 shares of common stock and the related carrying value was reclassified to common stock and additional paid-in capital. There were no shares of redeemable convertible preferred stock outstanding as of December 31, 2020.

Issued and outstanding redeemable convertible preferred stock as of December 31, 2019, and its principal terms during the year then ended were as follows (in thousands, except share and per share amounts):

		As of December 31, 2019			
Series	Shares Authorized	Shares Issued and Outstanding	Original Issue Price Per Share	Aggregate Liquidation Amount	Net Carrying Value
Series A redeemable convertible preferred stock	28,000,000	28,000,000	$ 1.0000	$ 28,000	$ 27,813

During 2020, the Company authorized and issued 73,333,330 shares of Series B preferred stock at $1.20 per share for aggregate net proceeds of $87.6 million.

The holders of redeemable convertible preferred stock had various rights and preferences, including the following:

Liquidation Preference

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or deemed liquidation event, the holders of redeemable convertible preferred stock were entitled to be paid out of the assets of

the Company, prior and in preference to any distribution to the holders of common stock, an amount equal to the original issuance price, meaning $1.00 per share for each share of Series A redeemable convertible preferred stock (Series A preferred stock) and $1.20 per share for each share of Series B preferred stock, plus all declared but unpaid dividends, if any.

If the assets available for distribution to stockholders were insufficient to pay the holders of shares of the redeemable convertible preferred stock the full amount to which they are entitled, then the entire assets of the Company legally available for distribution would be distributed ratably among the holders of redeemable convertible preferred stock in proportion to the respective amounts each such holder is otherwise entitled to receive.

After the payment to the holders of redeemable convertible preferred stock of the full preferential amount specified above, any remaining assets would be distributed pro rata to the holders of redeemable convertible preferred stock and common stock based upon the respective shares of common stock held by each holder (assuming conversion of all such redeemable convertible preferred stock into common stock). The redeemable convertible preferred stockholders were entitled to receive the greater of the maximum participation amount, meaning $4.00 per share for each share of Series A preferred stock and $4.80 per share for each share of Series B preferred stock, or the amount they would have received if all shares of redeemable convertible preferred stock were converted into common stock immediately prior to such liquidation, dissolution, or wind up.

Conversion

The shares of redeemable convertible preferred stock were convertible into such number of shares of common stock as is determined by dividing the original issue price by the applicable conversion price in effect at the time of conversion, at the option of the holder. The conversion price was initially equal to $6.541 per share for each share of Series A preferred stock and $7.849 per share for each share of Series B preferred stock, subject to certain anti-dilution adjustments. Additionally, each share of redeemable convertible preferred stock would be automatically converted into common stock (i) immediately prior to the closing of the Company's sale of its common stock in a firm commitment underwritten public offering pursuant to a registration statement under the Securities Act of 1933, as amended, in which (a) the gross cash proceeds to the Corporation (before underwriting discounts, commissions and fees) were at least $50.0 million, (b) the price per share in the public offering was at least $15.6984 per share, and (c) the Company's shares were listed for trading on the New York Stock Exchange, Nasdaq Global Select Market or Nasdaq Global Market, or (ii) upon the affirmative election of the holders of a majority shares of then-outstanding shares of redeemable convertible preferred stock, voting together as a single class on an as-converted basis, which majority must include the approval of certain holders of Series B preferred stock.

In October 2020, pursuant to the closing of the IPO, the holders of Series A and Series B redeemable convertible preferred stock elected to automatically convert all outstanding shares of Series A and Series B redeemable convertible preferred stock into the Company's common stock, at the then-effective and applicable conversion rate.

Voting

The holders of redeemable convertible preferred stock were entitled to one vote for each share of common stock into which such redeemable convertible preferred stock could then be converted; and with respect to such vote, such holders have full voting rights and powers equal to the voting rights and powers of the holders of common stock in addition to certain separate voting requirements in favor of the holders of Series A preferred stock and Series B preferred stock.

The holders of Series A preferred stock, voting as a separate class, were entitled to elect two directors to the Board of Directors. The holders of Series B preferred stock, voting as a separate class, were entitled to elect three directors to the Board of Directors. The holders of common stock, voting as a separate class, were entitled to elect one director to the Board of Directors. All common and redeemable convertible preferred stockholders, voting together as a single class on an as-converted basis, were entitled to elect the balance of the total number of directors to the Board of Directors.

Dividends

The holders of the Series B preferred stock were entitled to receive non-cumulative dividends at an annual rate of 8% of the original issue price of $1.20 per share of the Series B preferred stock when and if declared by the Board of Directors and in preference to any dividends paid to the holders of any other class or series of redeemable convertible preferred stock or common stock. After payment of such Series B preferred stock dividend, the holders of Series A preferred stock were entitled to receive non-cumulative dividends at an annual rate of 8% of the original issue price of $1.00 per share of Series A preferred stock when and if declared by the Board of Directors and in preference to any dividends paid to the holders of common stock. After payment of such Series A preferred stock dividends and Series B preferred stock dividends, any additional dividends would be distributed among the holders of redeemable convertible preferred stock and common stock on a pro rata basis based upon the respective shares of common stock held by each holder (assuming conversion of all such redeemable convertible preferred stock into common stock). No dividends were declared during the years ended December 31, 2020 and 2019.

9. Equity Incentive Plan and Stock-Based Compensation Expense

2020 Equity Incentive Plan

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. Any shares subject to outstanding stock options or other stock awards that were granted under the 2016 Plan that terminate or expire prior to exercise or settlement; are settled in cash; are forfeited or repurchased because of the failure to vest; or are reacquired or withheld to satisfy a tax withholding obligation or the purchase or exercise price in accordance with the terms of the 2016 Plan will also be reserved for issuance under the 2020 Plan.

Under the 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, 2020.

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, 2018	430,354	$ 0.89	8.4	$ 123
Granted	485,150	1.43	—	—
Exercised	—	—	—	—
Forfeited/Cancelled	(56,182)	0.85	—	—
Balance as of December 31, 2019	859,322	1.20	7.9	209
Granted	1,775,808	3.33	—	—
Exercised	(57,614)	0.89	—	—
Forfeited/Cancelled	(298,745)	1.86	—	—
Balance as of December 31, 2020	2,278,771	$ 2.78	8.6	$ 49,059
Vested and expected to vest as of December 31, 2020	2,132,726	$ 2.76	8.5	$ 45,965
Vested and exercisable as of December 31, 2020	603,963	$ 1.42	6.2	$ 13,822

Stock options vested and expected to vest differs from total stock options outstanding as it excludes performance-based stock options for which the performance criteria have not been achieved as of December 31, 2020. During 2020, the Company granted options to purchase 127,042 shares of common stock with performance criteria stipulating that no shares will vest unless certain financing and other related milestones are achieved. In January 2021, the Board of Directors determined that the performance-based vesting criteria of such options had been satisfied. Additionally, the Company granted an option to purchase 19,003 shares of common stock with the performance criteria stipulating that no shares will vest unless certain clinical development milestones are achieved. As of December 31, 2020, the option awardee had not yet achieved this performance criteria.

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 for the year ended December 31, 2020. There were no options exercised during the years ended December 31, 2019.

As of December 31, 2020, a total of 2,647,684 shares were authorized to be issued under the 2020 Plan and 2,637,076 shares remained available for issuance, and a total of 2,268,163 shares were authorized to be issued under the 2016 Plan and no shares remained available for issuance.

As of December 31, 2019, a total of 863,920 shares were authorized to be issued and 4,598 shares remained available for issuance under the 2016 Plan.

Stock Options Granted to Employees

The Company recognizes compensation expense for stock option awards granted to employees on a straight-line basis over the requisite service period of the award, generally four years. During the years ended December 31, 2020 and 2019, the Company granted options to purchase an aggregate of 1,775,808 and 427,055 shares of common stock to grantees with a weighted-average exercise price of $3.33 and $1.43 per share, respectively. For the years ended December 31, 2020 and 2019, the weighted-average fair value of options granted was $3.56 and $0.98 per

share, respectively, and was estimated using the Black-Scholes option-pricing model, with the following weighted-average assumptions:

	2020	2019
Expected term (in years)	6.0	6.0
Expected volatility	80.1%	80.0%
Risk-free interest rate	0.4%	1.8%
Expected dividend rate	0.0%	0.0%

The total fair value of options that vested during the years ended December 31, 2020 and 2019 was $0.6 million and $0.1 million, respectively.

Stock Options Granted to Nonemployees

The Company recognizes compensation expense for stock option awards granted to nonemployees as the stock options are earned over the vesting period of the award. During the year ended December 31, 2019, the Company granted options to purchase an aggregate of 58,095 shares of common stock to nonemployees with a weighted-average exercise price of $1.44 per share. The Company did not grant any stock options to nonemployees during the year ended December 31, 2020.

2020 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. As of December 31, 2020, 220,640 shares of common stock remained available for issuance under the ESPP.

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. The initial offering period runs from October 8, 2020 to December 31, 2022.

The Company recognizes compensation expense for its ESPP awards on a straight-line basis over the requisite service period for the entire award, typically two years. Total compensation expense related to the ESPP for the year ended December 31, 2020 was $32 thousand. The following range of assumptions were used to calculate stock-based compensation for each stock purchase right granted under the ESPP:

	2020	2019
Expected term (in years)	0.7 - 2.2	—
Expected volatility	89.2 - 93.0%	—
Risk-free interest rate	0.1 - 0.2%	—
Expected dividend rate	0.0%	—

Fair Value of Equity-Settled Awards

Prior to the IPO, the fair value of the Company's common stock was determined by the Board of Directors since it was not publicly traded. The Board of Directors determined fair value of the common stock at the time of

grant of the option by considering a number of objective and subjective factors including valuation of comparable companies, sales of redeemable convertible preferred stock to third parties, operating and financial performance, the lack of liquidity of capital stock, and general and industry specific economic outlook, amongst other factors. Following the IPO, the fair market value of the Company's common stock is determined based on the closing price of its common stock on the Nasdaq Global Select Market.

Estimating the fair value of equity-settled awards as of the grant date using the Black-Scholes option pricing model is affected by assumptions regarding several complex variables. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop. These inputs are as follows:

- *Expected Term*. The expected term for employees 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. The expected term for non-employees is based on the remaining contractual term.
- *Expected Volatility*. The expected volatility is estimated based on the historical volatilities for 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 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.

Stock-Based Compensation Expense

The following table summarizes the components of stock-based compensation expense recognized in the Company's statement of operations during the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,	
	2020	2019
Research and development	$ 327	$ 119
General and administrative	428	77
Total stock-based compensation expense	$ 755	$ 196

Unrecognized stock-based compensation expense as of December 31, 2020 was approximately $5.0 million, which is expected to be recognized over a weighted-average vesting term of 3.5 years.

10. License Agreement

In May 2016, the Company entered into a license agreement (the License Agreement), with Eli Lilly and Company (Lilly). Pursuant to the terms of the 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 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 License Agreement remains in effect, of certain milestones relating to the clinical development and commercial sales of products licensed under the 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 License Agreement.

The 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.

11. Income Taxes

The Company has incurred cumulative domestic net operating losses (NOL) since inception and, consequently, has not recorded any income tax expense for the years ended December 31, 2020 and 2019 due to its net operating loss position.

The reconciliation of the federal statutory income tax rate to the Company's effective tax rate is as follows:

	December 31,	
	2020	2019
Federal statutory tax rate	21.00 %	21.00 %
State tax, net of federal benefit	6.98 %	— %
Nondeductible expenses	(0.09)%	0.14 %
Tax credits	6.15 %	2.02 %
Change in valuation allowance	(41.38)%	(23.15)%
Prior year true-up for state net operating losses	6.96 %	— %
Other	0.38 %	(0.01)%
Effective tax rate	0 %	0 %

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. Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The net valuation allowance increased by approximately $12.2 million and $3.0 million during the years ended December 31, 2020 and 2019, respectively.

Significant components of the Company's net deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 16,381	$ 6,259
Accruals	326	151
Intangible assets	143	119
Tax credits	2,500	682
Other	109	25
Total gross deferred tax assets	19,459	7,236
Valuation allowance for deferred tax assets	(19,459)	(7,236)
Total net deferred tax assets	$ —	$ —

As of December 31, 2020, the Company had federal net operating loss carryforwards of approximately $58.6 million and $58.4 million in state net operating loss carryforwards. If not utilized, the federal net operating loss carryforwards incurred before January 1, 2018 will begin to expire in 2036, and state net operating loss carryforwards will begin to expire in 2036. The federal net operating losses of $51.4 million incurred in 2018 and beyond do not expire.

Under Sections 382 and 383 of the Internal Revenue Code (IRC) of 1986, as amended (the Code), if a corporation undergoes an “ownership change,” the company’s ability to use its pre-change net operating loss carryforwards and other pre-change attributes, such as research tax credits, to offset its post-change income may be limited. In general, an “ownership change” will occur if there is a cumulative change in ownership by “5% shareholders” that exceeds 50 percentage points over a rolling three-year period. Tax credits are subject to IRC Section 383. In the event of a change in ownership as defined by this code section, the usage of the credits may be limited. Similar rules may apply under state tax laws. As of December 31, 2020, the Company determined that an ownership change occurred on May 2, 2016 and August 7, 2020. As a result of the ownership changes, the Company derecognized an immaterial amount of net operating loss-related deferred tax assets for federal and state purposes as of December 31, 2020. The ability of the Company to use its remaining net operating loss carryforwards is subject to Section 382 limitation and may be further limited if the Company experiences a Section 382 ownership change as a result of future changes in its stock ownership.

As of December 31, 2020, the Company had federal and state tax credit carryforwards of approximately $3.0 million and $0.6 million, respectively. If not utilized, the federal tax credits will begin to expire in 2036 and the state tax credits do not expire. As a result of the previously mentioned ownership changes, the Company has derecognized approximately $2 thousand of gross federal tax credit-related deferred tax assets due to the Section 383 limitation as of December 31, 2020. The Company has not derecognized any of the state tax credit-related deferred tax assets because the credits do not expire.

On March 27, 2020, the Coronavirus Aid, Relief and Economic Security (CARES) Act (the Act) was signed into law. The Act includes provisions relating to refundable payroll tax credits, deferment of the employer portion of certain payroll taxes, net operating loss carryback periods, alternative minimum tax credit refunds, modifications to the net interest deduction limitations, and technical corrections to tax depreciation methods for qualified improvement property. The Company analyzed the provisions of the Act and determined there was no significant impact to its 2020 tax provision.

On June 29, 2020, the California Governor signed Assembly Bill 85 (A.B. 85), which became California law, A.B. 85, which includes several tax measures, provided for a three-year suspension of the use of net operating losses for medium and large businesses and a three-year cap on the use of business incentive tax credits to offset no more than $5.0 million of tax per year. Generally, A.B. 85 suspends the use of net operating losses for taxable years 2020, 2021 and 2022 for taxable income of $1.0 million or more. Since the Company is not expected to generate California source taxable income of more than $1.0 million, no material impact is anticipated at this time.

On December 27, 2020, the “Consolidated Appropriations Act, 2021” (the CAA) was signed into law. The CAA includes provisions meant to clarify and modify certain items put forth in the CARES Act, while providing aid to business affected by the pandemic. The CAA allows deductions for expenses paid for by Paycheck Protection Program (PPP) and Economic Injury Disaster Loan (EIDL) Program, clarifies forgiveness of EIDL advances, and other business provisions. The Company analyzed the provisions of the CAA and determined there was no significant impact to its 2020 tax provision.

Uncertain Income Tax Positions

The Company accounts for uncertainty in income taxes in accordance with ASC 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 does not expect the amount of unrecognized tax benefits to materially change in the next 12 months.

The Company had approximately $1.1 million and $0.4 million of unrecognized tax benefits as of December 31, 2020 and 2019, respectively. As the Company has a full valuation allowance on its deferred tax assets, the unrecognized tax benefits have reduced the net deferred tax assets and the valuation allowance in the same amount.

A reconciliation of the beginning and ending balance of the unrecognized tax benefits is as follows (in thousands):

	December 31,	
	2020	2019
Balance at the beginning of the year	$ 398	$ 230
Increase of unrecognized tax benefits taken in prior years	10	—
Increase of unrecognized tax benefits related to current year	686	168
Balance at the end of the year	$ 1,094	$ 398

Interest and penalty related to unrecognized tax benefits would be included as income tax expense in the Company's statements of operations. As of December 31, 2020 and 2019, the Company had not recognized any tax-related penalties or interest in its financial statements.

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.

12. 401(k) Retirement Savings Plan

In December 2017, the Company adopted a 401(k) plan (the 401(k) Plan) for all employees who have met certain eligibility requirements. Under the agreement, employees may elect to contribute a portion of their eligible compensation, subject to certain limitations. The Company did not make any matching employer contributions to the 401(k) Plan as of and for the years ended December 31, 2020 and 2019.

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,	
	2020	2019
Numerator:		
Net loss	$ (29,539)	$ (13,088)
Denominator:		
Weighted-average common shares outstanding	5,991,213	764,408
Net loss per share, basic and diluted	$ (4.93)	$ (17.12)

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,	
	2020	2019
Series A redeemable convertible preferred stock (on an if-converted basis)	—	4,280,690
Shares subject to outstanding common stock options	2,278,771	859,322
Estimated shares issuable under the employee stock purchase plan	24,118	—
Shares subject to common stock warrants	—	49,609
Total	2,302,889	5,189,621

14. Subsequent Events

Stock Option Grants and Modification

In January 2021, the Company granted options to purchase an aggregate of 351,000 shares of common stock to employees pursuant to the 2020 Plan.

During 2020, the Company granted options to certain executive officers to purchase 127,042 shares of common stock with performance criteria stipulating that no shares will vest unless certain financing and other related milestones are achieved. In January 2021, the Board of Directors determined that the performance-based vesting criteria of such options had been satisfied, which was deemed as a modification.

First Amendment to Loan and Security Agreement

In March 2021, the Company and SVB entered into a First Amendment to Loan and Security Agreement (the First Amendment), pursuant to which the Company and SVB amended the Loan Agreement. The First Amendment increases the aggregate principal amount of the Term Loan commitment by SVB to up to $30.0 million dollars. Up to $20.0 million is available under the first tranche of the Term Loan (the First Tranche), $5.0 million of which was advanced immediately to repay the outstanding obligations under the Term Loan prior to the First Amendment with the remainder of the First Tranche commitments available through December 31, 2021, and up to $10.0 million is available under the second tranche (the Second Tranche) subject to the completion of certain clinical and financial milestones which Second Tranche commitment is available through December 31, 2022. Pursuant to the First Amendment, the Term Loan will mature on January 1, 2026.

Pursuant to the First Amendment, the Company is required to make monthly payments of interest only commencing on the first day of the month following the funding date of each respective tranche and continuing thereafter through December 31, 2022 to the extent that the Company does not borrow any part of the Second Tranche or December 31, 2023 if the Company has borrowed some or all of the Second Tranche. Outstanding principal balances under the Term Loan, as amended by the First Amendment, bear interest at a floating per annum rate equal to (A) if the Company does not borrow under the Second Tranche, the greater of (x) 1% above the prime rate or (y) 4.25%; or (B) if the Company does borrow under the Second Tranche, the greater of (x) 3% above the prime rate or (y) 6.25%.

Following the interest-only period, the outstanding Term Loan balance will be payable in (i) 37 consecutive monthly payments (or 25 if the Company borrows under the Second Tranche) after the end of the Amendment 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 interest-only period, over the repayment period, plus (ii) monthly payments of accrued but unpaid interest. The final payment due on the maturity date shall include all outstanding principal and all accrued unpaid interest and an End of Term Payment totaling (x) 6% of the original funded principal amount of the First Tranche if the Company does not borrow under the Second Tranche, or (y) 9.5% of the total original funded principal amount under the First and Second Tranche if the Company does borrow under the Second Tranche. 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 End of Term Payment, a prepayment fee between 1% and 3% of the commitment amount of the First and Second Tranches, and any bank expenses become due and payable.

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, or 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 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, 2020. Based on the evaluation of our disclosure controls and procedures as of December 31, 2020, 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

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting due to a transition period established by rules of the SEC for newly public companies.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies. Additionally, our independent registered public accounting firm will not be required to opine on our internal control over financial reporting until we are no longer an emerging growth company.

Changes in Internal Controls over Financial Reporting

Other than disclosed below, there were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) that occurred during the period covered by this Annual Report that has materially affected or is reasonably likely to materially affect, our internal control over financial reporting.

Remediation of Material Weakness

Our management previously identified a material weakness in our internal control over financial reporting primarily related to a lack of timely review over the financial statement close process in connection with the audit of our financial statements as of and for the year ended December 31, 2019. A "material weakness" is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Our management determined that we did not have a sufficient complement of qualified personnel within the accounting function and had a lack of segregation of duties to adequately conduct review and analysis of certain routine transactions. In response to the material weakness identified, management developed and implemented the following remedial actions to address the underlying causes of the material weakness, which were subject to senior management review and Audit Committee oversight:

- Hired a Chief Financial Officer, Corporate Controller and other accounting personnel with appropriate technical accounting and financial reporting experience;

- Segregated incompatible duties and implemented controls where segregation of duties could not be achieved;
- Implemented a formal process for our review procedures during the financial close process; and
- Developed and formally documented policies and procedures relating to our internal control over financial reporting.

Our management has concluded, based on evidence obtained in validating the design and operating effectiveness of the controls, that the efforts undertaken to enhance the design of our controls would lead to the prevention or detection of a material misstatement of our financial statements. As such, our management concluded that we have remediated this material weakness as of December 31, 2020.

Other than described above, there was no change in our internal control over financial reporting during the quarter ended December 31, 2020, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

On March 19, 2021, the Company and SVB entered the First Amendment, pursuant to which the Company and SVB amended the Loan Agreement. The First Amendment increases the aggregate principal amount of the Term Loan commitment by SVB to up to $30.0 million dollars. Up to $20.0 million is available under the First Tranche of the Term Loan, $5.0 million of which was advanced immediately to repay the outstanding obligations under the Term Loan prior to the First Amendment with the remainder of the First Tranche commitments available through December 31, 2021, and up to $10.0 million is available under the Second Tranche subject to the completion of certain clinical and financial milestones which Second Tranche commitment is available through December 31, 2022. Pursuant to the First Amendment, the Term Loan will mature on January 1, 2026.

Pursuant to the First Amendment, the Company is required to make monthly payments of interest only commencing on the first day of the month following the funding date of each respective tranche and continuing thereafter through December 31, 2022 to the extent that the Company does not borrow any part of the Second Tranche or December 31, 2023 if the Company has borrowed some or all of the Second Tranche. Outstanding principal balances under the Term Loan, as amended by the First Amendment, bear interest at a floating per annum rate equal to (A) if the Company does not borrow under the Second Tranche, the greater of (x) 1% above the prime rate or (y) 4.25%; or (B) if the Company does borrow under the Second Tranche, the greater of (x) 3% above the prime rate or (y) 6.25%.

Following the interest-only period, the outstanding Term Loan balance will be payable in (i) 37 consecutive monthly payments (or 25 if the Company borrows under the Second Tranche) 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 interest-only period, over the repayment period, plus (ii) monthly payments of accrued but unpaid interest. The final payment due on the maturity date shall include all outstanding principal and all accrued unpaid interest and an End of Term Payment totaling (x) 6% of the original funded principal amount of the First Tranche if the Company does not borrow under the Second Tranche, or (y) 9.5% of the total original funded principal amount under the First and Second Tranche if the Company does borrow under the Second Tranche. 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 End of Term Payment, a prepayment fee between 1% and 3% of the commitment amount of the First and Second Tranches, and any bank expenses become due and payable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is set forth in our definitive proxy statement to be filed with respect to the 2021 annual meeting of stockholders (the "Proxy Statement"), all of which is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this item is set forth in our Proxy Statement, all of which 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 is set forth in our Proxy Statement, all of which is incorporated herein by reference.

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

The information required by this item is set forth in our Proxy Statement, all of which is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item is set forth in our Proxy Statement, all of which is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

We have filed the following documents as part of this Annual Report:

(a)(1) Financial Statements

The financial statements are included in Item 8. “Financial Statements and Supplementary Data.”

(a)(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.

(a)(3) Exhibits

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation (filed as Exhibit 3.1 to the registrant’s Current Report on Form 8-K, filed with the SEC on October 14, 2020, and incorporated by reference herein).
3.2	Amended and Restated Bylaws (filed as Exhibit 3.2 to the registrant’s Current Report on Form 8-K, filed with the SEC on October 14, 2020, and incorporated by reference herein).
4.1	Form of Common Stock Certificate (filed as Exhibit 4.1 to the registrant’s Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on October 5, 2020, and incorporated by reference herein).
4.2	Amended and Restated Investors’ Rights Agreement, by and among the registrant and certain of its stockholders, dated February 19, 2020 (filed as Exhibit 4.2 to the registrant’s Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
4.3	Warrant to Purchase Common Stock issued to Silicon Valley Bank, dated September 23, 2019 (filed as Exhibit 4.3 to the registrant’s Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
4.4*	Description of Common Stock of the registrant.
10.1+	Spruce Biosciences, Inc. Amended and Restated 2016 Equity Incentive Plan (filed as Exhibit 10.1 to the registrant’s Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
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 (filed as Exhibit 10.2 to the registrant’s Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.3+	Spruce Biosciences, Inc. 2020 Equity Incentive Plan (filed as Exhibit 10.3 to the registrant’s Current Report on Form 8-K, filed with the SEC on October 5, 2020, and incorporated by reference herein).
10.4+	Forms of Grant Notice, Stock Option Agreement and Notice of Exercise under the Spruce Biosciences, Inc. 2020 Equity Incentive Plan (filed as Exhibit 10.4 to the registrant’s Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.5+	Spruce Biosciences, Inc. 2020 Employee Stock Purchase Plan (filed as Exhibit 10.5 to the registrant’s Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on October 5, 2020, and incorporated by reference herein).
10.6+*	Spruce Biosciences, Inc. 2020 Employee Stock Purchase Plan Offering Document.
10.7+	Spruce Biosciences, Inc. 2020 Non-Employee Director Compensation Policy (filed as Exhibit 10.6 to the registrant’s Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on October 5, 2020, and incorporated by reference herein).

10.8+	Form of Indemnification Agreement by and between the registrant and its directors and executive officers (filed as Exhibit 10.7 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.9+	Spruce Biosciences, Inc. Severance and Change in Control Plan (filed as Exhibit 10.9 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.10+¥	Employment Agreement, by and between the registrant and Richard King, dated October 1, 2019 (filed as Exhibit 10.11 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.11+¥	Offer Letter, by and between the registrant and Samir Gharib, dated April 8, 2020 (filed as Exhibit 10.16 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.12+¥	Offer Letter, by and between the registrant and Rosh Dias, M.D., M.R.C.P., dated July 28, 2020 (filed as Exhibit 10.17 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.13+	Letter Agreement, by and between the registrant and Michael Grey, dated March 24, 2017 (filed as Exhibit 10.18 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.14+	Letter Agreement, by and between the registrant and Camilla V. Simpson, dated October 11, 2017 (filed as Exhibit 10.19 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.15+	Letter Agreement, by and between the registrant and Daniel Spiegelman, dated August 31, 2020 (filed as Exhibit 10.20 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.16	Office Lease Agreement, by and between the registrant and DC Station Owner, LLC, dated February 13, 2020 (filed as Exhibit 10.21 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.17#	License Agreement, by and between the registrant and Eli Lilly and Company, dated May 2, 2016 (filed as Exhibit 10.22 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.18	Loan and Security Agreement, by and between the registrant and Silicon Valley Bank, dated September 23, 2019 (filed as Exhibit 10.23 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-248924), filed with the SEC on September 18, 2020, and incorporated by reference herein).
10.19*	First Amendment to Loan and Security Agreement, by and between the registrant and Silicon Valley Bank dated March 19, 2021.
23.1*	Consent of BDO USA, LLP, independent registered public accounting firm.
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.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*†	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*†	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document

101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

\+ 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 not material and would likely cause competitive harm to the registrant if publicly disclosed.

¥ 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.

March 22, 2021

By: /s/ *Richard King*
Richard King
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Richard King 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/ *Richard King* Richard King	Chief Executive Officer and Director (Principal Executive Officer)	March 22, 2021
/s/ *Samir Gharib* Samir Gharib	Chief Financial Officer (Principal Financial Officer)	March 22, 2021
/s/ *Michael Grey* Michael Grey	Executive Chairman	March 22, 2021
/s/ *Tiba Aynechi, Ph.D.* Tiba Aynechi, Ph.D.	Director	March 22, 2021
/s/ *Dina Chaya, Ph.D., C.F.A.* Dina Chaya, Ph.D., C.F.A.	Director	March 22, 2021
/s/ *Jonas Hansson, M.Sc.* Jonas Hansson, M.Sc.	Director	March 22, 2021
/s/ *Bali Muralidhar, M.D, Ph.D.* Bali Muralidhar, M.D, Ph.D.	Director	March 22, 2021
/s/ *Niall O'Donnell, Ph.D.* Niall O'Donnell, Ph.D.	Director	March 22, 2021
/s/ *Camilla V. Simpson, M.Sc.* Camilla V. Simpson, M.Sc.	Director	March 22, 2021
/s/ *Daniel Spiegelman* Daniel Spiegelman	Director	March 22, 2021

Exhibit 4.4

DESCRIPTION OF COMMON STOCK

General

The following description summarizes the terms of the common stock of Spruce Biosciences, Inc., or we, our or us. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description of the matters set forth in this "Description of Common Stock," you should refer to our amended and restated certificate of incorporation and amended and restated bylaws, which are included as exhibits to our Annual Report on Form 10-K, and to the applicable provisions of the Delaware General Corporation Law. Our amended and restated certificate of incorporation authorizes us to issue 200,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share. Our board of directors is authorized, without stockholder approval except as required by the listing standards of The Nasdaq Stock Market LLC, to issue additional shares of our capital stock. In addition, under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock.

Voting Rights

Our common stock is entitled to one vote per share on any matter that is submitted to a vote of our stockholders. Our amended and restated certificate of incorporation does not provide for cumulative voting for the election of directors. Our amended and restated certificate of incorporation establishes a classified board of directors that is divided into three classes with staggered three-year terms. Only the directors in one class will be subject to election by a plurality of the votes cast at each annual meeting of our stockholders, with the directors in the other classes continuing for the remainder of their respective three-year terms.

Economic Rights

Except as otherwise expressly provided in our amended and restated certificate of incorporation or required by applicable law, all shares of common stock have the same rights and privileges and rank equally, share ratably and be identical in all respects for all matters, including those described below.

Dividends. Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine.

Liquidation Rights. On our liquidation, dissolution or winding-up, the holders of our common stock will be entitled to share equally, identically and ratably in all assets remaining after the payment of any liabilities, liquidation preferences and accrued or declared but unpaid dividends, if any, with respect to any outstanding preferred stock, unless a different treatment is approved by the affirmative vote of the holders of a majority of the outstanding shares of such affected class, voting separately as a class.

No Preemptive or Similar Rights

The holders of shares of our common stock are not entitled to preemptive rights and are not subject to conversion, redemption or sinking fund provisions.

Exchange Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "SPRB."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent's address is 250 Royal Street, Canton, Massachusetts 02021.

Anti-Takeover Provisions

The provisions of Delaware law, our amended and restated certificate of incorporation and amended and restated bylaws, which are summarized below, may have the effect of delaying, deferring or discouraging another person from acquiring control of our company. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Certificate of Incorporation and Bylaws

Because our stockholders do not have cumulative voting rights, stockholders holding a majority of the voting power of our shares of common stock will be able to elect all of our directors. Our amended and restated certificate of incorporation and amended and restated bylaws provide that stockholders may only take action at a duly called meeting of stockholders. A special meeting of stockholders may be called by a majority of our board of directors, the chair of our board of directors or our chief executive officer. Our amended and restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors. In accordance with our amended and restated certificate of incorporation, our board of directors is divided into three classes with staggered three-year terms.

The foregoing provisions will make it more difficult for another party to obtain control of us by replacing our board of directors. Since our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of deterring hostile takeovers or delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, subject to certain exceptions.

Choice of Forum

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) shall be the sole and exclusive forum for the following claims or causes of action under the 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 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 amended and restated bylaws (as each may be amended from time to time); (v) any claim or cause of action as to which the Delaware General Corporation Law confers jurisdiction on 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 having personal jurisdiction over the indispensable parties named as defendants; provided these provisions of our amended and restated certificate of incorporation and amended and restated bylaws will not apply to claims or causes of action brought to enforce a duty or liability created by the Securities Act of 1933, Securities Exchange Act of 1934, as amended, or any other claim for which the federal courts have exclusive jurisdiction. Our amended and restated certificate of incorporation and amended and restated bylaws further provide that, to the fullest extent permitted by law, the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act of 1933, as amended, unless we consent in writing to the selection of an alternative forum.

Exhibit 10.6

SPRUCE BIOSCIENCES, INC.

2020 EMPLOYEE STOCK PURCHASE PLANOFFERING DOCUMENT

ADOPTED BY THE BOARD OF DIRECTORS: SEPTEMBER 9, 2020

In this document, capitalized terms not otherwise defined will have the same definitionsof such terms as in the Spruce Biosciences, Inc. 2020 Employee Stock Purchase Plan.

1. GRANT; OFFERING DATE.

(a) The Board hereby authorizes a series of Offerings pursuant to the terms of this Offering Document.

(b) The first Offering hereunder (the "***Initial Offering***") will begin on the IPO Date and will end on December 31, 2022, unless terminated earlier as provided below. The Initial Offering will consist of four Purchase Periods with the first Purchase Period ending on June 30, 2021, the second Purchase Period ending on December 31, 2021, the third Purchase Period ending on June 30, 2022 and the fourth Purchase Period (and the Initial Offering) ending on December 31, 2022.

(c) After the Initial Offering commences, a new Offering will thereafter automatically begin on July 1, 2021, and every six (6) months thereafter over the term of the Plan. Each Offering will be approximately twenty-four (24) months in duration, and Offerings will be concurrent. Each Offering will consist of four (4) Purchase Periods of approximately six (6) months in duration ending on June 30 and December 31 each year. Except as provided below, a Purchase Date is the last day of a Purchase Period or of an Offering, as the case may be.

(d) Notwithstanding the foregoing: (i) if any Offering Date falls on a day that is not a Trading Day, then such Offering Date will instead fall on the next subsequent Trading Day, and
(ii) if the last day of either a Purchase Period or an Offering (and therefore any Purchase Date) falls on a day that is not a Trading Day, then such last day of the Purchase Period or Offering (and therefore the Purchase Date) will instead fall on the immediately preceding Trading Day.

(e) Prior to the commencement of any Offering, the Board or Committee may changeany or all terms of such Offering and any subsequent Offerings. The granting of Purchase Rightspursuant to each Offering hereunder will occur on each respective Offering Date unless (i) prior to such date the Board or Committee determines that such Offering will not occur, or (ii) no shares of Common Stock remain or will be available for issuance under the Plan in connection with such Offering.

(f) Notwithstanding anything in this Section 1 to the contrary, if the Fair Market Value of a share of Common Stock on any Offering Date of a subsequent Offering (the "***New Offering***") is less than or equal to the Fair Market Value of a share of Common Stock on the

Offering Date for an ongoing Offering (the "***Ongoing Offering***"), then such Ongoing Offering shall terminate immediately following the purchase of shares of Common Stock on the Purchase Date of such Ongoing Offering, and Participants in the terminated Ongoing Offering automatically shall be enrolled in the New Offering. Thereafter, notwithstanding the provisions of Section 1(c) above, instead of a new Offering commencing pursuant to Section 1(c), a new Offering shall begin on the date that is six (6) months after the New Offering that commences pursuant to this Section 1(f) and every six (6) months thereafter, and each such Offering shall end on the date that is twenty-four (24) months after its Offering Date.

2. ELIGIBLE EMPLOYEES.

(a) "***Eligible Employee***" means an Employee as of the applicable enrollment deadline who is either: (i) an Employee of the Company; or (ii) an Employee of a Related Corporation incorporated in the United States; or (iii) an Employee of a Related Corporation that is not incorporated in the United States but whose employees the Board or Committee has designated as eligible to participate in the Offering. Each Eligible Employee as of an Offering Date who has completed the necessary enrollment paperwork (including any enrollment form) by the applicable deadline, will be granted a Purchase Right on the Offering Date of such Offering.

(b) Each person who first becomes an Eligible Employee during an Offering shall not be granted a Purchase Right under such ongoing Offering, but shall be eligible to participate in the next subsequent Offering and shall be granted a Purchase Right under such subsequent Offering; *provided*, *however*, that as a condition to the grant of a Purchase Right under such subsequent Offering, the Eligible Employee must submit the necessary enrollment paperwork (including any enrollment form) required by the Company at least seven (7) business days (or such other period of time as determined by the Company and communicated to Participants) before the start of such Offering.

(c) Notwithstanding the foregoing, the following Employees will ***not*** be Eligible Employees or be granted Purchase Rights under an Offering:

(i) five percent stockholders (including ownership through unexercised and/or unvested stock options) as described in Section 5(c) of the Plan; or

(ii) Employees in jurisdictions outside of the United States if, as of the Offering Date of the Offering, the grant of such Purchase Rights under this Offering Document would not be in compliance with the applicable laws, regulations or requirements of any jurisdiction in which the Employee resides or is employed, as determined in the sole discretion of the Board or Committee.

3. PURCHASE RIGHTS; PURCHASE LIMITS.

(a) Subject to the limitations herein and in the Plan, a Participant's Purchase Right will permit the purchase of the number of shares of Common Stock purchasable with up to 15% of such Participant's Earnings paid during the Offering, beginning as of the date such Participant first commences participation in that Offering; *provided*, *however*, that no Participant may have more than 15% of such Participant's Earnings applied to purchase shares of Common Stock

under all ongoing Offerings under the Plan and all other plans of the Company and Related Corporations that are intended to qualify as employee stock purchase plans under Section 423 of the Code. In the case of a payroll date that falls after the Purchase Date of one Purchase Period but prior to the first Trading Day of the immediately following Purchase Period, if applicable, Earnings from such payroll will be included in the new Purchase Period. In the case of a payroll date that falls after the last Purchase Date of an Offering but prior to the Offering Date of the next new Offering, Earnings from such payroll will be included in the new Offering (provided the Eligible Employee continues to participate in the new Offering).

(b) For Offerings hereunder, "***Earnings***" means the cash compensation paid to a Participant, consisting of the Participant's base salary or base wage rate, including the value of amounts elected to be deferred by such Participant under any 401(k) plan or other deferred compensation program or arrangement established by the Company or a Related Corporation, but excluding all of the following: bonuses, commissions and overtime pay, if applicable, and all other cash remuneration paid directly to the Participant, including, without limitation, profit sharing contributions, the cost of employee benefits paid for by the Company or a Related Corporation, education or tuition reimbursements, imputed income (whether or not arising under any Company or Related Corporation group insurance or benefit program), traveling expenses, business expense reimbursements, moving expense reimbursements, housing and living allowances, income received, reported or otherwise recognized in connection with stock options and other equity awards, contributions made by the Company or a Related Corporation underany employee benefit plan, and other similar items of compensation.

(c) However, the maximum number of shares of Common Stock that a Participant may purchase on any Purchase Date in an Offering will be such number of shares as has a Fair Market Value (determined as of the Offering Date for such Offering) equal to (1) US $25,000 multiplied by the number of calendar years in which the Purchase Right under such Offering has been outstanding at any time, minus (2) the Fair Market Value of any other shares of Common Stock (determined as of the relevant Offering Date with respect to such shares) that, for purposesof the limitation of Section 423(b)(8) of the Code, are attributed to any of such calendar years in which the Purchase Right has been outstanding. In all cases, this US $25,000 limit will be determined in accordance with regulations applicable under Section 423(b)(8) of the Code. In particular, the amount in clause (2) will be determined based on (i) the number of shares previously purchased with respect to such calendar years pursuant to such Offering or any other Offering under the Plan, and pursuant to any other Company or Related Corporation plans intended to qualify as an employee stock purchase plan under Section 423 of the Code, and (ii) the number of shares subject to other Purchase Rights outstanding on the Offering Date for such Offering pursuant to the Plan and any other such Company or Related Corporation plan intended to qualify as an Employee Stock Purchase Plan.

(d) In addition, the maximum number of shares of Common Stock that may bepurchased on any single Purchase Date by any one Participant is 20,000 shares.

(e) Notwithstanding the foregoing, in all cases, the maximum aggregate number of shares of Common Stock available to be purchased by all Participants under an Offering will be the number of shares of Common Stock remaining available under the Plan on the Offering Date,

rounded down to the nearest whole share, taking into account the Purchase Rights granted or to be granted under all other contemporaneous Offerings under the Plan. If the aggregate number of shares of Common Stock to be purchased upon the exercise of all outstanding Purchase Rights on a single Purchase Date under all on-going Offerings would exceed the foregoing limit, the Board or Committee will make a pro rata allocation (based on each Participant's accumulated Contributions) on the applicable Purchase Date of the shares available (as of the Offering Date) in a uniform and equitable manner.

(f) Any Contributions not applied to the purchase of shares of Common Stock as a result of the application of the limits set forth in this Section 3 will be refunded to the Participants at the end of the Offering without interest (unless otherwise required by applicable laws or regulations).

4. PURCHASE PRICE.

The purchase price of shares of Common Stock under an Offering will be the lesser of:
(i) 85% of the Fair Market Value of such shares of Common Stock on the Offering Date, and
(ii) 85% of the Fair Market Value of such shares of Common Stock on the applicable Purchase Date, in each case rounded up to the nearest whole cent per share. For the Initial Offering, the Fair Market Value of the shares of Common Stock on the Offering Date will be the price per share at which shares are first sold to the public in the Company's initial public offering, as specified in the final prospectus for that initial public offering.

5. PARTICIPATION.

(a) Contributions may be made through payroll deductions only, unless payroll deductions are prohibited by applicable laws or regulations or unless the Company or a Participant's employer determines that another means of contributing is required or advisable forlegal or administrative reasons.

(b) An Eligible Employee's election to participate in an Offering is effective on the Offering Date. An Eligible Employee must elect his or her Contribution rate on the enrollment form provided by the Company (the "***Enrollment and Change Request Form***"). The completed Enrollment and Change Request Form must be delivered to the Company at least seven (7) business days prior to the Offering Date, unless a different time is set by the Company for all Eligible Employees with respect to a given Offering. Contribution rates must be expressed in whole percentages of Earnings, with a minimum percentage of 1% (except as otherwise providedherein) and a maximum percentage of 15%.

(c) A Participant may increase or decrease his or her Contribution level, with such change effective as of the next Purchase Period or Offering, by delivering the required Enrollment and Change Request Form at least seven (7) business days (or such other period of time as determined by the Company and communicated to Participants) prior to the start of the Purchase Period or Offering, as applicable, for which it is to be effective. However, the Company may determine in its sole discretion at any time, including at any time following the commencement of an Offering, that it will no longer accept Participant requests to increase or

decrease Contribution levels.

(d) Unless otherwise determined by the Company and communicated to Participants with respect to the Purchase Period or Offering, a Participant may not increase his or her Contribution level as to Contributions to be made during a Purchase Period. A Participant may decrease (including a decrease to 0%) his or her Contribution level no more than one time per Purchase Period, with such change effective as to Contributions to be made during such ongoing Purchase Period. The Participant must deliver an Enrollment and Change Request Form stating the new decreased Contribution level at least seven (7) business days (or such other period of time as determined by the Company and communicated to Participants) prior to the payroll date for which it is to be effective. Any Participant who has not increased his or her Contribution level as to Contributions to be made for the next Offering from 0% to at least 1% at least seven (7) business days (or such other period of time as determined by the Company and communicated to Participants) prior to the start of a new Offering will be withdrawn from the Plan effective as of the first day of that new Offering.

(e) A Participant may withdraw from an Offering and receive a refund of his or her Contributions (reduced to the extent, if any, such Contributions have been used to acquire shares of Common Stock for the Participant on any prior Purchase Date) without interest, at any time prior to the end of the Offering, but excluding the seven (7) business day period immediately preceding a Purchase Date (or such other period of time determined by the Company and communicated to Participants), by delivering the required Enrollment and Change Form. A Participant who has withdrawn from an Offering may not again participate in that Offering, but may participate in subsequent Offerings.

(f) Eligible Employees may not make an investment decision regarding participation in an Offering, including electing a Contribution level, until a registration statement covering the shares reserved under the Plan for that Offering has been filed by the Company and has become effective. The Company may establish procedures to enable the purposes of the Plan to be satisfied while complying with applicable securities laws.

(g) For the Initial Offering only, each Eligible Employee who is employed on the Offering Date for the Initial Offering automatically will be enrolled in the Initial Offering, with aPurchase Right to purchase up to the number of shares of Common Stock that are purchasable with 15% of the Eligible Employee's Earnings attributable to the Initial Offering, subject to the limitations set forth in Section 3 above. Immediately following the filing of an effectiveregistration statement pursuant to a Form S-8, Eligible Employees will have a period of approximately two (2) weeks, unless a different period is selected by the Company (with the last such day of that period referred to as the "***Election Date***") within which to (i) withdraw from the Plan or (ii) authorize Contributions through payroll deductions for the purchase of shares during the Initial Offering (which may be for a percentage that is less than 15% of the Eligible Employee's Earnings, including 0%). Authorized payroll deductions will begin on the first regularly scheduled payroll paydate that occurs at least seven (7) business days following the Election Date (unless an earlier paydate is selected by the Company). If an Eligible Employee fails to authorize payroll deductions at a Contribution level of at least 1% by the Election Date, the Eligible Employee will be deemed to have elected a 0% Contribution Rate for the first

Purchase Period of the Initial Offering and no shares will be purchased for the Eligible Employeeon the first Purchase Date of the Initial Offering. However, the Eligible Employee's Purchase Right will remain outstanding and he or she may still authorize payroll deductions for the secondPurchase Period of the Initial Offering. If the Eligible Employee has not timely elected payroll deductions at the rate of at least 1% before the start of the second Purchase Period of the Initial Offering, his or her Purchase Right for the Initial Offering will be immediately terminated, he or she will be automatically withdrawn from the Plan, and he or she must affirmatively enroll and authorize payroll deductions in accordance with Section 5(a) above to participate in futureOfferings.

(h) Once an Eligible Employee affirmatively enrolls in an Offering and authorizes Contributions (including in connection with the Initial Offering), the Eligible Employee automatically will be enrolled for all subsequent Offerings that begin after the end of theOffering in which the Eligible Employee is a Participant until he or she elects to withdraw from an Offering pursuant to Section 5(e) above, is deemed to have withdrawn pursuant to Section 5(d) above, or otherwise terminates his or her participation in the Plan (including through termination of employment with the Company or a Related Corporation).

6. PURCHASES.

Subject to the limitations contained herein, on each Purchase Date, each Participant's Contributions (without any increase for interest) will be applied to the purchase of whole shares of Common Stock, up to the maximum number of shares permitted under the Plan and the Offering. On a Purchase Date, each Participant's purchases shall first be made under the Offering for which purchases are being made on such Purchase Date that results in stock being purchased for such Participant at the lowest price under all Offerings in which such Participant has been granted Purchase Rights and under which stock is then being purchased on such Purchase Date. The Company may require that such shares of Common Stock be retained with a particular broker or agent for a designated period of time and/or may establish other procedures to permit tracking of qualifying and disqualifying dispositions of such shares of Common Stock.

7. NOTICES, FORMS AND AGREEMENTS.

Any notices, forms or agreements provided for in an Offering or the Plan will be given in writing, in a form provided by the Company (including documents delivered in electronic form, if authorized by the Committee). Unless specifically provided for in the Plan or this Offering document, notices, forms and agreements will be deemed effectively given upon receipt (including documents delivered in electronic form).

8. EXERCISE CONTINGENT ON STOCKHOLDER APPROVAL.

The Purchase Rights granted under an Offering are subject to the approval of the Plan by the stockholders of the Company as required for the Plan to obtain treatment as an Employee Stock Purchase Plan.

9. OFFERING SUBJECT TO PLAN.

Each Offering is subject to all the provisions of the Plan, and the provisions of the Plan are hereby made a part of the Offering. The Offering is further subject to all interpretations, amendments, rules and regulations which may from time to time be promulgated and adopted pursuant to the Plan. In the event of any conflict between the provisions of an Offering and those of the Plan (including interpretations, amendments, rules and regulations which may from time to time be promulgated and adopted pursuant to the Plan), the provisions of the Plan will control.

10. CHANGES TO ONGOING OFFERINGS.

Notwithstanding anything in this Offering Document to the contrary, the Board and/or the Committee are entitled to: (i) establish the exchange ratio applicable to Contributions in a currency other than U.S. dollars, if applicable; (ii) permit Contributions in excess of the amount designated by a Participant to adjust for mistakes in the Company's processing of properly completed Contribution elections; (iii) establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of Common Stock for each Participant properly correspond with that Participant's Contributions;
(iv) amend any outstanding Purchase Rights or clarify any ambiguities regarding the terms of any Offering to enable the Purchase Rights to qualify under and/or comply with Section 423 of the Code; and (v) establish other limitations or procedures as the Board and/or the Committee determines in its sole discretion advisable that are consistent with the Plan. The actions of the Board or Committee pursuant to this paragraph will not be considered to alter or impair the Purchase Rights granted under this Offering Document as they are part of the initial terms of each Purchase Period and the Purchase Rights granted under this Offering Document.

Exhibit 10.19

FIRST AMENDMENT
TO
LOAN AND SECURITY AGREEMENT

This First Amendment to Loan and Security Agreement (this "Amendment") is entered into as of March 19, 2021, by and between Silicon Valley Bank ("Bank") and Spruce Biosciences, Inc., a Delaware corporation ("Borrower"), whose address is 2001 Junipero Serra Blvd., Suite 640, Daly City, CA 94014.

RECITALS

A. Bank and Borrower have entered into that certain Loan and Security Agreement dated as of September 23, 2019 (as the same may from time to time be amended, modified, supplemented or restated, the "Loan Agreement").

B. Bank has extended credit to Borrower for the purposes permitted in the Loan Agreement.

C. Borrower has requested that Bank amend the Loan Agreement to (i) make available to Borrower an additional term loan facility and (ii) make certain other revisions to the Loan Agreement as more fully set forth herein.

D. Bank has agreed to so amend certain provisions of the Loan Agreement, but only to the extent, in accordance with the terms, subject to the conditions and in reliance upon the representations and warranties set forth below.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing recitals and other good and valuable consideration, the receipt and adequacy of which is hereby acknowledged, and intending to be legally bound, the parties hereto agree as follows:

1. Definitions. Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.

2. Amendments to Loan Agreement.

2.1 Section 2.1.1 (**Term Loans**). Sections 2.1.1(b) and (c) are amended in their entirety and replaced with the following:

(b) Repayment. All Term Loans shall be repaid in accordance with Section 2.1.2(a)(i) below.

(c) Final Payment. Borrower shall pay the Final Payment in accordance with Section 2.1.2(a)(i) below.

2.2 Section 2.1.2 (**Supplemental Term Loans**). A new Section 2.1.2 is added to the Loan Agreement as follows:

2.1.2 Supplemental Term Loans.

(a) Availability. Subject to the terms and conditions of this Agreement, Bank agrees to make advances to Borrower (each a "**Supplemental Term Loan**" and collectively the "**Supplemental Term Loans**"), from time to time, prior to the Supplemental Term Loan Commitment Termination Date (Supplemental Second Tranche), in an aggregate amount not to exceed the Supplemental Term Loan Commitment. Each Supplemental Term Loan must be in an amount of not less than Five Million Dollars ($5,000,000). After repayment, no Supplemental Term Loan may be reborrowed.

(i) Up to Twenty Million Dollars ($20,000,000) of the Supplemental Term Loan Commitment (the "**Supplemental First Tranche**") shall be available through the Supplemental Term Loan Commitment Termination Date (Supplemental First Tranche). Subject to the terms and conditions hereof, on or about the First Amendment Date Bank shall advance to Borrower a Supplemental Term Loan under the Supplemental First Tranche in an amount equal to Five Million Dollars ($5,000,000), the proceeds of which shall immediately be used to repay all Obligations (including the Final Payment) owing with respect to the Term Loans.

(ii) The remaining Ten Million Dollars ($10,000,000) of the Supplemental Term Loan Commitment (the "**Supplemental Second Tranche**") shall be available through the Supplemental Term Loan Commitment Termination Date (Supplemental Second Tranche), provided Borrower achieves the Supplemental Second Tranche Milestone. Funds will be available under the Supplemental Second Tranche as soon as Borrower delivers to Bank evidence satisfactory to Bank that Borrower has achieved the Supplemental Second Tranche Milestone.

(b) Repayment of Supplemental Term Loans.

(i) Interest-Only Payments. For each Supplemental Term Loan, Borrower shall make monthly payments of interest-only commencing on the first (1st) Business Day of the first (1st) month following the month in which the Funding Date occurs with respect to such Supplemental Term Loan and continuing thereafter during the Supplemental Interest-Only Period, on the first (1st) Business Day of each successive month.

(ii) Principal and Interest Payments. For each Supplemental Term Loan outstanding as of the last day of the Supplemental Interest-Only Period, Borrower shall make (i) thirty-seven (37) (or twenty-five (25), if a Supplemental Term Loan has been made under the Supplemental Second Tranche) consecutive equal monthly payments of principal commencing on the first (1st) Business Day of the first (1st) month after the Supplemental Interest-Only Period (the "**Supplemental Conversion Date**") and continuing on the first (1st) Business Day of each month thereafter, in amounts that would fully amortize the applicable Supplemental Term Loan, as of the Supplemental Conversion Date, over the Supplemental Repayment Period plus (ii) monthly payments of accrued but unpaid interest. The Supplemental Final Payment and all unpaid principal and accrued and

unpaid interest on each Supplemental Term Loan is due and payable in full on the Supplemental Term Loan Maturity Date.

(c) Voluntary Prepayment. Borrower shall have the option to prepay all Supplemental Term Loans in full, provided Borrower (i) shall provide written notice to Bank of its election to prepay the Supplemental Term Loans at least five (5) Business Days prior to such prepayment and (ii) pays, on the date of such prepayment, (A) all outstanding principal and accrued but unpaid interest, plus (B) the Supplemental Prepayment Fee, plus (C) the Supplemental Final Payment, plus (D) all other sums, including Bank Expenses, if any, that shall have become due and payable.

(d) Mandatory Prepayment Upon an Acceleration. If the Supplemental Term Loans are accelerated following the occurrence of an Event of Default, Borrower shall immediately pay to Bank an amount equal to the sum of (i) all outstanding principal and accrued but unpaid interest, plus (ii) the Supplemental Prepayment Fee, plus (iii) the Supplemental Final Payment, plus (iv) all other sums, including Bank Expenses, if any, that shall have become due and payable.

2.3 Section 2.3 (**Payment of Interest on the Credit Extensions**). Section 2.3(a) is amended by adding a new clause (ii) to the end thereof as follows:

(ii) Supplemental Term Loans. Subject to Section 2.3(b), the principal amount outstanding for each Supplemental Term Loan shall accrue interest at a floating per annum rate equal to (A) if no Supplemental Term Loan has been made under the Supplemental Second Tranche, the greater of (x) one percentage point (1.00%) above the Prime Rate or (y) four and one-quarter percent (4.25%), or (B) if a Supplemental Term Loan has been made under the Supplemental Second Tranche, the greater of (x) three percentage points (3.00%) above the Prime Rate or (y) six and one-quarter percent (6.25%), in each case, which shall be payable monthly in accordance with Section 2.3(d) hereof.

2.4 Section 2.4 (**Fees**). Sections 2.4(a) and (b) are amended in their entirety and replaced with the following:

(a) Supplemental Final Payment. The Supplemental Final Payment when due hereunder;

(b) Supplemental Prepayment Fee. The Supplemental Prepayment Fee, if and when due hereunder; and

2.5 Section 3.5 (**Procedures for Borrowing**). Section 3.5(a) is amended by deleting each reference to "Term Loan" and "Term Loans" and substituting in lieu thereof the terms "Credit Extension" and "Credit Extensions", respectively.

2.6 Section 6.2 (**Financial Statements, Reports**). Sections 6.2(a), (b), (e), (f) and (h) are amended in their entirety and replaced with the following:

(a) Quarterly Financial Statements. No later than forty-five (45) days after the last day of each fiscal quarter (other than the last fiscal quarter of each fiscal year),

Borrower's 10-Q filing for such quarter including a consolidated balance sheet, statement of cash flows and income statement covering Borrower's consolidated operations for such quarter prepared in accordance with GAAP (other than for the absence of footnotes and subject to year-end audit adjustments) as filed by Borrower with the SEC (the "**Quarterly Financial Statements**");

(b) Quarterly Compliance Statement. Within forty-five (45) days after the last day of each fiscal quarter (other than the last fiscal quarter of each fiscal year) and together with the Quarterly Financial Statements, a duly completed Compliance Statement, confirming that as of the end of such quarter, Borrower was in full compliance with all of the terms and conditions of this Agreement, and setting forth such other information as Bank may reasonably request;

(e) Annual Financial Statements. No later than ninety (90) days after the last day of Borrower's fiscal year end, Borrower's 10-K filing for such fiscal year including audited and certified consolidated financial statements prepared under GAAP, consistently applied, as filed by Borrower with the SEC, together with an unqualified opinion (other than a qualification as to going concern typical for venture backed companies similar to Borrower) on the financial statements from an independent certified public accounting firm reasonably acceptable to Bank (the "**Annual Financial Statements**");

(f) Annual Compliance Statement. Within ninety (90) days after the last day of Borrower's fiscal year end and together with the Annual Financial Statements, a duly completed Compliance Statement, confirming that as of the end of such fiscal year, Borrower was in full compliance with all of the terms and conditions of this Agreement, and setting forth such other information as Bank may reasonably request;

(h) SEC Filings. Within five (5) days of filing, copies of all periodic and other reports, proxy statements and other materials filed by Borrower with the SEC, any Governmental Authority succeeding to any or all of the functions of the SEC or with any national securities exchange, or distributed to its shareholders, as the case may be Documents required to be delivered pursuant to the terms of this Section 6.2 (to the extent any such documents are included in materials otherwise filed with the SEC) may be delivered electronically and if so delivered, shall be deemed to have been delivered on the date on which Borrower notifies SVB in writing (which may be by electronic mail) that Borrower has (i) posted such documents, or provided a link thereto, on Borrower's website on the Internet at Borrower's website address or (ii) made such documents available in the SEC's EDGAR filing system.

2.7 Section 6.6 (**Operating Accounts**). Section 6.6(a) is amended in its entirety and replaced with the following:

(a) (i) Borrower shall maintain at least eighty percent (80%) of its operating account balances and excess cash with Bank or Bank's Affiliates and (ii) Borrower shall obtain any business credit cards exclusively from Bank.

2.8 Section 8.1 (**Payment Default**). Section 8.1 is amended by deleting the reference to "Term Loan Maturity Date" and substituting in lieu thereof "Supplemental Term Loan Maturity Date".

2.9 Section 12.1 (**Termination Prior to Term Loan Maturity Date; Survival**). Section 12.1 is amended by (a) renaming the section as "Termination Prior to Maturity Date; Survival" and (b) deleting the phase to "prior to the Term Loan Maturity Date by Borrower, effective three (3) Business Days after written notice of termination is given to Bank" and substituting in lieu thereof the phrase "prior to the Supplemental Term Loan Maturity Date in accordance with Section 2.1.2(c)".

2.10 Section 13 (**Definitions**). The following term and its definition set forth in Section 13.1 are amended in their entirety and replaced with the following:

"**Credit Extension**" is any Term Loan, Supplemental Term Loan or any other extension of credit by Bank for Borrower's benefit under this Agreement.

2.11 Section 13 (**Definitions**). The following terms and their respective definitions are added to Section 13.1 in appropriate alphabetical order:

"**Annual Financial Statements**" is defined in Section 6.2(e).

"**First Amendment Date**" is March 19, 2021.

"**Quarterly Financial Statements**" is defined in Section 6.2(a).

"**Supplemental Conversion Date**" is defined in Section 2.1.2(b)(ii).

"**Supplemental Final Payment**" is a payment (in addition to and not a substitution for the regular monthly payments of principal plus accrued interest) due in accordance with Section 2.1.2 above, equal to the original principal amount of the Supplemental Term Loans multiplied by the Supplemental Final Payment Percentage.

"**Supplemental Final Payment Percentage**" is (a) if no Supplemental Term Loan has been made under the Supplemental Second Tranche, six percent (6.00%), or (b) if a Supplemental Term Loan has been made under the Supplemental Second Tranche, nine and one-half percent (9.50%).

"**Supplemental First Tranche**" is defined in Section 2.1.2(a)(i).

"**Supplemental Interest-Only Period**" means, with respect to each Supplemental Term Loan, the period commencing on the Funding Date of such Supplemental Term Loan and continuing through (a) if no Supplemental Term Loan has been made under the Supplemental Second Tranche, December 31, 2022, or (b) if a Supplemental Term Loan has been made under the Supplemental Second Tranche, December 31, 2023.

"**Supplemental Prepayment Fee**" shall be, with respect to the prepayment of the Supplemental Term Loans, an amount equal to (i) three percent (3.0%) of the Supplemental

Term Loan Commitment if such prepayment occurs prior to the first (1st) anniversary of the First Amendment Date, (ii) two percent (2.0%) of the Supplemental Term Loan Commitment if such prepayment occurs on or after the first (1st) anniversary of the First Amendment Date but prior to the second (2nd) anniversary of the First Amendment Date, or (iii) one percent (1.0%) of the Supplemental Term Loan Commitment if such prepayment occurs on or after the second (2nd) anniversary of the First Amendment Date.

"**Supplemental Repayment Period**" is the period of time commencing on the Supplemental Conversion Date and continuing through the Supplemental Term Loan Maturity Date.

"**Supplemental Second Tranche**" is defined in Section 2.1.2(a)(ii).

"**Supplemental Second Tranche Milestone**" means Bank's receipt of evidence satisfactory to Bank that Borrower has either (a) received positive data in pivotal Phase 2b studies sufficient to submit a New Drug Application for tildacerfont in congenital adrenal hyperplasia or (b) received gross cash proceeds of at least Seventy-Five Million Dollars ($75,000,000) from the sale and issuance of Borrower's equity interests in a public offering to investors, and on terms and conditions, satisfactory to Bank.

"**Supplemental Term Loan**" is defined in Section 2.1.2(a).

"**Supplemental Term Loan Commitment**" is Thirty Million Dollars ($30,000,000).

"**Supplemental Term Loan Commitment Termination Date (Supplemental First Tranche)**" is December 31, 2021.

"**Supplemental Term Loan Commitment Termination Date (Supplemental Second Tranche)**" is December 31, 2022.

"**Supplemental Term Loan Maturity Date**" is January 1, 2026.

2.12 Section 13 (Definitions). The following term and its definition are deleted from Section 13.1 in their entirety:

"**Monthly Financial Statements**"

2.13 Exhibit D (Compliance Statement). Exhibit D to the Loan Agreement is amended in its entirety and replaced with Exhibit D attached hereto.

3. Limitation of Amendments.

3.1 The amendments set forth in Section 2, above, are effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right or remedy which Bank may now have or may have in the future under or in connection with any Loan Document.

3.2 This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents, except as herein amended, are hereby ratified and confirmed and shall remain in full force and effect.

4. Representations and Warranties. To induce Bank to enter into this Amendment, Borrower hereby represents and warrants to Bank as follows:

4.1 Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct as of such date), and (b) no Event of Default has occurred and is continuing;

4.2 Borrower has the power and authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

4.3 The organizational documents of Borrower most recently delivered to Bank remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

4.4 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, have been duly authorized;

4.5 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not and will not contravene (a) any law or regulation binding on or affecting Borrower, (b) any contractual restriction with a Person binding on Borrower, (c) any order, judgment or decree of any court or other governmental or public body or authority, or subdivision thereof, binding on Borrower, or (d) the organizational documents of Borrower;

4.6 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not require any order, consent, approval, license, authorization or validation of, or filing, recording or registration with, or exemption by any governmental or public body or authority, or subdivision thereof, binding on Borrower, except as already has been obtained or made; and

4.7 This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

5. Integration. This Amendment and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements. All prior

agreements, understandings, representations, warranties, and negotiations between the parties about the subject matter of this Amendment and the Loan Documents merge into this Amendment and the Loan Documents.

6. Counterparts. This Amendment may be executed in any number of counterparts and all of such counterparts taken together shall be deemed to constitute one and the same instrument.

7. Electronic Execution of Documents. Each party hereto may execute this Amendment by electronic means and recognizes and accepts the use of electronic signatures and records by any other party hereto in connection with the execution and storage hereof.

8. Effectiveness. This Amendment shall be deemed upon (a) the due execution and delivery to Bank of this Amendment by each party hereto, and (b) payment of Bank's legal fees and expenses in connection with the negotiation and preparation of this Amendment (Bank acknowledges receipt of a good faith deposit in the amount of Twenty-Five Thousand Dollars ($25,000), which will be applied to Bank Expenses on the First Amendment Date with any remainder to be refunded to Borrower).

[Signature page follows.]

In Witness Whereof, the parties hereto have caused this Amendment to be duly executed and delivered as of the date first written above.

BANK	**BORROWER**
Silicon Valley Bank	Spruce Biosciences, Inc.
By: /s/ Shawn Perry	By: /s/ Samir Gharib
Name: Shawn Perry	Name: Samir Gharib
Title: Managing Director	Title: Chief Financial Officer

EXHIBIT D

COMPLIANCE CERTIFICATE

TO: SILICON VALLEY BANK Date: _____
FROM: SPRUCE BIOSCIENCES, INC.

Under the terms and conditions of the Loan and Security Agreement between Borrower and Bank dated as of the Effective Date (the "**Agreement**"), Borrower is in complete compliance for the period ending _____ with all required covenants except as noted below**.** Attached are the required documents evidencing such compliance, except as explained in an accompanying letter or footnotes. Capitalized terms used but not otherwise defined herein shall have the meanings given them in the Agreement.

Please indicate compliance status by circling Yes/No under "Complies" column.

Reporting Covenants	**Required**	**Complies**
Quarterly 10-Q with financial statements (consolidated balance sheet, statement of cash flows, and income statement) with Compliance Statement	Within 45 days of quarter end (except for the last quarter of each FY)	Yes No
Annual 10-K with financial statement (CPA Audited) + CS	Within 90 days of FYE	Yes No
Annual Projections	FYE within 30 days; and more frequently as updated	Yes No
8-K and other filings with SEC	Within 5 days after filing with SEC	Yes No

Other Matters

Have there been any amendments of or other changes to the Operating Documents of Borrower or any of its Subsidiaries? If yes, provide copies of any such amendments or changes with this Compliance Statement.	Yes	No
Have there been any material amendments of or other material changes to the capitalization table of Borrower or any of its Subsidiaries (excluding, for the avoidance of doubt, changes relating to stock options and issuances)? If yes, provide copies of any such amendments or changes with this Compliance Statement.	Yes	No

The following are the exceptions with respect to the statements above: (If no exceptions exist, state "No exceptions to note.")

Exhibit 23.1

Tel: 408-278-0220
Fax: 408-278-0230
www.bdo.com

300 Park Avenue, Suite 900
San Jose, CA 95110

Consent of Independent Registered Public Accounting Firm

Spruce Biosciences, Inc.
Daly City, California

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-249431) of Spruce Biosciences, Inc. of our report dated March 22, 2021, relating to the financial statements which appear in this Form 10K.

/s/ BDO USA, LLP
San Jose, California

March 22, 2021

Exhibit 31.1

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

I, Richard King, certify that:

1. I have reviewed this Annual Report on Form 10-K of Spruce Biosciences, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 22, 2021

By: /s/ Richard King

Richard King
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

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

I, Samir Gharib, certify that:

1. I have reviewed this Annual Report on Form 10-K of Spruce Biosciences, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 22, 2021

By: /s/ Samir Gharib

Samir Gharib
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

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

In connection with the Annual Report of Spruce Biosciences, Inc. (the "Company") on Form 10-K for the period ending December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 22, 2021

By: /s/ Richard King

Richard King
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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

In connection with the Annual Report of Spruce Biosciences, Inc. (the "Company") on Form 10-K for the period ending December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 22, 2021

By: /s/ Samir Gharib

Samir Gharib
Chief Financial Officer
(Principal Financial Officer)