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: 001-36310

CONCERT PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**20-4839882**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
65 Hayden Avenue, Suite 3000N Lexington, Massachusetts	**02421**
(Address of principal executive offices)	**(Zip code)**

(781) 860-0045
(Registrant's telephone number, including area code)

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

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

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2020 was approximately $173,586,000 based on the closing price of the registrant's common stock on the Nasdaq Global Market on that date.

The number of shares outstanding of the registrant's common stock as of February 19, 2021: 32,173,778

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2021 Annual Meeting of Stockholders. Portions of such proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

CONCERT PHARMACEUTICALS, INC.
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REFERENCES TO CONCERT

Throughout this Annual Report on Form 10-K, "Concert," "the Company," "we," "us" and "our," except where the context requires otherwise, refer to Concert Pharmaceuticals, Inc. and its consolidated subsidiaries, and "our board of directors" refers to the board of directors of Concert Pharmaceuticals, Inc.

FORWARD-LOOKING STATEMENTS

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

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

- ongoing and planned clinical trials for our product candidates, whether conducted by us or by our collaborators, including the timing of initiation, enrollment and completion of these trials and of the anticipated results;
- our plans to identify, develop and commercialize novel small molecule drugs based on our knowledge of deuterium chemistry;
- our plans to enter into collaborations for the development and commercialization of product candidates;
- our expected benefits from our current and any future collaboration, development or license arrangements;
- our ability to receive research and development funding and achieve anticipated milestones under our collaborations;
- our expectations regarding any future milestone payments we may receive as part of our asset purchase agreement with Vertex Pharmaceuticals, Inc. with respect to VX-561;
- our expectations regarding any future milestone payments or royalties we may receive as part of our agreement with Avanir Pharmaceuticals Inc. with respect to AVP-786 and payments from our other collaboration and license arrangements;
- the timing of and our ability to obtain and maintain marketing approvals for our product candidates;
- the rate and degree of market acceptance and clinical utilization of our products;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- the outcome of our inter partes review proceeding regarding U.S. Patent No. 9,249,149 covering CTP-543 and the post grant review petition challenging U.S. Patent No. 10,561,659 covering CTP-543;
- our freedom to operate with respect to third-party patents;
- our expectations regarding our DCE Platform® and the potential advantages of our product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- conditions and events that raise doubt about our ability to continue as a going concern;
- risks associated with the COVID-19 pandemic, which may adversely impact our business, clinical trials and supply chain;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in Part I, Item 1A. Risk Factors, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking

statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations or investments that we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

SUMMARY OF THE MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous risks and uncertainties, including those described in the "Risk Factors" section in Part I, Item 1A. of this Annual Report on Form 10-K. The principal risks and uncertainties affecting our business include the following:

- Our business may be adversely affected by the ongoing COVID-19 pandemic.
- We have incurred significant losses since inception, expect to incur losses for at least the next several years and may never sustain profitability.
- Based on our current operating plan, there is substantial doubt regarding our ability to continue as a going concern.
- We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our development programs or commercialization efforts.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome.
- We may not be able to continue further clinical development of our wholly owned development programs, including CTP-543. If we are unable to develop, obtain marketing approval for or commercialize our wholly owned development programs, ourselves or through a collaboration, or experience significant delays in doing so, our business could be materially harmed.
- If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or our collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.
- If we, or our collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our product candidates, potential marketing approval or commercialization of our product candidates could be delayed or prevented.
- If we, or our collaborators, experience delays or difficulties in the enrollment of patients in clinical trials, our, or their, receipt of necessary marketing approvals could be delayed or prevented.
- Serious adverse events, undesirable side effects or other unexpected properties of our product candidates, including those that we have licensed to collaborators, may be identified during development that could delay or prevent the product candidate's marketing approval.
- We rely on third parties to conduct our clinical trials and some aspects of our research and nonclinical testing. If they terminate their relationships with us or do not perform satisfactorily, our business may be materially harmed.
- We depend on collaborations with third parties for the development and commercialization of some of our product candidates and expect to continue to do so in the future. Our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.
- We expect to seek to establish additional collaborations, and if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.
- If we are unable to obtain and maintain sufficient patent protection for our product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates may be adversely affected.
- Third parties may sue us alleging that we are infringing their intellectual property rights, and such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.
- We contract with third parties for the manufacture and distribution of our product candidates for nonclinical and clinical testing and expect to continue to do so in connection with our future development and commercialization efforts. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, or that the product candidates will not be of sufficient quality or reproducibility or produced on our desired schedule, which could delay, prevent or impair our development or commercialization efforts.
- Even if we complete the necessary nonclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and we may not obtain approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or our collaborators, will obtain marketing approval to commercialize a product candidate.

- We face substantial competition from other pharmaceutical and biotechnology companies and our operating results may suffer if we fail to compete effectively.

The summary risk factors described above should be read together with the text of the full risk factors below, in the section entitled "Risk Factors" and the other information set forth in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes, as well as in other documents that we file with the SEC. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us, or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

Part I

Item 1. Business

OVERVIEW

We are a clinical stage biopharmaceutical company that is developing small molecule drugs that we discovered through the application of our deuterated chemical entity platform, or DCE Platform®. Selective incorporation of deuterium into known molecules has the potential, on a case-by-case basis, to provide better pharmacokinetic or metabolic properties, thereby enhancing their clinical safety, tolerability or efficacy. Our lead product candidate is in late-stage development for the treatment of alopecia areata, a serious autoimmune dermatological condition. We are also assessing a number of earlier-stage pipeline candidates.

OUR STRATEGY

Our strategy is to apply our deuterium technology to previously studied molecules, including approved drugs, in which deuterium substitution has the potential to enhance clinical safety, tolerability or efficacy. We select pipeline candidates based on the medical needs of patients, commercial opportunity, regulatory considerations and competitive landscape. We use deuterium technology to develop deuterated product candidates that we believe are promising in view of the known biology of previously studied compounds, including approved drugs, in which deuterium substitution has the potential to enhance clinical safety, tolerability or efficacy. Our strategy includes potential commercialization of product candidates on our own, or with strategic partners.

Deuterium

Due to its natural abundance, the average adult human body contains approximately two grams of deuterium. While essentially identical to hydrogen in size and shape, deuterium differs from hydrogen in that it contains an additional neutron. As a result, deuterium forms a more stable chemical bond with carbon than does hydrogen. The deuterium-carbon bond is typically six to nine times more stable than the hydrogen-carbon bond. This has important implications for drug development because drug metabolism often involves the breaking of hydrogen-carbon bonds.

Because deuterium forms more stable bonds with carbon, deuterium substitution can in some cases alter drug metabolism, including through improved metabolic stability, reduced formation of toxins, increased formation of desired active metabolites or a combination of these effects. At the same time, these improvements in drug metabolism are possible without materially altering the intrinsic biological activity of a compound. Deuterated compounds with enhanced metabolic properties can generally be expected to retain biochemical potency and selectivity similar to their hydrogen analogs. The effects, if any, of deuterium substitution on metabolic properties are highly dependent on the specific molecular positions at which deuterium is substituted for hydrogen. In addition, the metabolic effects of deuterium substitution, if any, are unpredictable, even in compounds that have similar chemical structures.

Potential advantages of product candidates based on our DCE Platform

Using our DCE Platform, we create novel drugs designed to have superior properties - including enhanced clinical safety, tolerability or efficacy - based on compounds that have established pharmacological activity. In many instances, Phase 1 clinical evaluation has the potential to demonstrate whether there will be product differentiation.

Potential advantages of our DCE Platform include the following:

- *Improved metabolic profile.* An improved metabolic profile may potentially reduce or eliminate unwanted side effects or undesirable drug interactions or increase efficacy. Metabolic profile refers to the relative amounts and exposure profile of the parent drug and its metabolites or metabolic by-products in the body.

- *Increased half-life.* A longer half-life may decrease the number of doses that a patient is required to take per day or provide more consistent exposure of the compound in comparison to the corresponding non-deuterated compound, potentially improving the drug's therapeutic profile. Half-life is usually defined as the time it takes for the body to clear half of a given concentration of the drug from the plasma.

- *Avoidance of undesirable metabolism.* By avoiding first pass metabolism, we may be able to improve oral bioavailability, which could potentially lead to better efficacy at a lower dose of drug. First pass metabolism is metabolism that occurs before the drug reaches the circulatory system.

- *Improved biodistribution*. Changes in the rate of drug metabolism in a specific organ can alter drug exposure in the organ, relative to plasma concentrations. If a deuterated drug achieves higher organ levels relative to plasma levels than its non-deuterated analog, therapeutically-relevant drug concentrations in that organ may be achieved by administering a smaller amount of the deuterated drug.

OUR PRODUCT CANDIDATES

Our lead product candidate, CTP-543, is in late-stage development for the treatment of alopecia areata, a serious autoimmune dermatological condition. We are also assessing a number of earlier-stage pipeline candidates.

CTP-543

Background on Alopecia Areata

Alopecia areata is a serious, chronic autoimmune disease affecting approximately 700,000 Americans at any given time that results in partial or complete loss of hair on the scalp and/or body. Alopecia areata occurs when the immune system attacks the hair follicles and is characterized as non-scarring hair loss. It presents in a number of patterns including:

- Patchy: coin-sized or larger patch or patches of hair loss;
- Totalis: no hair on the head; and
- Universalis: no hair anywhere on the body.

Onset can occur at any age including childhood, and it affects both women and men equally. The average age of onset is between 25-35 years. The emotional effect of alopecia areata can be considerable and may result in anxiety and depression or affect personal attributes such as self-esteem and confidence. Alopecia areata may also be associated with other autoimmune conditions such as allergic rhinitis, asthma, atopic dermatitis, lupus, rheumatoid arthritis, thyroid disease, ulcerative colitis and vitiligo. The most common form of treatment is corticosteroids including intralesional injections or topical application. However, corticosteroids are typically not well tolerated and often provide limited efficacy. There are currently no treatments approved by the U.S. Food and Drug Administration, or FDA, for alopecia areata.

CTP-543 Opportunity

CTP-543 is an oral selective inhibitor of Janus kinases JAK1 and JAK2 that we are developing for the treatment of moderate to severe alopecia areata. CTP-543 was discovered by applying our deuterium chemistry technology to modify ruxolitinib, a Janus kinase, or JAK, inhibitor, which is commercially available under the name Jakafi® in the United States for the treatment of certain blood disorders and for graft versus host disease. The FDA has granted CTP-543 Breakthrough Therapy designation for the treatment of adult patients with moderate to severe alopecia areata and Fast Track designation for the treatment of alopecia areata. CTP-543 is currently in Phase 3 development.

Clinical Development of CTP-543

We have completed multiple Phase 2 trials of CTP-543 for the treatment of moderate to severe alopecia areata to support the advancement of the program into Phase 3 development. In September 2019, we announced results from a Phase 2 double-blind, randomized, dose-ranging trial to evaluate three sequential doses of CTP-543 (4, 8 and 12 mg twice-daily) and a placebo control in 149 patients with moderate to severe alopecia areata. Patients treated with either 8 mg twice-daily or 12 mg twice-daily doses of CTP-543 met the primary efficacy endpoint with statistically significant differences ($p < 0.001$) relative to placebo in the percentage of patients achieving a $\geq$ 50% relative change from baseline at 24 weeks. The 8 mg twice-daily and 12 mg twice-daily dose groups were also significantly different from placebo in the number of patients achieving $\geq$ 75% and $\geq$ 90% relative change in Severity of Alopecia Tool, or SALT, score between baseline at 24 weeks. A numerically but not statistically greater percentage of patients treated with the 4 mg twice-daily dose of CTP-543 met the primary efficacy endpoint. At 24 weeks, patients treated with 8 mg twice-daily and 12 mg twice-daily doses compared to placebo also rated significantly greater improvement in their alopecia areata on the Patient Global Impression of Improvement Scale. Treatment with CTP-543 was generally well tolerated. The most common side effects in the 8 mg or 12 mg twice-daily dose groups were headache, nasopharyngitis, upper respiratory tract infection, acne, nausea and low-density lipoprotein increase. One serious adverse event of facial cellulitis was reported in the 12 mg twice-daily dose group as possibly related to treatment; however, after a brief interruption, treatment continued and this patient completed the trial. No thromboembolic events were reported during the trial.

In June 2020, we released new data analyses from our Phase 2 dose-ranging trial of CTP-543 supporting the design of our Phase 3 program. The new data analyses revealed that statistically significant results were reported for the 8 mg twice-daily and 12 mg twice-daily doses of CTP-543 at more stringent response thresholds, which may be more clinically meaningful to patients, and positive findings were reported for clinician and patient reported outcome measures of scalp hair loss. At 24 weeks, 26% and 42% of patients who received CTP-543 in the 8 mg twice-daily and 12 mg twice-daily cohorts, respectively, achieved an absolute SALT score $\leq$ 20 ($p < 0.05$ vs. placebo), indicating a clinically-meaningful 80% or greater scalp hair present. Data from the Clinician Global Impression of Improvement scale showed 75% of clinicians rated the response in the 12 mg twice-daily cohort and 61% of clinicians rated the response in the 8 mg twice-daily cohort as "much improved" or "very much improved" at 24 weeks. For both doses, there was a statistically significant difference from placebo ($p < 0.001$).

In December 2019, we announced that we completed an open label Phase 2 trial evaluating 8 mg twice-daily compared to 16 mg once-daily dosing of CTP-543 in 57 patients with moderate to severe alopecia areata. Results in the 8 mg twice-daily arm were consistent with the previously-reported 8 mg twice-daily results from our Phase 2 dose-ranging trial of CTP-543. The trial measured the relative change in SALT score between baseline and 24 weeks. Treatment was generally well tolerated in both arms of the study. All but one of the patients who completed this trial elected to continue in an ongoing open label, long-term extension study. A second open label Phase 2 trial evaluating 12 mg twice-daily compared to 24 mg once-daily dosing of CTP-543 in patients with moderate to severe alopecia areata was completed in 2020. We are utilizing the 8 mg twice-daily and 12 mg twice-daily doses in our ongoing clinical development program for CTP-543.

We conducted an end of Phase 2 meeting with the FDA in March 2020 and initiated a Phase 3 trial of CTP-543, THRIVE-AA1, in November 2020. The THRIVE-AA1 trial is a double-blind, randomized, placebo-controlled clinical trial of CTP-543 to evaluate hair regrowth using the SALT score after 24 weeks of dosing in approximately 700 adult patients with moderate to severe alopecia areata. The trial will evaluate 8 mg and 12 mg twice-daily doses of CTP-543 compared to placebo at sites in the United States, Canada and Europe. We expect to report topline results from the THRIVE-AA1 trial in 2022. We expect to begin a second Phase 3 trial of CTP-543, THRIVE-AA2, in the first half of 2021.

Eligible patients from our efficacy and safety studies with CTP-543 may also enroll in an open label, long-term extension study that we are conducting.

CTP-692

On February 1, 2021, we announced that our Phase 2 trial to evaluate CTP-692 as an adjunctive treatment for schizophrenia did not meet the primary endpoint or other secondary endpoints. As a result, we have ceased development of CTP-692. CTP-692 is a deuterated form of D-serine, an endogenous amino acid that is a co-agonist of the NMDA receptor.

In December 2019, we initiated a double-blind, randomized, placebo-controlled Phase 2 trial to evaluate the safety and efficacy of CTP-692 as an adjunctive treatment for schizophrenia. A total of 325 adult patients who are stable on an antipsychotic medication were randomized to receive 1, 2 or 4 grams of CTP-692 or placebo once-daily. The primary outcome measure was the change in the Positive and Negative Syndrome Scale (PANSS) total score at 12 weeks compared to baseline. CTP-692 did not show a statistically significant improvement over placebo at any of the doses. In addition, CTP-692 did not meet any of the secondary endpoints, including the positive or negative symptoms subscales of PANSS, at any of the doses. In the Phase 2 trial,

treatment with CTP-692 was generally well tolerated. The adverse events reported were predominantly mild in severity and equally distributed across the dose groups, including placebo.

Earlier-Stage Pipeline

We are currently assessing a number of earlier-stage pipeline candidates as potential development candidates.

COLLABORATION PRODUCT CANDIDATES

In addition to our wholly owned development programs, we have entered into collaborative arrangements with companies to develop deuterium-modified versions of their marketed products. Our partners are currently responsible for all development and future commercialization activities under these arrangements. In each of these collaborations, the deuterium-modified compound was independently discovered by us. For example, on February 24, 2012, we entered into a development and license agreement with Avanir Pharmaceuticals, Inc., or Avanir, a subsidiary of Otsuka Pharmaceuticals Co., Ltd. for the worldwide rights to develop, manufacture and commercialize AVP-786. AVP-786 is a combination of deudextromethorphan hydrobromide (d6-DM) and quinidine sulfate (Q), a CYP2D6 inhibitor, being investigated for the treatment of neurologic and psychiatric disorders. In 2019, Avanir completed two Phase 3 trials evaluating AVP-786 for the treatment of agitation associated with dementia of the Alzheimer's type. The second of the Phase 3 trials did not meet its primary or key secondary endpoints; however, following additional data analysis, Avanir decided to continue developing AVP-786 for the treatment of agitation associated with dementia of the Alzheimer's type. Three additional Phase 3 trials and an open label, long-term extension study for Alzheimer's agitation are ongoing. Additionally, Avanir is conducting a Phase 2/3 trial evaluating AVP-786 for the treatment of negative symptoms of schizophrenia.

ASSET PURCHASE AGREEMENT WITH VERTEX PHARMACEUTICALS FOR CTP-656

In July 2017, we completed the sale of worldwide development and commercialization rights to CTP-656 and other assets related to the treatment of cystic fibrosis to Vertex Pharmaceuticals, Inc., or Vertex. CTP-656, now known as VX-561, is an investigational cystic fibrosis transmembrane conductance regulator, or CFTR, potentiator that has the potential to be used as part of future once-daily combination regimens of CFTR modulators that treat the underlying cause of cystic fibrosis. We received $160.0 million in cash upon closing, and if VX-561 is approved as part of a combination regimen to treat cystic fibrosis, we are eligible to receive up to $90.0 million in the form of two additional milestones based on marketing approval in the United States and agreement for reimbursement in the first of the United Kingdom, Germany or France.

INTELLECTUAL PROPERTY

We protect our product candidates through the use of patents, trade secrets and careful monitoring of our proprietary know-how. Our patents and patent applications, if they issue as patents, for our lead programs expire between 2028 and 2038. The expected expiration dates are before any patent term extension to which we may be entitled under the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly referred to as the Hatch-Waxman Amendments) or equivalent laws in other jurisdictions where we have issued patents.

CTP-543

We hold various patents and pending applications covering the composition of matter of deuterated analogs of ruxolitinib, including CTP-543, and methods of treating hair loss, including alopecia areata, with certain doses of CTP-543.

We hold U.S. Patent No. 9,249,149, or the '149 patent, covering the composition of matter of deuterated analogs of ruxolitinib, including CTP-543, and we have a corresponding U.S. patent application. We also have a corresponding allowed patent application in Europe and a corresponding patent and allowed patent application in Japan. Such patents and patent applications, if issued, are expected to expire in 2033.

We also hold U.S. Patent No. 10,561,659, or the '659 patent, covering methods of treating hair loss, including alopecia areata, with certain doses of CTP-543, and we have a corresponding U.S. patent application. We have corresponding patent applications in Europe and Japan. Such patent and patent applications, if issued, are expected to expire in 2037.

In April 2018, the Patent Trial and Appeal Board, or PTAB, instituted an inter partes review, or IPR, brought against the '149 patent by Incyte Corporation, or Incyte. In April 2019, the PTAB issued a final written decision in connection with the IPR that held that the claims of the '149 patent were unpatentable as obvious. In January 2020, the U.S. Court of Appeals for the Federal Circuit, or Federal Circuit, granted our motion to vacate and remand the PTAB final written decision in light of the Federal Circuit ruling on the Constitution's Appointments Clause in *Arthrex, Inc. v. Smith & Nephew, Inc.,* 941 F.3d 1320 (Fed. Cir. 2019). As a result, the IPR was remanded for reconsideration by a new panel of PTAB judges. However, the reconsideration is currently on hold while the Supreme Court considers certain questions raised by *Arthrex*. The '149 patent remains valid and

enforceable while the IPR is being reconsidered by the PTAB and until any future appeals by us have been exhausted in the event that the PTAB reaches a similar decision to invalidate the '149 patent.

In addition, in October 2020, Incyte filed a post grant review, or PGR, petition with the PTAB challenging the validity of the '659 patent. We filed our response in February 2021 and expect the PTAB to make a decision on whether to institute the PGR by mid-May 2021. We intend to vigorously defend the '659 patent.

We have retained all of the CTP-543 patent rights.

AVP-786

We hold U.S. patents and pending applications covering the composition of matter and methods of use of deudextromethorphan and other deuterated dextromethorphan analogs. Such U.S. patents and patent applications, if issued, are expected to expire between 2028 and 2030. We hold corresponding patents and patent applications in Europe and Japan. Such foreign patents and patent applications, if issued, are expected to expire in 2028. We have granted exclusive licenses under these patent rights to Avanir.

Other Product Candidates

We also have patent portfolios that are related to a number of other programs. These patent portfolios are wholly owned by us. These include issued patents or patent applications that claim deuterated analogs of a number of non-deuterated drugs and drug candidates.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In the United States and other countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

Under U.S. patent law, the patent term may be extended by patent term adjustment due to certain failures of the PTO to act in a timely manner. The patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Amendments permit a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other non-U.S. jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents that we believe are eligible for such extension. We also intend to seek patent term extensions in other jurisdictions where these are available. However, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

We also rely on trade secrets and careful monitoring of our proprietary know-how to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection, including our DCE Platform.

MANUFACTURING AND SUPPLY

We currently rely, and expect to continue to rely, on third parties for the manufacture of product candidates for our clinical trials. We obtain these manufacturing services, including both the manufacture of the active pharmaceutical ingredients and finished drug product, on a purchase order basis and have not entered into long-term supply contracts with any of these third-party manufacturers. We expect to rely on third parties for commercial manufacturing for any of our product candidates that receive marketing approval.

When manufacturing our product candidates, we incorporate deuterium using either deuterium oxide or deuterated chemical reagents (which themselves are derived from deuterium oxide). As a result, we rely on being able to obtain and transport deuterated materials in order to manufacture our product candidates.

We purchase our raw materials on a purchase order basis and have not entered into long-term supply contracts with any of these third-party suppliers. We believe that the raw materials for our product candidates are readily available and that the cost of manufacturing for our product candidates will not preclude us from selling them profitably, if approved for sale.

COMMERCIALIZATION

We have not yet established a sales, marketing or product distribution infrastructure. We plan to use a combination of third-party collaboration, licensing and distribution arrangements and a focused in-house commercialization capability to sell any of our products that receive marketing approval. With respect to the United States, we plan to seek to retain full commercialization rights for products that we can commercialize with a specialized sales force and to retain co-promotion or similar rights when feasible in indications requiring a larger commercial infrastructure. We plan to collaborate with third parties for commercialization in the United States of any products that require a large sales, marketing and product distribution infrastructure. We also plan to collaborate with third parties for commercialization outside the United States.

We plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. We expect the responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with thought leaders in relevant fields of medicine.

COMPETITION

The development and commercialization of new drug products is highly competitive. We expect that we, and our collaborators, will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to our product candidates that we, or they, may seek to develop or commercialize in the future. Specifically, there are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of autoimmune and CNS disorders. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, simpler to use, have fewer or more tolerable side effects or are less costly than any product candidates that we are currently developing or that we may develop or acquire, which could render our product candidates obsolete and noncompetitive.

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

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

Many pharmaceutical and biotechnology companies have begun to cover deuterated analogs of their product candidates in patent applications and may develop these deuterated compounds. Some of these pharmaceutical and biotechnology companies may have significantly greater financial resources and expertise in research and development, manufacturing, nonclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. In some cases, these competitors may be interested in developing deuterated compounds that we may be interested in developing for ourselves. Our competitors may succeed in obtaining patents that dominate our products, preventing our operational freedom. In addition, these competitors may enter into collaborative arrangements or business combinations that result in their ability to research and develop deuterated compounds more effectively than us. Our potential competitors also include academic institutions, government agencies and other public and private research organizations.

CTP-543 is a deuterated analog of ruxolitinib that we are developing as an oral agent for the treatment of moderate to severe alopecia areata. If CTP-543 receives marketing approval for this indication, it may face competition from a number of other product candidates that are being studied for alopecia areata. Other companies pursuing development of oral JAK inhibitors for the treatment of alopecia areata include Eli Lilly and Company and Pfizer Inc.

GOVERNMENT REGULATIONS

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, sales, distribution, marketing and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable federal, state, local and foreign statutes and regulations, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. 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 and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, voluntary product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practices, or GLPs;
- production of well-characterized drug substance and drug product, and potentially matching placebos;
- submission to the FDA of an investigational new drug application, or IND application, which allows human clinical trials to begin unless the FDA otherwise informs the drug's sponsor within 30 days;
- agreement by clinical investigators and their clinical trial sites, followed by approval by an independent institutional review board, or IRB, representing each clinical site, before the clinical trial may be initiated at that site;
- performance of adequate and well-controlled human clinical trials in accordance with the FDA's good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a New Drug Application, or NDA;
- review of the NDA by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the drug product, and the active pharmaceutical ingredient or active ingredients thereof, are produced to assess compliance with the FDA's current good manufacturing practices, or cGMPs, and to assure that the facilities, methods and controls are adequate to ensure the product's identity, strength, quality and purity;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including a risk evaluation and mitigation strategy, or REMS, and any post-approval studies required by the FDA.

Nonclinical Studies and an IND

Nonclinical studies can include *in vitro* and animal studies to assess the potential for efficacy and adverse events and, in some cases, to establish a rationale for human therapeutic use. The conduct of nonclinical studies is subject to federal regulations and requirements, including GLPs. Other studies include laboratory evaluation of the purity, stability and physical form of the manufactured drug substance or active pharmaceutical ingredient and the physical properties, stability and reproducibility of the formulated drug or drug product. An IND sponsor must submit the results of the relevant nonclinical tests, including all tests conducted under GLPs, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some nonclinical testing, such as longer-term toxicity testing, animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or

questions related to a proposed clinical trial and places the trial on clinical hold or partial clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

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

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institute of Health, or NIH, for public dissemination on their ClinicalTrials.gov website. Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and dosage for Phase 3 studies.
- Phase 3: The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

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 investigators for serious and unexpected suspected adverse events, any findings from other studies or animal or in vitro testing that suggests a significant risk for human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the 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 the data monitoring committee, or DMC, or board. This group provides recommendations for whether or not a trial may move forward at designated check points based on review of certain data from the trial. The FDA will often inspect one or more clinical sites in late-stage clinical trials to assure compliance with GCPs and the integrity of the clinical data submitted.

A manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This

requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug or, as applicable, 15 days after the drug receives a designation as a Breakthrough Therapy, Fast Track product or regenerative advanced therapy.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the nonclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to a user fee.

Under certain circumstances, the FDA will waive the application fee for the first human drug application that a small business, defined as a company with less than 500 employees, or its affiliate submits for review. An affiliate is defined as a business entity that has a relationship with a second business entity if one business entity controls, or has the power to control, the other business entity, or a third party controls, or has the power to control, both entities.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMPs and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs.

The FDA also may require submission and agreement of a REMS to mitigate any identified or suspected serious risks prior to approving an NDA. The REMS could include medication guides, physician communication plans, assessment plans and elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools.

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

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities and clinical sites, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. Additionally, the FDA has issued complete response letters or has deferred action on applications where inspections of manufacturing facilities or clinical sites could not be completed during the review cycle due to COVID-19 related restrictions. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution restrictions or other risk management mechanisms, including a REMS, which can materially affect the potential market and profitability of the product. In addition, the FDA could

require that a "black box" warning be included in the product label at the time of approval of a product or following approval of a product based on the drug class, even if the safety concern is not known to be associated with that specific product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

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

Expedited development and review programs

The FDA has various programs, including Fast Track designation, Breakthrough Therapy designation, priority review and accelerated approval, which are intended to expedite or facilitate the development and review of new drugs that meet certain criteria and/or provide for approval on the basis of surrogate endpoints.

New drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address an unmet medical need for the condition. Fast Track designation is intended to facilitate early and frequent meetings between the FDA and the sponsor company during development and the FDA may agree to review sections of an NDA on a rolling basis before the complete NDA is submitted. A drug may be eligible for Breakthrough Therapy designation if the drug is intended to treat a serious or life-threatening disease and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies. Breakthrough Therapy designation provides for frequent meetings between the sponsor and the FDA, involving senior and experienced review staff, as appropriate, in a collaborative, cross-functional review and the assignment of an FDA project lead to facilitate efficient review of the development program and serve as a scientific liaison with the sponsor. Although Fast Track and Breakthrough Therapy designation do not affect the regulatory standards for approval, the frequent interactions with the FDA may facilitate a more efficient development program. In addition, the NDAs for drugs granted Fast Track and Breakthrough Therapy designation may become eligible for priority review. Priority review is designed for drug candidates that offer significant improvements in safety or effectiveness or fill an unmet medical need and provides for an initial review within six months of acceptance of the NDA for filing, as compared to a standard review of ten months after acceptance for filing. Accelerated approval provides an earlier approval of drugs that treat serious diseases, and that fill an unmet medical need, based on a surrogate endpoint that the FDA determines is reasonably likely to predict a clinical benefit. As a condition of approval, the FDA may require that the sponsor of a drug receiving accelerated approval perform post-marketing confirmatory clinical trials.

Even if a drug candidate qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review will not be shortened. Regardless of any accelerated review period under these programs, the review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Section 505(b)(2) NDAs

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

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain nonclinical or clinical studies of the new product. The FDA may also require companies to perform additional

studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

If our partners submit NDAs for approval of deuterated analogs of marketed compounds for which they are the NDA holder, we believe that in certain cases the FDA may allow referencing of data from the non-deuterated compound in support of the application for approval of the deuterated product. Since this referencing by our partners would involve use of their own data and not require the use of another party's data, it would constitute a Section 505(b)(1) application.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also is an annual prescription drug user fee for any marketed products, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMPs. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMPs and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMPs.

Once an approval is granted, the FDA may withdraw the 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 or problems with manufacturing processes of unanticipated severity or frequency, 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 or other restrictions under a REMS. Other potential consequences include, among other things:

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

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications 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, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

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.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with the passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the nonclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the "reference listed drug." To reference that information, however, the ANDA applicant must demonstrate, and the FDA must conclude, that the generic drug does, in fact, perform in the same way as the reference listed drug it purports to copy.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the reference listed drug with respect to the active ingredients, the route of administration, the dosage form and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a reference listed drug if "the rate and extent of absorption of the generic drug do not show a significant difference from the rate and extent of absorption of the reference listed drug. . ."

Upon approval of an ANDA, the FDA indicates that the generic product is "therapeutically equivalent" to the reference listed drug and it assigns a therapeutic equivalence rating to the approved generic drug in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider the therapeutic equivalence rating to mean that a generic drug is fully substitutable for the reference listed drug. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of a therapeutic equivalence rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of data exclusivity for new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity is a drug that contains no active moiety that has been previously approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such new chemical entity exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five year new chemical entity exclusivity, an award of three year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product.

Hatch-Waxman Patent Certification and the 30 Month Stay

NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

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

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

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

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

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

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, as amended, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans within 60 days of an end of Phase 2 meeting, or as may be agreed between the sponsor and the FDA. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The applicant, the FDA and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after efficacy and safety has been established in adults, or full or partial waivers from the pediatric data requirements. Generally, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Amendments. Those Amendments permit a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and ultimate approval. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. The PTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of its products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial applications must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a drug under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the European Medicines Agency, or EMA, is responsible for issuing an Opinion following the initial assessment of an MAA. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days. Following a positive Opinion by the CHMP, the final authorization is issued by the European Commission.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days after receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Data and Market Exclusivity in the European Union

In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the drug if such company can complete a full MAA with a complete database of pharmaceutical tests, nonclinical tests and clinical trials and obtain marketing approval of its product.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care

organizations, provide coverage and establish adequate reimbursement levels for such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged for medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has also become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products and re-importation of products sold outside of the United States. Adoption of price controls and cost-containment measures, including importation of drugs into the United States from lower-cost countries, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could adversely affect our net revenue and results.

Outside of the United States, ensuring adequate coverage and payment for products remains challenging. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

As a result, the marketability of any product which receives regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. In particular, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. Even if favorable coverage and reimbursement status is attained for one or more products that receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Since enactment of the PPACA, there have been numerous judicial, administrative, executive and legislative challenges to certain aspects of the PPACA, and we expect there will be additional challenges and amendments to the PPACA in the future. Various portions of the PPACA are currently undergoing legal and constitutional challenges in the U.S. Supreme Court; the Trump Administration issued various Executive Orders that eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers or manufacturers of pharmaceuticals or medical devices; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the PPACA. As implementation of the PPACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

At the state level, legislatures have increasingly passed legislation and implemented regulations that are designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, that are designed to encourage importation from other countries and bulk purchasing.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on

healthcare costs in general, particularly prescription drugs, has become 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 competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements for any of our products.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal healthcare Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the False Claims Act, which imposes civil monetary penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- the federal anti-inducement law, which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a federal or state governmental program;

- the federal transparency requirements under the PPACA, which requires certain manufacturers of covered drugs to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare providers and teaching hospitals, as well as physician ownership and investment interests. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, including environmental, health and safety laws and regulations, we may be subject to penalties, including administrative, civil and criminal penalties, imprisonment, exclusion from participation in government healthcare programs such as Medicare and Medicaid, damages, fines 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.

HUMAN CAPITAL RESOURCES

As of December 31, 2020, we had 71 employees on a full-time or part-time basis, 46 of whom were primarily engaged in research and development activities. A total of 41 employees hold Ph.D., master's or other post-graduate degrees. In addition, we retain expert consultants on an ad-hoc basis as required in connection with our development programs. We believe that our future success will depend, in part, on our ability to continue to attract, hire and retain qualified personnel. We monitor our compensation programs closely and believe that we offer competitive compensation (including salary, incentive bonus and equity awards) and benefits packages. None of our employees are represented by a labor union, and we believe that our relations with our employees are good.

FACILITIES

We lease approximately 56,000 square feet of office and laboratory space at our headquarters in Lexington, Massachusetts. The lease expires on January 1, 2029.

RESEARCH AND DEVELOPMENT

We have dedicated a significant portion of our resources to our efforts to develop our pipeline and product candidates. We incurred research and development expenses of $61.6 million and $59.8 million during the years ended December 31, 2020 and 2019, respectively. We anticipate that a significant portion of our operating expenses in future periods will continue to be related to research and development as we continue to advance our product candidates through clinical development.

AVAILABLE INFORMATION

We file reports and other information with the Securities and Exchange Commission, or SEC, as required by the Securities Exchange Act of 1934, as amended, or Exchange Act. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at www.sec.gov.

We were incorporated under the laws of the State of Delaware on April 12, 2006 as Concert Pharmaceuticals, Inc. Our principal executive offices are located at 65 Hayden Avenue, Suite 3000N, Lexington, Massachusetts 02421, and our telephone number is (781) 860-0045. Our website is www.concertpharma.com. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. In addition, we regularly use our website to post information regarding our business, development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors," as a source of information about us.

The foregoing references to our website are not intended to, nor shall they be deemed to, incorporate information on our website into this Annual Report on Form 10-K by reference.

Item 1A. Risk Factors.

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

Risks Related to the COVID-19 Pandemic

Our business may be adversely affected by the ongoing COVID-19 pandemic.

Our business could be adversely affected by health epidemics in regions where we have concentrations of clinical trial sites or other business activities and could cause significant disruption in the operations of clinical research organizations and contract manufacturers upon whom we rely. For example, the COVID-19 pandemic has grown to affect most regions of the world.

As a result of the COVID-19 pandemic, we may experience disruptions that could severely impact our business, clinical trials and supply chain, including:

- We believe that the COVID-19 pandemic has had, and will continue to have, an impact on our clinical trials, including our Phase 3 clinical trial and open label long-term extension study of CTP-543 for alopecia areata. Due to changes to study site operations and local travel restrictions, in some cases, these impacts include the potential need for remote assessments and delivery of study medication directly to patients. Some patients may choose to withdraw from our studies or we may choose to, or be required to, pause enrollment or patient dosing in order to preserve health resources and protect trial participants. As a result, the timelines to complete our clinical trials may be delayed.
- We believe that the COVID-19 pandemic may also have an impact on the clinical trials of our collaborators. For instance, AVP-786 is being developed under a collaboration with Avanir. Screening and enrollment in ongoing AVP-786 clinical trials were temporarily paused due to restrictions associated with the COVID-19 pandemic, but have since resumed. As a result, our collaborators' timelines to complete clinical trials may be delayed.
- We currently rely on third parties to, among other things, manufacture raw materials, manufacture our product candidates for our clinical trials, ship our product candidates to study sites, perform quality testing and supply other goods and services to run our business. If any such third party in our supply chain is adversely impacted by restrictions resulting from the COVID-19 pandemic, including staffing shortages, production slowdowns or disruptions in delivery systems, our supply chain may be disrupted, limiting our ability to manufacture our product candidates for our clinical trials and conduct our research and development operations.
- We have limited our on-site staff to personnel that work in our laboratories or perform other essential activities on-site, and have requested that all other personnel continue to work remotely. Our increased reliance on personnel working from home may negatively impact productivity or disrupt, delay or otherwise adversely impact our business. In addition, this could increase our cyber security risk, create data accessibility concerns and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, clinical trial sites and other important agencies and contractors. General protective measures put into place at various governmental levels, including quarantines, travel restrictions and business shutdowns, may also negatively affect our operations.
- Health regulatory agencies globally have experienced disruptions in their operations as a result of the COVID-19 pandemic. The FDA and comparable foreign regulatory agencies may have had slower response times or been under resourced. It is unknown how long these disruptions may continue. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, the FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates.
- The trading prices for our common stock and the stock of other biopharmaceutical 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. In addition, a recession, depression or other sustained adverse market event resulting from the COVID-19 pandemic could materially and adversely affect our business and the value of our common stock.

The COVID-19 pandemic continues to rapidly evolve. The ultimate impact of the COVID-19 pandemic on our business operations is highly uncertain and subject to change and will depend on future developments, which cannot be accurately predicted, including the duration of the pandemic, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19 and the actions taken to contain or address its impact in the short and long term, among others. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy. We will continue to monitor the situation closely.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception, expect to incur losses for at least the next several years and may never sustain profitability.

As of December 31, 2020, we had an accumulated deficit of $269.4 million. We have not generated any revenues from product sales and have financed our operations to date primarily through the public offering and private placement of our equity, debt financing, funding from collaborations and patent assignments, an asset sale and other arrangements. We have not completed development of any product candidate and have devoted substantially all of our financial resources and efforts to research and development. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct nonclinical studies and clinical trials with respect to our product candidates;
- seek to identify additional product candidates;
- in-license or acquire additional product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain marketing approval;
- require the manufacture of larger quantities of product candidates for clinical development and potentially commercialization;
- maintain, expand and protect our intellectual property portfolio;
- incur delays to the initiation or completion of our clinical trials due to the COVID-19 pandemic;
- incur any disruptions or delays to the supply of our product candidates due to the COVID-19 pandemic;
- hire additional personnel;
- add equipment and physical infrastructure to support our research and development; and
- continue to implement the infrastructure necessary to support our product development and help us comply with our obligations as a public company.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we are, or one of our collaborators is, able to successfully commercialize one or more of our product candidates. Doing so will require success in a range of challenging activities, including completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we, or our collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. We, and our collaborators, may never succeed in these activities and, even if we do, or one of our collaborators does, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our Company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations. A decline in the value of our Company could cause our stockholders to lose all or part of their investments in us.

Based on our current operating plan, there is substantial doubt regarding our ability to continue as a going concern.

Based on our current operating plan, we believe that our cash, cash equivalents and investments as of December 31, 2020 will enable us to fund our operating expenses and capital expenditure requirements through 2021. However, without significant

changes to our current operating plan or raising additional capital, there is substantial doubt regarding our ability to continue as a going concern for a period of at least twelve months from the issuance date of this Annual Report on Form 10-K.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our development programs or commercialization efforts.

Developing pharmaceutical products, including conducting nonclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we initiate new clinical trials of, initiate new research and nonclinical development efforts for and seek marketing approval for our product candidates, or if we in-license or acquire product candidates. In addition, if we obtain marketing approval for any of our product candidates, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of one of our collaborators. In particular, the costs that we may be required to incur for the manufacture of any product candidate that receives marketing approval may be substantial. Manufacturing a drug at commercial scale may require specialized facilities, processes and materials. Furthermore, we will continue to incur costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

In any event, our existing cash, cash equivalents and investments will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates. Accordingly, we will be required to obtain further funding through a combination of equity offerings, debt financings, collaboration and licensing arrangements and other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. Our failure to raise capital when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

Based on our current operating plan, we believe that our cash, cash equivalents and investments as of December 31, 2020 will enable us to fund our operating expenses and capital expenditure requirements through 2021. Our estimate as to how long we expect our cash, cash equivalents and investments to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could 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. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the progress, timing, costs and results of clinical trials of, and research and nonclinical development efforts for, our product candidates and potential product candidates, including current and future clinical trials, including on account of the COVID-19 pandemic and its impact on our clinical trial sites;
- our current collaboration agreements and achievement of milestones under these agreements;
- our ability to enter into and the terms and timing of any additional collaborations, licensing, product acquisition or other arrangements that we may establish;
- the number of product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking marketing approvals;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims;
- potential litigation costs; and
- the costs of operating as a public company.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration and licensing arrangements and other sources. We do not have any committed external source of funds, other than potential milestone payments under our Asset Purchase Agreement with Vertex, or the Vertex Agreement, and potential milestone payments and royalties under our existing license agreements, each of which is subject to the achievement of development, regulatory and/or sales-based milestones with respect to our product candidates. To the extent that we raise additional capital through the sale of common stock, convertible securities or other

equity securities, the ownership interests of our stockholders may be materially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of our stockholders. In addition, debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

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

Any future indebtedness could adversely affect our ability to operate our business.

We could in the future incur indebtedness containing financial obligations and restrictive covenants, which could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, reducing money available to fund working capital, capital expenditures, product development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

Any financial obligations or restrictive covenants could negatively impact our ability to conduct our business.

We have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We began operations in April 2006. Our operations to date have been limited to financing and staffing our company, developing our technology and product candidates and establishing collaborations. We are conducting our first international, multi-center, pivotal clinical trial and have not yet demonstrated an ability to successfully obtain marketing approvals, manufacture product on a commercial scale or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

Risks Related to the Development of Our Product Candidates

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

Clinical testing is expensive, time-consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy in a clinical trial or across a broad or definable population of patients, the occurrence of severe or medically or commercially unacceptable adverse events, fraudulent conduct by clinical investigators, failure to comply with protocols, applicable regulatory requirements or other determinations made by the FDA, or any comparable foreign regulatory authority that a drug product is not approvable. It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials, we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

For example, on February 1, 2021, we announced that our Phase 2 trial to evaluate CTP-692 as an adjunctive treatment for schizophrenia did not meet the primary endpoint or other secondary endpoints. As a result, we have ceased development of CTP-692.

In addition to the risk of failure inherent in drug development, certain of the deuterated compounds that we, and our collaborators, are developing and may develop in the future may be particularly susceptible to failure to the extent they are based on compounds that others have previously studied or tested, but did not progress in development due to safety, tolerability or efficacy concerns or otherwise. Deuteration of these compounds may not be sufficient to overcome the problems experienced with the corresponding non-deuterated compound.

We may not be able to continue further clinical development of our wholly owned development programs, including CTP-543. If we are unable to develop, obtain marketing approval for or commercialize our wholly owned development programs, ourselves or through a collaboration, or experience significant delays in doing so, our business could be materially harmed.

We currently have no products approved for sale. The success of our wholly owned development programs will depend on several factors, including:

- in the case of CTP-543, our ability to treat moderate to severe alopecia areata with acceptable safety and efficacy;
- successful and timely completion of clinical trials, including the impact of the COVID-19 pandemic on the initiation or completion of our clinical trials and the supply of our product candidates;
- receipt of marketing approvals from applicable regulatory authorities;
- the performance of our future collaborators, if any, for our programs;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials suppliers and manufacturers;
- our ability to manufacture or arrange for the manufacture of our active pharmaceutical ingredients and drug products with sufficient quality, quantity and reproducibility to support clinical trials and potential future commercialization;
- establishment of arrangements with third-party manufacturers to obtain finished drug products that are appropriately packaged for sale;
- obtaining and maintaining patent, trade secret protection, regulatory exclusivity and freedom to operate, both in the United States and internationally;
- amount of commercial sales, if and when approved;
- a continued acceptable safety profile of our programs following any marketing approval; and
- agreement by third-party payors to reimburse patients for the costs of treatment with our products, and the terms of such reimbursement.

If we are unable to successfully develop, receive marketing approval for and commercialize our wholly owned development programs, or experience delays as a result of any of these factors or otherwise, our business could be materially harmed.

If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or our collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

We, or our collaborators, must complete nonclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans in order to obtain marketing approval from regulatory authorities for the sale of our product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. Further, the outcome of nonclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face similar setbacks.

Any inability to successfully complete nonclinical and clinical development could result in additional costs to us, or our collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if (1) we, or our collaborators, are required to conduct additional or larger clinical trials or other testing of our product candidates beyond the trials and testing that we, or they, contemplate, (2) we, or our collaborators, are unable to successfully complete clinical trials of our product candidates or other testing, (3) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or (4) there are unacceptable safety concerns associated with our product candidates, we, or our collaborators, in addition to incurring additional costs, may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

For instance, AVP-786 is being developed under a collaboration with Avanir. In 2019, Avanir completed two Phase 3 trials evaluating AVP-786 for the treatment of agitation associated with dementia of the Alzheimer's type. The second of the Phase 3 trials did not meet its primary or key secondary endpoints; however, following additional data analysis, Avanir decided to continue developing AVP-786 for the treatment of agitation associated with dementia of the Alzheimer's type in a number of ongoing Phase 3 trials. Additionally, Avanir is conducting a Phase 2/3 trial evaluating AVP-786 for the treatment of negative symptoms of schizophrenia. However, given the results of Avanir's second Phase 3 trial of AVP-786 for the treatment of agitation associated with dementia of the Alzheimer's type, there is no guarantee that any future trials of AVP-786 will meet their primary or key secondary endpoints.

Even if we, or our collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

If we, or our collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our product candidates, potential marketing approval or commercialization of our product candidates could be delayed or prevented.

We, or our collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent marketing approval of our product candidates, including:

- toxicity or serious adverse effects may be observed in our nonclinical studies causing us to delay or abandon clinical trials;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- unexpectedly high placebo response rates;
- rater variability in the assessment of clinical endpoints;
- we, or our collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials and or develop and or validate new clinical endpoints for our clinical trials, or abandon development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we, or our collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or our collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or our collaborators, anticipate;
- our third-party contractors, or those of our collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of our collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or our collaborators in a timely manner or at all;
- criminal or unauthorized misuse of computer systems may result in disruption to our, or our partners' or vendors', clinical trials, nonclinical activities or manufacturing, or may compromise data from our, or our partners' or vendors', clinical or nonclinical studies;
- regulators or institutional review boards may not authorize us, our collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or our collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients or the sites from the clinical trial, increase the needed enrollment size for the clinical trial, extend the clinical trial's duration or cause spurious results;
- investigators may provide inaccurate or false data, resulting in spurious clinical results, an inadequate data set or regulators' unwillingness to approve a product;
- regulators, institutional review boards or data monitoring committees may require that we, or our collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks,

undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;
- the FDA or comparable foreign regulatory authorities may disagree with our, or our collaborators', clinical trial design or our or their interpretation of data from nonclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may change their requirements for approvability for a given product or for an indication after we have initiated work based on their previous guidance;
- the COVID-19 pandemic may impact the FDA's or comparable foreign regulatory authorities' ability to continue its normal operations;
- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply, including as a result of shipping delays or vendor personnel shortages due to the COVID-19 pandemic;
- we, or our manufacturing vendors, may not produce, or may not consistently produce material, that meets necessary specifications for commercialization;
- the FDA or comparable foreign regulatory authorities may determine that our, or our manufacturing vendors, manufacturing or quality control processes fail to meet their specifications or guidelines; 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 to obtain marketing approval.

Product development costs for us, or our collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates. We, and our collaborators, do not know whether any nonclinical tests or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant nonclinical or clinical trial delays also could shorten any periods during which we, or our collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of our collaborators, to bring products to market before we, or our collaborators, do and impair our ability, or the ability of our collaborators, to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

Additionally, timely enrollment, conduct, progress and completion of clinical trials are reliant on clinical trial sites, which may be adversely affected by global health matters, including, among other things pandemics. For example, some of our clinical trial sites have been impacted by the COVID-19 pandemic. As the COVID-19 pandemic continues to evolve, the conduct of our clinical trials may be adversely affected, despite efforts to mitigate this impact.

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

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

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the availability or interest of clinical sites to enroll patients into our trials;
- the willingness or availability of patients to participate in our clinical trials, including due to the COVID-19 pandemic;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial, including any requirement to halt current therapy in connection with the trial;
- the potential need to discontinue investigational treatment at the completion of the study;
- the availability of other effective treatments for the indication we are assessing;
- access to relevant clinical trial sites;
- efforts to facilitate timely enrollment;
- competing clinical trials;
- support by relevant industry or patient organizations with influence over clinical trial sites; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved or used for the indications we are investigating.

Our inability, or the inability of our collaborators, to enroll a sufficient number of patients for our, or their, clinical trials could result in significant delays or may require us or them to abandon one or more clinical trials altogether. Enrollment delays in our, or their, clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our, or our collaborators', ability to commence sales of and generate revenues from our product candidates, which could cause the value of our Company to decline and limit our ability to obtain additional financing, if needed.

Serious adverse events, undesirable side effects or other unexpected properties of our product candidates, including those that we have licensed to collaborators, may be identified during development that could delay or prevent the product candidate's marketing approval.

All of our product candidates are in nonclinical and clinical development stages and their risk of failure is high. Serious adverse events or undesirable side effects caused by our product candidates, or competitor products with similar mechanisms of action, could cause us, one of our collaborators, an institutional review board, data monitoring committee or regulatory authorities to interrupt, amend, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. A dose of a deuterated compound could, in comparison to an equal dose of the corresponding non-deuterated compound, result in altered exposure levels, distribution and half-life in the body and alter the levels of particular metabolites that are present in the body. These changes may cause serious adverse events or undesirable side effects that we, or our collaborators, did not anticipate, whether based on the characteristics of the corresponding non-deuterated compound or otherwise. If any of our product candidates is associated with serious adverse events or undesirable side effects or have properties that are unexpected, we, or our collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound. In addition, unexpected adverse clinical effects of a deuterated product candidate, including either those identified by us or deuterated analogs of approved drugs being developed by any third parties, may create general concerns regarding deuteration technology that could delay the development of our product candidates.

Breakthrough Therapy and Fast Track designations by the FDA may not lead to faster development, regulatory review or approval.

Although the FDA has granted CTP-543 Breakthrough Therapy designation for the treatment of adult patients with moderate to severe alopecia areata and Fast Track designation for the treatment of alopecia areata, Breakthrough Therapy and Fast Track designations do not necessarily lead to a faster development pathway or regulatory review process and do not increase the likelihood of marketing approval. The FDA may later withdraw the designations if it believes that CTP-543 no longer meets the necessary conditions.

We may not be successful in our efforts to identify or discover additional potential product candidates.

If we are unable to identify suitable additional compounds for nonclinical and clinical development, our ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to our financial position and adversely impact our stock price.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials and some aspects of our research and nonclinical testing. If they terminate their relationships with us or do not perform satisfactorily, our business may be materially harmed.

We do not independently conduct clinical trials of any of our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct these clinical trials and expect to rely on these third parties to conduct clinical trials of any other product candidate that we develop. We also rely on third parties to conduct some aspects of our research and nonclinical testing and expect to rely on these third parties in the future. Any of these third parties may terminate their engagements with us under certain circumstances. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. Switching to or adding additional third parties would involve additional cost and require management time and focus. In addition, there is a natural transition period when a new third party commences work, which could result in delays in our product development activities. Although we seek to carefully manage our relationships with

our contract research organizations, any such challenges or delays could have a material adverse impact on our business, financial condition and prospects.

Our reliance on these third parties for clinical development activities limits our control over these activities but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. For example, notwithstanding the obligations of a contract research organization for a trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the marketing approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with GCPs.

Furthermore, these third parties are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct their services in accordance with our contracts, regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

We also rely on other third parties to store, label and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, such as ClinicalTrials.gov, within certain timeframes. Failure to do so can result in the inability to report our clinical results in certain publications, fines, adverse publicity and civil and criminal sanctions.

We depend on collaborations with third parties for the development and commercialization of some of our product candidates and expect to continue to do so in the future. Our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.

We have entered into collaborations for the development and commercialization of certain of our product candidates and expect to enter into additional collaborations in the future. We have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates, and our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, our collaborators have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving our product candidates pose a number of risks, including:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

- collaborators may conduct their clinical trials poorly or inadequately, harming our products, including our products' development in other territories;
- product candidates developed in collaboration with us, including in particular product candidates based on deuteration of a collaborator's marketed drugs or advanced clinical candidates, may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may steal our trade secrets or may hire valuable employees from us;
- collaborators may fail to protect our trade secrets;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

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

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We may seek one or more collaborators for the development and commercialization of one or more of our product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the potential differentiation of our product candidate from its corresponding non-deuterated analog, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the proposed collaborator's perception of our freedom to operate in a particular market or markets without challenge, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies that may be available for collaboration and whether such collaboration could be more attractive than the one with us for our product candidate.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We are also restricted under the terms of certain of our existing collaboration agreements from entering into collaborations regarding or otherwise developing specified compounds that are similar to the compounds that are subject to those agreements and collaboration agreements that we enter into in the future may contain further restrictions on our ability to enter into potential collaborations or to otherwise develop specified compounds.

We may not be able to negotiate collaborations for our product candidates on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to limit the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue. In cases where we seek a collaborator for a product compound that is a

deuterated analog of a compound that has been previously developed, failure to enter into a collaboration with the developer of the corresponding non-deuterated compound may result in a loss of the potential to obtain clearance from the FDA to follow expedited development programs that reference and rely on findings previously obtained from the developer's prior nonclinical or clinical studies of the corresponding non-deuterated compound.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for our product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary product candidates. If we do not adequately protect our intellectual property, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel product candidates that are important to our business. The patent application and approval process is expensive, uncertain and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Neither deuterium itself, nor the general concept of selective substitution of deuterium for hydrogen in existing pharmaceutical compounds, is patentable; therefore, we usually seek patents on a compound-by-compound basis or on a relatively narrow genus of compounds. We are not guaranteed that patents will issue protecting any particular deuterated compound for which we seek patent protection. We also cannot guarantee that another company will not be able to find a different pattern of deuterium substitution that is equally or more effective in improving the characteristics of a non-deuterated compound, then patenting that deuterated compound and competing with us.

Our ability to obtain and maintain patent protection for our product candidates may be limited if disclosures of non-deuterated compounds are held to anticipate or make obvious claims of deuterated analogs of the same or similar compounds in any given territory. In addition, several large pharmaceutical and biotechnology companies have begun to pursue patent protection for deuterated analogs of their products and product candidates, and may in the future obtain patent protection that covers deuterated analogs of those product candidates. If patents directed primarily to non-deuterated compounds are deemed to protect deuterated analogs of those compounds or patent claims on deuterated analogs of compounds become common in the biotechnology and pharmaceutical industries, these factors may substantially limit our ability to seek and obtain patent protection for new product candidates based on deuterium modification of compounds. It may also limit our ability to develop new product candidates based on deuterium modification of such compounds without obtaining a license from those patent holders. In certain cases, a company that owns the patent on a non-deuterated compound may be able to file a continuation or divisional patent on deuterated analogs of their compounds that successfully claims priority to the original filing date of the non-deuterated composition, causing their patent to have priority over ours, even if filed later than ours was.

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

Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the 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 were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

We may also become involved in opposition, derivation, reexamination, PGR, IPR or interference proceedings in the United States or elsewhere, challenging our patent rights or the patent rights of others. For example, in April 2018, the PTAB instituted an IPR brought against our '149 patent by Incyte. The '149 patent covers the composition of matter of deuterated analogs of ruxolitinib, including CTP-543. In April 2019, the PTAB issued a final written decision in connection with the IPR that held that the claims of the '149 patent were unpatentable as obvious. In January 2020, the Federal Circuit granted our motion to vacate and remand the PTAB final written decision in light of the Federal Circuit ruling on the Constitution's Appointments Clause in *Arthrex, Inc. v. Smith & Nephew, Inc.,* 941 F.3d 1320 (Fed. Cir. 2019). As a result, the IPR was remanded for reconsideration by a new panel of PTAB judges. However, the reconsideration is currently on hold while the Supreme Court considers certain questions raised by *Arthrex*. The '149 patent remains valid and enforceable while the IPR is being

reconsidered by the PTAB and until any future appeals by us have been exhausted in the event that the PTAB reaches a similar decision to invalidate the '149 patent.

In addition, in October 2020, Incyte filed a PGR petition with the PTAB challenging the validity of our '659 patent. The '659 patent covers methods of treating hair loss, including alopecia areata, with certain doses of CTP-543. We filed our response in February 2021 and expect the PTAB to make a decision on whether to institute the PGR by mid-May 2021. We intend to vigorously defend the '659 patent.

There can be no assurance that we will be successful in defending the '149 patent or the '659 patent. If both patents are found to be invalid, it could potentially shorten the timeframe during which we could prevent generic versions of CTP-543 from entering the market. In addition, adverse determinations in any other submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Our pending and future patent applications may not result in patents being issued that protect our product candidates, in whole or in part, or which effectively prevent others from commercializing competitive products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. In certain territories, losses to an infringing product may not be sufficiently great to justify the costs of challenging the infringer and asserting our rights. In some situations, governments have allowed or enabled the sale of competing products that infringe a company's intellectual property. Thus, even if we have valid and nominally enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad, including challenges through the PTO's PGR proceedings. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Third parties may sue us alleging that we are infringing their intellectual property rights, and such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates without infringing the intellectual property and other proprietary rights of third parties. Our CTP-543 compound is based, and potential future product candidates may be based, on products that are covered by issued patents or patent applications, the holders of which may attempt to assert claims against us. To date, we are not aware of any judicial decision holding that a patent that covers a non-deuterated compound should be construed to also cover deuterated analogs thereof, absent specific claims with respect to the deuterated analogs. However, any such judicial decision, or legal proceedings asserting such claims, could increase the likelihood of potential infringement claims being asserted against us. If any third-party patents or patent applications are found to cover our product candidates or their methods of use, we may not be free to manufacture or market our product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

For example, CTP-543 is a deuterated analog of ruxolitinib. Incyte owns patents covering ruxolitinib that may be unexpired if and when we seek marketing approval for CTP-543. Incyte also owns a U.S. patent that broadly claims deuterated analogs of ruxolitinib. On June 27, 2017, we filed a PGR with the PTAB seeking to invalidate all claims of Incyte's U.S. patent that covers deuterated analogs of ruxolitinib. In January 2018, the PTAB did not grant our petition to challenge the validity of Incyte's patent. In May 2018, our request for reconsideration was denied.

In addition, Columbia University is the assignee of patents licensed to Aclaris Therapeutics, Inc. claiming the use of ruxolitinib, isotopic forms of ruxolitinib and other named JAK inhibitors for the treatment of hair loss disorders, including alopecia areata, which may be unexpired if and when we seek marketing approval for CTP-543.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings with respect to our product candidates. Third parties may assert infringement claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the relevant patent claims or that these patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity under most circumstances requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. We may also assert that a patent claim for a corresponding non-deuterated compound does not cover our product. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party’s intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product and could be required to pay potentially significant damages. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys’ fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity and enforceability of such patents is upheld, the court will construe the patent’s claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition.

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

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

While we have obtained composition of matter patents with respect to our most advanced product candidates, our DCE Platform is not patented. In seeking to develop and maintain a competitive position through our DCE Platform and as to other aspects of our business, we rely on trade secrets, including unpatented know-how, technology and other proprietary information. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our consultants, independent contractors, advisors, corporate collaborators, outside scientific collaborators, contract manufacturers, suppliers and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

Risks Related to the Manufacturing of Our Product Candidates

We contract with third parties for the manufacture and distribution of our product candidates for nonclinical and clinical testing and expect to continue to do so in connection with our future development and commercialization efforts. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, or that the product candidates will not be of sufficient quality or reproducibility or produced on our desired schedule, which could delay, prevent or impair our development or commercialization efforts.

We currently rely, and expect to continue to rely, on third-party contractors to manufacture nonclinical and clinical supplies of our product candidates and to package, label and ship these supplies. We expect to rely on third-party contractors to manufacture, formulate, package, label and distribute commercial quantities of any product candidate that we commercialize following approval for marketing by applicable regulatory authorities. Reliance on such third-party contractors entails risks, including:

- manufacturing delays, including if our third-party contractors give greater priority to the supply of other products over our product candidates or if they otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- potentially incorrect data analysis, resulting in falsely-positive, falsely-negative or misleading or uninterpretable results;
- potential industrial accidents such as fires or explosions that compromise our product candidates or the ability of the contractors to timely deliver them;
- natural disasters, public health crises, pandemics and epidemics, including the COVID-19 pandemic;
- the possible termination or non-renewal of agreements by our third-party contractors at a time that is costly or inconvenient for us;
- potentially limited numbers of available contractors due to the need for uncommon equipment or expertise, or pre-existing conflicts of interest;
- the possible breach by the third-party contractors of our agreements with them;
- possible theft of intellectual property or trade secrets;
- possible theft of our materials, including starting materials, intermediates, active pharmaceutical ingredients or drug products;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- possible contamination, or non-conformance with product or packaging specifications, of our product during or after its manufacture;
- possible interruptions in our contractors' operations, including departure of key personnel, disruption due to merger and acquisitions activities or supply chain disruptions;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

If any of our product candidates are approved by any regulatory agency, we plan to enter into agreements with third-party contract manufacturers for the commercial production and distribution of those products. It may be difficult for us to reach agreement with a contract manufacturer on satisfactory terms or in a timely manner, especially if the manufacturer believes it is uniquely suited to use our deuterium chemistry manufacturing processes or otherwise has unusual market power, or that our deuterium chemistry manufacturing processes bear greater production risks than manufacture of non-deuterated compounds. In addition, we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization efforts.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be inspected by the FDA after we submit an NDA and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in foreign countries. We do not directly control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. If our manufacturers fail to consistently manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, or if they unacceptably deviate from standard operating procedures in the production of our product candidates, they will not be able to secure the applicable approval for or a regulatory authority may find deficiencies with their manufacturing facilities. If deficiencies are found at these facilities or if these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate.

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

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Because there are limited commercial suppliers of deuterated materials and the import/export of deuterated materials may be controlled by governments, we, and our collaborators, are exposed to a number of risks and uncertainties associated with our supply of deuterated materials.

When manufacturing our product candidates, we incorporate deuterium using either deuterium oxide or deuterated chemical reagents (which themselves are derived from deuterium oxide). As a result, we rely on being able to obtain and transport deuterated materials in order to manufacture our product candidates.

We rely on third parties to both supply deuterated materials and to manufacture our product candidates. However, our suppliers of deuterated materials are often located in different countries than the manufacturers of our product candidates, which would require the deuterated materials to be transported across country borders.

Transporting deuterated materials across country borders often requires licenses or other government approvals. The import and export of deuterated materials into or out of the United States is regulated and may require a license from the Nuclear Regulatory Commission or other government agency. Similarly, the import and export of deuterated materials into or out of other countries may require local government license or approvals. Licenses and certain other required documents may specify the maximum amount of deuterated materials that we, or our suppliers, are permitted to import or export per year. We, or our suppliers, may not be able to obtain such licenses or approvals in a timely manner or at all. In addition, our current import and export licenses may be insufficient to meet our future requirements.

We estimate that our current sources of deuterated materials will be sufficient to meet our anticipated requirements; however, we do not currently have long-term agreements with our suppliers. If we are not able to establish or maintain supply arrangements, or any relevant foreign governments decide to withhold authorizations for the import or export of deuterated materials that we seek, we may be unable to secure alternative sources. If we are unable to obtain sufficient supplies of deuterated materials from our current suppliers, we would be forced to seek alternative suppliers of deuterated materials, likely in other countries. Such alternative supplies may not be available to us on acceptable terms, or at all.

If we are unable to obtain sufficient supplies of deuterated materials, our ability to produce our product candidates would be impeded and our business, financial condition and prospects could be harmed. Additionally, the inability to import or export deuterated materials to our third-party manufacturers could have a particularly severe impact on our ability to develop or commercialize our product candidates.

Similarly, to develop and commercialize any of our licensed product candidates, our collaborators will need to obtain supplies of deuterated materials and will be subject to risks and requirements in connection with sourcing deuterated materials that are similar to the ones that we face. Any adverse impact on our collaborators' ability to obtain deuterated materials could delay or prevent the development or commercialization of our licensed product candidates, which could have a material adverse effect on our business.

Risks Related to Marketing Approval of Our Product Candidates

Even if we complete the necessary nonclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and we may not obtain approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or our collaborators, will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drug products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, which regulations differ from country to country. Failure to obtain marketing approval for a product candidate in a given territory will prevent us, and our collaborators, from commercializing the product candidate in that territory. Our product candidates are in various stages of development and are subject to the risks of failure inherent in drug development. We, and our collaborators, have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction. We have limited experience in filing and supporting the applications necessary to gain marketing approvals.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. This is the case even though the deuterated compounds that we produce and seek to develop can have similar pharmacological properties as their corresponding non-deuterated compounds. Even if, as a result of any such similarities, we, or our collaborators, obtain clearance from the FDA and other regulatory authorities to follow expedited development programs for some deuterated compounds that reference and rely on previous findings for non-deuterated compounds, the review and approval of our product candidates may still take a substantial period of time. Conversely, in certain countries regulators may consider our deuterated compounds to be equivalent to non-deuterated compounds that possess regulatory exclusivity and therefore refuse to approve our compounds until the expiration of that exclusivity.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional nonclinical, clinical or other studies. In addition, varying interpretations of the data obtained from nonclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we, or our collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

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

Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell our products in the European Union and many other jurisdictions, we, or our collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many territories outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that territory. Our products may not

receive commercially feasible prices in any given territory, or the price offered for our products in a territory may have an adverse effect on their prices in other territories if we were to accept such price. We, and our collaborators, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

Even if we, or our collaborators, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and our collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we, and our collaborators, will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or our collaborators, receive marketing approval for one or more of our product candidates, we, and our collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and our collaborators, are not able to comply with post-approval regulatory requirements, we, and our collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or our collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

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

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

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

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

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the indication, patient population or other parameters for which the drug is approved;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- reputational damage;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Risks Related to Commercialization and Market Acceptance of Our Product Candidates

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

The development and commercialization of new drug products is highly competitive. We expect that we, and our collaborators, will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to our product candidates that we, or they, may seek to develop or commercialize in the future. Specifically, there are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of autoimmune and CNS disorders, which are key indications for our development programs. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that attain preferred reimbursement by payors or are more effective, simpler to use, have fewer or more tolerable side effects or are less costly than any product candidates that we are currently developing or that we may develop or acquire, or which are marketed more effectively, which could render our product candidates obsolete and noncompetitive.

We are developing CTP-543 as an oral agent for the treatment of moderate to severe alopecia areata. If CTP-543 receives marketing approval for this indication, it may face competition from a number of other product candidates that are being studied for alopecia areata. Other companies pursuing development of oral JAK inhibitors for the treatment of alopecia areata include Eli Lilly and Company and Pfizer Inc.

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

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

Even if one of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for the product candidate may be smaller than we estimate.

Even if one of our product candidates, including those licensed to our collaborators, is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-

party payors, formulary decision-makers and others in the medical or patient communities. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies. If any of our product candidates receive negative publicity, patients may choose not to request them even if approved, or may not comply with taking them as prescribed.

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

- the efficacy and safety of the product;
- the potential advantages of the product compared to alternative treatments;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy;
- limitations or warnings, including distribution or use restrictions or burdensome prescription requirements contained in the product's approved labeling;
- our ability, or the ability of our collaborators, to offer the product for sale at commercially acceptable prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- the strength of sales, marketing and distribution support;
- the approval of other new products for the same indications;
- the extent and success of counter-detailing efforts by our competitors;
- the pricing, extent of discounts or bundled products offered by our competitors;
- the organization stability of our collaborators, if any;
- changes in the standard of care for the targeted indications for the product;
- the timing of market introduction of our approved products as well as competitive products; and
- the availability and amount of reimbursement from government payors, managed care plans and other third-party payors.

The potential market opportunities for our product candidates are difficult to precisely estimate. Our estimates of the potential market opportunities are predicated on many assumptions, including industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidates could be smaller than our estimates of the potential market opportunities.

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less pure, homogeneous or stable than believed, less effective than previously believed, or causes undesirable side effects that were not previously identified or at a higher rate than was projected during clinical development, our ability to market the drug, or that of our collaborators, could be compromised.

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

- regulatory authorities may withdraw their approval of the drug and/or seize the drug;
- we, or our collaborators, may need to recall the drug or change the way the drug is administered;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug, including the addition of labeling statements, such as a "black box" warning or a contraindication;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- we, or our collaborators, may be required to operate under a REMS;
- we, or our collaborators, could be sued and held liable for harm caused to patients; and

- the drug may become less competitive.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

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

We do not have a sales, marketing or distribution infrastructure and as a company have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We expect to use a combination of third-party collaboration, licensing and distribution arrangements and a focused in-house commercialization capability to sell any products that receive marketing approval.

We generally plan to seek to retain full commercialization rights for the United States for products that we can commercialize with a specialized sales force and to retain co-promotion or similar rights for the United States when feasible in indications requiring a larger commercial infrastructure. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe that we could otherwise develop and commercialize the product independently.

We currently expect to collaborate with third parties for commercialization in the United States of any products that require a large sales, marketing and product distribution infrastructure. We also expect to commercialize our product candidates outside the United States through collaboration, licensing and distribution arrangements with third parties, if at all. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively, or may actively sell a competing product at the expense of selling ours.

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

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

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

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the

reference listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference listed drug. While we believe that our product candidates contain active ingredients that would be treated as new chemical entities by the FDA and, therefore, if approved, should be afforded at least five years of data exclusivity, the FDA may disagree with that conclusion and may approve generic products after a period that is less than five years. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that our products may face from generic versions of our products could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

To the extent we, or our collaborators, market products that are deuterated analogs of generic drugs that are approved or will be approved while we market our products in territories in which the generic drug is available, our products may compete against these generic products and the sales of our products could be adversely affected.

We anticipate that some of the products that we, or our collaborators, may develop will be deuterated analogs of approved drugs that are or will then be available on a generic basis. In addition, if we develop a product that is a deuterated analog of a non-generic approved drug, the FDA or comparable foreign regulatory authorities may also approve generic versions of the corresponding non-deuterated drug. If approved, we expect that our deuterated products will compete against these generic non-deuterated compounds if they are used in the same indications. Even if the approved indications are different for the deuterated and non-deuterated drugs, the generic non-deuterated drug may be used off-label, negatively affecting sales of our product. Efforts to educate the medical community and third-party payors on the benefits of any product that we develop as compared to the corresponding non-deuterated compound, or generic versions of it, may require significant resources and may not be successful. If physicians, rightly or wrongly, do not believe that a product that we, or our collaborators, develop offers substantial advantages over the corresponding non-deuterated compound, or generic versions of the corresponding non-deuterated compound, or that the advantages offered by our product as compared to the corresponding non-deuterated compound, or its generic versions, are not sufficient to merit the increased price over the corresponding non-deuterated compound, or its generic versions, that we, or our collaborators, would seek, physicians might not prescribe that product. In addition, third-party payors may refuse to provide reimbursement for a product that we, or our collaborators, develop when the corresponding non-deuterated compound, or generic versions of the corresponding non-deuterated compound, offer a cheaper alternative therapy in the same indication, or may otherwise encourage use of the corresponding non-deuterated compound, or generic versions of the corresponding non-deuterated compound, over our product, even if our product possesses favorable pharmaceutical properties or is labeled for a different indication.

Competition that our product candidates may face from any generic non-deuterated product on which our product candidate is based or a later-approved generic version of a branded non-deuterated product on which our product is based, could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

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

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of our collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of our collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or our collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If reimbursement is not available, or is available only to limited levels, we, or our collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or our collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our, or their, investments.

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

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

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

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, such as the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we, or our collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

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

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we, or our collaborators, commercially sell any product that we may, or they may, develop. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend litigation;
- distraction to our management diverting focus from business operations and strategy;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

Although we maintain product liability insurance coverage, it may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to

increase our insurance coverage if and when we begin selling any product candidate that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Healthcare Regulations

Recently enacted and future legislation may increase the difficulty and cost for us and our collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of our collaborators, to profitably sell any products for which we, or they, obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the MMA only addresses drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the PPACA.

Among the provisions of the PPACA of potential importance to our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program new requirements to report financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; 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.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and our collaborators to more stringent product labeling and post-marketing testing and other requirements.

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

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third-party payors and customers, if any, will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws and regulations may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations in the United States include the following:

- *Anti-Kickback Statute*. The federal Healthcare Anti-Kickback statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- *False Claims Act*. The federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;
- *HIPAA*. HIPAA imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services and, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information;
- *Transparency Requirements*. Federal transparency laws require certain manufacturers of covered drugs to report payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and other healthcare providers and their immediate family members; and
- *Analogous State and Foreign Laws*. Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services. In addition, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Risks Related to Legal Compliance Matters

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time, our operations may involve the use of hazardous materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, including any laws and regulations that may be imposed as a result of the COVID-19 pandemic. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

The increasing use of social media platforms presents risks and challenges.

The increasing use of social media platforms presents risks and challenges. Social media increasingly is being used by third parties to communicate about our product candidates and the diseases they are designed to treat. We believe that members of the alopecia areata community may be more active on social media as compared to other patient populations due to the demographics of this patient population. Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients in clinical trials may use social media platforms to comment on the effectiveness of, or adverse experiences with, a product candidate, which could result in reporting obligations. In addition, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business.

Risks Related to Data Protection and Cybersecurity

Our failure to comply with data protection laws and regulations could lead to government enforcement actions, private litigation and/or adverse publicity and could negatively affect our operating results and business.

We are subject to data protection laws and regulations that address privacy and data security. The legislative and regulatory landscape for data protection continues to evolve, and in recent years there has been an increasing focus on privacy and data security issues. 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 govern the collection, use, disclosure and protection of health-related and other personal information. Failure to comply with data protection laws and regulations could result in 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. In addition, we may obtain health information from third parties that are subject to privacy and security requirements under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act. We could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information in a manner that is not authorized or permitted.

The collection and use of personal health data in the European Union is governed by the provisions of the General Data Protection Regulation, or the GDPR, which came into effect in May 2018. This regulation imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States may result in significant fines and other administrative penalties.

Significant disruptions of information technology systems or security breaches could adversely affect our business.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit large amounts of confidential information (including, among other things, trade secrets or other intellectual property, proprietary business information and personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We also have outsourced elements of our operations to third parties, and as a result we manage a number of third-party vendors who may or could have access to our confidential information. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, and the large amounts of confidential information stored on those systems, make such systems vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, consultants, third-party vendors, and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks could also include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

Significant disruptions of our information technology systems, or those of our third-party vendors, or security breaches could adversely affect our business operations and/or result in the loss, misappropriation and/or unauthorized access, use or disclosure of, or the prevention of access to, confidential information, including, among other things, trade secrets or other intellectual property, proprietary business information and personal information, and could result in financial, legal, business and reputational harm to us. For example, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, require us to comply with federal and/or state breach notification laws and foreign law equivalents, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our Chief Executive Officer and other key executives and to attract, retain and motivate qualified personnel.

Our industry has experienced a high rate of turnover of management personnel in recent years. 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 clinical personnel. We are highly dependent on the pharmaceutical research and development and business development expertise of Roger D. Tung, our President and Chief Executive Officer, as well as the other principal members of our management, scientific and development team. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. In addition, although we maintain a key-man insurance policy with respect to Dr. Tung, we do not carry key-man insurance on any of our other executive officers or employees and may not carry any key-man insurance in the future.

If we lose one or more of our executive officers, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

We expect to grow our organization and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As our pipeline grows and matures, we expect to experience significant growth in the number of our employees and the scope of our operations, including in the areas of drug manufacturing, regulatory affairs and sales, clinical development, marketing and distribution. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected expansion of our operations may lead to significant costs and may divert our business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to an Investment in Our Common Stock

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

The trading price of our comment stock has been, and may continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- the success or failure of existing or new competitive products or technologies;
- the timing, advancement of and results of nonclinical studies and clinical trials of any of our product candidates;
- commencement or termination of collaborations for our development programs;
- failure, delays, changes to or discontinuation of any of our development programs;
- regulatory or legal developments in the United States and other countries;
- regulatory actions relating to our product candidates;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- disclosures by our collaborators relating to our product candidates or competitive programs;
- merger or acquisition activity of our collaborators;
- the level of expenses related to any of our product candidates or development programs;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- receipt or expectation of receipt of revenues such as milestones, royalties, grants and license fees;
- sales of our common stock by us, our insiders or other stockholders;
- programmed trading based on technical stock chart or other inputs;
- portfolio restructuring by large stockholders or decisions by stockholders to rapidly acquire or sell our shares;
- addition or removal of our stock from stock indices;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts that cover our stock;
- actions by short-sellers or supporters of our stock, including social media postings or reports;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- legalization or the anticipation of possible legalization of drug reimportation from other countries;
- actual or anticipated changes in FDA practices;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

An active trading market for our common stock may not be sustained.

Although we have listed our common stock on the Nasdaq Global Market, an active trading market for our common stock may not be sustained. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the price at which they acquired their shares or at the times that they would like to sell. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

We have broad discretion in the use of our cash reserves and may not use them effectively.

Our management has broad discretion to use our cash reserves and could use our cash reserves in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

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

We are a smaller reporting company under applicable SEC regulations. For so long as we remain a smaller reporting company, we are permitted and plan to rely on exemptions from certain disclosure requirements applicable to other public companies, including reduced disclosure obligations regarding executive compensation. We cannot predict whether investors will find our common stock less attractive if we 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 will continue to incur increased costs as a result of operating as a public company.

As a public company, we are incurring and expect to continue to incur significant legal, accounting and other expenses. We expect that these expenses will further increase now that we are no longer an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, as of January 1, 2020.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or SOX, we are required to evaluate the effectiveness of our internal control over financial reporting as of the end of each fiscal year and to report on this evaluation in our Annual Report on Form 10-K for the year. We will need to continue to dedicate internal resources, engage outside consultants and maintain a detailed work plan to assess and document the adequacy of our internal control over financial reporting, continue to improve control processes as appropriate, validate through testing that controls are functioning as documented and maintain a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that in the future we will not be able to conclude that our internal control over financial reporting is effective as required by SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

A significant portion of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

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

In addition, as of February 19, 2021, there were 6,181,151 shares subject to outstanding options and restricted stock units under our equity compensation plans, all of which shares are registered under the Securities Act of 1933, as amended, or the Securities Act. These shares will be able to be freely sold in the public market upon exercise, as permitted by any applicable vesting requirements, except to the extent they are held by our affiliates, in which case such shares will become eligible for sale in the public market as permitted by Rule 144 under the Securities Act. Furthermore, as of February 19, 2021, there were 1,861,273 shares subject to outstanding warrants to purchase common stock, 1,800,000 shares of which are registered under the Securities Act. The remaining 61,273 shares will become eligible for sale in the public market, to the extent such warrant is exercised, as permitted by Rule 144 under the Securities Act.

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

We have never declared or paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. Furthermore, any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to substantially influence all matters submitted to stockholders for approval.

Our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding common stock, and all affiliates, in the aggregate, beneficially own a substantial percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to substantially influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would substantially influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

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

Future sales of a substantial number of our common shares by our principal stockholders could depress the trading price of our common stock.

If our principal stockholders sell substantial amounts of shares of our common stock in the public market or if the market anticipates that these sales could occur, the market price of shares of our common stock could decline. These sales may make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem appropriate, or to use equity as consideration for future acquisitions.

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

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

Risks Related to Our Charter and By-Laws

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our by-laws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

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

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of

our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

Our by-laws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our by-laws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of or based on a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or our charter or by-laws, (4) any action to interpret, apply, enforce or determine the validity of our charter or by-laws, or (5) any action asserting a claim governed by the internal affairs doctrine of the State of Delaware. In addition, pursuant to our by-laws, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. These forum selection clauses in our by-laws may limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Risks Related to Income Taxes

Changes in tax law could adversely affect our business and financial condition or holders of our common stock.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge stockholders to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

ITEM 1B. Unresolved Staff Comments

None.

ITEM 2. Properties

We lease our principal facilities, which consist of approximately 56,000 square feet of office and laboratory space located at 65 Hayden Avenue, Lexington, Massachusetts. The lease expires on January 1, 2029. We believe that our facilities are sufficient for our current needs for the foreseeable future.

ITEM 3. Legal Proceedings

In April 2018, the PTAB instituted an IPR brought against the '149 patent by Incyte. In April 2019, the PTAB issued a final written decision in connection with the IPR that held that the claims of the '149 patent were unpatentable as obvious. In January 2020, the Federal Circuit granted our motion to vacate and remand the PTAB final written decision in light of the Federal Circuit ruling on the Constitution's Appointments Clause in *Arthrex, Inc. v. Smith & Nephew, Inc.,* 941 F.3d 1320 (Fed. Cir. 2019). As a result, the IPR was remanded for reconsideration by a new panel of PTAB judges. However, the reconsideration is currently on hold while the Supreme Court considers certain questions raised by *Arthrex*. The '149 patent remains valid and enforceable while the IPR is being reconsidered by the PTAB and until any future appeals by us have been exhausted in the event that the PTAB reaches a similar decision to invalidate the '149 patent.

In addition, in October 2020, Incyte filed a PGR petition with the PTAB challenging the validity of the '659 patent. The '659 patent covers methods of treating hair loss, including alopecia areata, with certain doses of CTP-543. We filed our response in February 2021 and expect the PTAB to make a decision on whether to institute the PGR by mid-May 2021. We intend to vigorously defend the '659 patent.

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 has been publicly traded on the Nasdaq Global Market under the symbol "CNCE" since February 13, 2014.

HOLDERS

As of February 19, 2021, there were 12 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

DIVIDENDS

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay any cash dividends to the holders of our common stock in the foreseeable future.

EQUITY COMPENSATION PLANS

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Part III, Item 12. of this Annual Report on Form 10-K.

ITEM 6. Selected Financial Data

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required by this Item.

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 together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve significant risks and uncertainties. You should read the "Risk Factors" section in Part I, Item 1A. of this Annual Report on Form 10-K for a discussion of important factors that could cause our actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

OVERVIEW

We are a clinical stage biopharmaceutical company that is developing small molecule drugs that we discovered through the application of our DCE Platform. Selective incorporation of deuterium into known molecules has the potential, on a case-by-case basis, to provide better pharmacokinetic or metabolic properties, thereby enhancing their clinical safety, tolerability or efficacy. As discussed in detail in the "Business" section in Part I, Item 1. of this Annual Report on Form 10-K, our lead product candidate is in late-stage development for the treatment of alopecia areata, a serious autoimmune dermatological condition. We are also assessing a number of earlier-stage pipeline candidates.

On February 1, 2021, we announced that our Phase 2 trial to evaluate CTP-692 as an adjunctive treatment for schizophrenia did not meet the primary endpoint or other secondary endpoints. As a result, we have ceased development of CTP-692.

Since our inception in 2006, we have devoted substantially all of our resources to our research and development efforts, including activities to develop our DCE Platform and our core capabilities in deuterium chemistry, identify potential product candidates, undertake nonclinical studies and clinical trials, manufacture clinical trial material in compliance with cGMPs, provide general and administrative support for these operations and establish our intellectual property. We have generated an accumulated deficit of $269.4 million since inception through December 31, 2020 and will require substantial additional capital to fund our research and development. We do not have any products approved for sale and have not generated any revenue from product sales.

We have financed our operations to date primarily through the public offering and private placement of our equity, debt financing, funding from collaborations and patent assignments, an asset sale and other arrangements. In February 2014, we completed our initial public offering, whereby we sold 6,649,690 shares of common stock at a price to the public of $14.00 per share, raising aggregate net proceeds of $83.1 million. In March 2015, we sold 3,300,000 shares of common stock through an underwritten public offering at a price to the public of $15.15 per share, raising aggregate net proceeds of $46.7 million. In January 2020, we sold 5,735,283 shares of common stock through an underwritten public offering at a price to the public of $9.92 per share. At the same time, we sold to a certain existing investor pre-funded warrants to purchase up to an aggregate of 1,800,000 shares of common stock at a purchase price of $9.919 per pre-funded warrant, which represents the per share public offering price for the common stock less the $0.001 per share exercise price for each pre-funded warrant. The aggregate net proceeds from the January 2020 offering was $70.1 million.

In March 2019, we entered into an Open Market Sale Agreement, or the ATM Agreement, with Jefferies LLC, or Jefferies. As of December 31, 2020, we had sold 2,044,364 shares of our common stock pursuant to the ATM Agreement for net proceeds of $23.2 million, after payment of cash commissions of 3.0% of the gross proceeds to Jefferies.

In July 2017, we completed the sale of worldwide development and commercialization rights to CTP-656, now known as VX-561, and other assets related to the treatment of cystic fibrosis to Vertex pursuant to the Vertex Agreement. We received $160.0 million in cash upon closing, with $16.0 million initially held in escrow, which was released to us in February 2019. If VX-561 is approved as part of a combination regimen to treat cystic fibrosis, we are eligible to receive up to $90.0 million in the form of two additional milestones based on marketing approval in the United States and agreement for reimbursement in the first of the United Kingdom, Germany or France. Additional information concerning the sale of CTP-656 is discussed in Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Our operating results may fluctuate significantly from year to year, depending on the timing and magnitude of cash payments received pursuant to collaboration and licensing arrangements and other agreements and the timing and magnitude of clinical trial and other development activities under our current development programs. We generated net losses of $74.8 million and $78.2 million for the years ended December 31, 2020 and 2019, respectively.

We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect our expenses will increase substantially in connection with our ongoing activities as we continue research and development efforts and develop and conduct additional nonclinical studies and clinical trials with respect to our product candidates.

We do not expect to generate revenue from product sales unless and until we, or our collaborators, obtain marketing approval for one or more of our product candidates, which we expect will take a number of years and is subject to significant uncertainty. If we obtain, or believe that we are likely to obtain, marketing approval for any product candidates for which we retain commercialization rights, and intend to commercialize a product, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We expect to seek to fund our operations through a combination of equity offerings, debt financings, collaboration and licensing arrangements and other sources for at least the next several years. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would force us to delay, limit, reduce or terminate our research and development programs and could have a material adverse effect on our financial condition and our ability to develop our products. We will need to generate significant revenues to achieve sustained profitability, and we may never do so.

COLLABORATIONS

We have entered into a number of collaborations for the research, development and commercialization of deuterated compounds. To date, our collaborations have provided us with significant funding for both our specific development programs and our DCE Platform. Our collaborators also have applied their considerable scientific, development, regulatory and commercial capabilities to the development of our compounds. In addition, in some instances, where we develop and seek to collaborate with respect to deuterated analogs of marketed drugs or of drug candidates that are more advanced in clinical trials, our collaborators may be eligible for an expedited development or regulatory pathway by relying on previous clinical data regarding their corresponding non-deuterated compound. We believe that our collaborations have contributed to our ability to progress our product candidates and build our DCE Platform.

Our collaborations are discussed further in Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

ASSET PURCHASE AGREEMENT

In July 2017, we completed the sale of worldwide development and commercialization rights to CTP-656, now known as VX-561, and other assets related to the treatment of cystic fibrosis to Vertex pursuant to the Vertex Agreement. We received $160.0 million in cash upon closing, with $16.0 million initially held in escrow, which was released to us in February 2019. Additionally, upon the achievement of certain milestone events, Vertex has agreed to pay us an aggregate of up to $90.0 million. Of this amount, $50.0 million will become payable to us upon receipt of FDA marketing approval for a combination treatment regimen containing VX-561 for patients with cystic fibrosis, and $40.0 million will become payable to us upon completion of a pricing and reimbursement agreement in the first of the United Kingdom, Germany or France with respect to a combination treatment regimen containing VX-561 for patients with cystic fibrosis. Additional information concerning the sale of CTP-656 is discussed in Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

COVID-19 PANDEMIC

The COVID-19 pandemic continues to spread throughout the United States and worldwide. We could be materially and adversely affected by the risks, or the public perception of the risks, related to an epidemic, pandemic or other public health crisis, such as the COVID-19 pandemic, including but not limited to potential delays in our clinical trials. The ultimate extent of the impact of any epidemic, pandemic or other public health crisis on our business, financial condition and results of operations will depend on future developments, which are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of such epidemic, pandemic or other public health crisis and actions taken to contain or prevent the further spread, among others. Accordingly, we cannot predict the extent to which our business, financial condition and results of operations may be affected by the COVID-19 pandemic, but we are monitoring the situation closely.

FINANCIAL OPERATIONS OVERVIEW

Revenue

We have not generated any revenue from the sales of products. All of our revenue to date has been generated through collaboration, license and research arrangements with collaborators and nonprofit organizations for the development and commercialization of product candidates, a patent assignment agreement and an asset sale.

The terms of these agreements may include one or more of the following types of payments: non-refundable license fees, payments for research and development activities, payments based on the achievement of specified milestones, payment of license exercise or option fees relating to product candidates and royalties on any net product sales. To date, we have received non-refundable upfront payments, several milestone payments, payments for research and development services provided to our collaborators, a change in control payment pursuant to a patent assignment agreement and a payment for the sale of an asset. However, we have not yet earned any license exercise or option fees, sales-based milestone payments or royalty revenue as a result of product sales.

In the future, we will seek to generate revenue from a combination of product sales and milestone payments and royalties on product sales in connection with our current collaborations, our asset sale with Vertex or other collaborations we may enter into.

Research and development expenses

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- employee-related expenses, including salary, benefits, travel and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations and investigative sites that conduct our clinical trials;
- the cost of acquiring, developing and manufacturing clinical trial materials;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies;
- platform-related lab expenses, which includes costs related to synthesis, analysis and *in vitro* and *in vivo* characterization of deuterated compounds to support the selection and progression of potential product candidates;
- expenses related to consultants and advisors; and
- costs associated with nonclinical activities and regulatory operations.

Research and development costs are expensed as incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

A significant portion of our research and development costs have been external costs, which we track on a program-by-program basis. These external costs include fees paid to investigators, consultants, central laboratories and contract research organizations in connection with our clinical trials, and costs related to acquiring and manufacturing clinical trial materials. Our internal research and development costs are primarily personnel-related costs, depreciation and other indirect costs. We do not track our internal research and development expenses on a program-by-program basis, as they are deployed across multiple projects under development.

The successful development of any of our product candidates is highly uncertain. As such, at this time, we cannot reasonably predict with certainty the duration and completion costs of the current or future clinical trials of any of our product candidates or if, when or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain marketing approval. We may never succeed in achieving marketing approval for any of our product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope and rate of progress of our ongoing as well as any additional clinical trials and other research and development activities;
- successful enrollment in and completion of clinical trials, including on account of the COVID-19 pandemic and its impact on clinical trial sites;
- conduct of and results from ongoing as well as any additional clinical trials and research and development activities;
- significant and changing government regulation;
- the terms and timing and receipt of any marketing approvals;
- the performance of our collaborators;
- our ability to manufacture any of our product candidates that we are developing or may develop in the future; and

- the expense and success of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights, including potential claims that we infringe other parties' intellectual property.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the cost and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials or other research and development activities beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, due to the increased size and duration of later-stage clinical trials and the manufacturing that is typically required for those later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our product candidate development programs progress, but we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our development programs and plans.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses for our employees in executive, operational, finance, legal, business development and human resource functions. Other general and administrative expenses include facility-related costs, depreciation and other expenses not allocated to research and development expense and professional fees for directors, accounting and legal services and expenses associated with obtaining and maintaining patents. In both 2020 and 2019, we incurred expenses for intellectual property matters related to CTP-543.

We anticipate that our general and administrative expenses will increase in the future as our pipeline grows and matures. Additionally, if and when we believe that a marketing approval of the first product candidate that we intend to commercialize on our own appears likely, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales, marketing and distribution of our product candidates.

Investment income

Investment income consists of interest income earned on cash equivalents and investments. The amount of investment income earned in any particular period may vary primarily as a result of the amount of cash equivalents and investments held during the period and the types of securities included in our portfolio during the period. Our current investment policy is to maintain a diversified investment portfolio of U.S. government-backed securities and money market mutual funds consisting of U.S. government-backed securities.

Unrealized loss on marketable equity securities

Unrealized loss on marketable equity securities consists of changes in the fair value of shares of common stock of Processa Pharmaceuticals, Inc., or Processa, held by us, as discussed further in Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Income taxes

We record a provision or benefit for income taxes on pre-tax income or loss based on our estimated effective tax rate for the year. We had a pre-tax net loss of $74.9 million and recorded a benefit for income taxes of $85 thousand during the year ended December 31, 2020. We had a pre-tax net loss of $78.2 million and recorded no income tax provision or benefit during the year ended December 31, 2019.

CRITICAL ACCOUNTING POLICIES AND SIGNIFICANT JUDGMENTS AND ESTIMATES

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances. Actual results may differ from these estimates. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies used in the preparation of our financial statements require the most significant judgments and estimates:

- revenue recognition;
- prepaid and accrued research and development expenses; and
- stock-based compensation.

Revenue recognition

We have primarily generated revenue through arrangements with collaborators for the development and commercialization of product candidates.

We adopted Accounting Standards Codification, or ASC, 606 effective January 1, 2018. ASC 606 is a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. The revenue standard is based on the principle that an entity should recognize revenue to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The revenue standard also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts and costs to obtain or fulfill contracts. We applied ASC 606 on January 1, 2018 to all contracts using the modified retrospective approach. For additional details regarding our adoption of ASC 606 and our associated accounting policies, see Notes 2 and 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Prepaid and accrued research and development expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- contract research organizations in connection with clinical trials;
- investigative sites in connection with clinical trials;
- vendors in connection with nonclinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We generally accrue expenses related to research and development activities based on the services received and efforts expended pursuant to contracts with multiple contract research organizations that conduct and manage clinical trials on our behalf as well as other vendors that provide research and development services. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period. To date, there have been no material differences from our estimates to the amounts actually incurred.

Stock-based compensation

Since our inception in April 2006, we have applied the fair value recognition provisions of ASC Topic 718, *Compensation-Stock Compensation*, to account for stock-based compensation arrangements with our employees. Stock-based compensation arrangements with non-employees has not been significant. We use the Black-Scholes-Merton option pricing model for determining the estimated fair value for stock-based awards on the date of grant, which requires the use of subjective assumptions to determine the fair value of stock-based awards, including the award's expected term and the price volatility of the underlying stock. We recognize the value of the portion of the awards that is ultimately expected to vest as expense over the requisite vesting periods on a ratable basis for the entire award. Our stock option awards granted to employees generally have a ten-year term and typically vest over a four-year period.

Prior to the year ended December 31, 2020, expected volatility was estimated using a weighted average of our historical volatility of our common stock and the historical volatility of the common stock of a representative group of publicly traded companies from the biopharmaceutical industry with similar characteristics as us, including stage of product development and therapeutic focus. Having accumulated sufficient historical trading data, we transitioned to calculating expected volatility for the year ended December 31, 2020 based on the historical volatility of only our common stock.

The expected term of awards represents the period of time that the awards are expected to be outstanding. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin, or SAB, No. 107, *Share-Based Payment,* as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees.

We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention of paying cash dividends. The risk-free interest rate was estimated using an average of treasury bill interest rates over a period commensurate with the expected term of the option at the time of grant. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

We have computed the fair value of employee stock options at the date of grant using the following weighted-average assumptions:

	Year ended December 31,	
	2020	**2019**
Expected volatility	68.60 %	76.83 %
Expected term	6.0 years	6.0 years
Risk-free interest rate	1.31 %	2.16 %
Expected dividend yield	— %	— %

We have granted restricted stock units and performance stock units to our employees and members of our senior management team. We recognize compensation expense for restricted stock units ratably over the required service period. For awards with performance conditions in which the award does not vest unless the performance condition is met, we recognize expense only if we estimate that achievement of the performance condition is probable. If we conclude that vesting is probable, we recognize expense from the date that we reach this conclusion through the estimated vesting date using an accelerated attribution method.

PENDING AND RECENTLY ADOPTED ACCOUNTING PRONOUNCEMENTS

For detailed information regarding recently issued accounting pronouncements and the actual and expected impact on our consolidated financial statements, see Note 2 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

RESULTS OF OPERATIONS

Discussion of the year ended December 31, 2020

The following table summarizes our results of operations for the year ended December 31, 2020.

(in thousands)	Year ended December 31, 2020
Revenue:	
License and research and development revenue	$ 7,902
Total revenue	7,902
Operating expenses:	
Research and development	61,624
General and administrative	18,925
Total operating expenses	80,549
Loss from operations	(72,647)
Investment income	1,202
Unrealized loss on marketable equity securities	(3,406)
Loss before income taxes	(74,851)
Income tax benefit	85
Net loss	$ (74,766)

License and research and development revenue

License and research and development revenue was $7.9 million for the year ended December 31, 2020, an increase of $6.8 million compared to the $1.1 million in revenue recognized for the year ended December 31, 2019. The revenue recognized in 2020 was primarily due to the expiration of two licensing options under our previous collaboration agreement with Celgene Corporation, or Celgene, and the satisfaction of obligations to perform research and development services and to supply nonclinical and clinical trial material in connection with the termination of the agreement with Celgene. We recognized $7.8 million in revenue associated with this arrangement for the year ended December 31, 2020. For additional details related to the revenue arrangement with Celgene, see Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

As of December 31, 2020, we had deferred revenue of $2.8 million related to a payment received from GlaxoSmithKline, or GSK. For additional details related to our contractual liabilities, see Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Research and development expenses

The following table summarizes our research and development expenses for the year ended December 31, 2020, with our external research expenses separately classified by program and our internal research expenses separately classified by category.

(in thousands)	Year ended December 31, 2020
CTP-543 external costs	$ 18,006
CTP-692 external costs	17,295
External costs for other programs	972
Employee and contractor-related expenses	20,012
Facility and other expenses	5,339
Total research and development expenses	$ 61,624

Research and development expenses were $61.6 million for the year ended December 31, 2020. CTP-543 expenses for the year ended December 31, 2020 were $18.0 million, an increase of $0.6 million compared to $17.4 million for the year ended December 31, 2019. CTP-543 expenses in 2020 primarily related to clinical development, including preparations for the Phase 3 clinical trial that we initiated in November 2020. CTP-692 expenses for the year ended December 31, 2020 were $17.3

million, an increase of $3.2 million compared to $14.1 million for the year ended December 31, 2019. CTP-692 expenses in 2020 primarily related to the Phase 2 dose-ranging clinical trial. External expenses for other programs consisted of costs incurred to develop our research pipeline. External expenses for other programs decreased by $2.3 million compared to $3.3 million for the year ended December 31, 2019 primarily due to a decrease in lab activity in 2020 related to the COVID-19 pandemic and a $0.5 million payment to the non-profit organization Fast Forward in the first quarter of 2019 under an existing agreement related to CTP-354 between Fast Forward and us, which was triggered by the upfront payment pursuant to our License Agreement, or the Cipla Agreement, with Cipla Technologies LLC, or Cipla. Employee-related expenses consisted primarily of cash and non-cash stock-based compensation expenses. Facility-related expenses consisted primarily of rent and maintenance of our premises. For additional details related to the Cipla Agreement, see Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

General and administrative expenses

The following table summarizes our general and administrative expenses for the year ended December 31, 2020.

(in thousands)	Year ended December 31, 2020
Employee salaries and benefits	$ 10,939
External professional service and legal expenses	3,669
Facility, technology and other expenses	4,016
Depreciation and amortization	301
Total general and administrative expenses	$ 18,925

General and administrative expenses for the year ended December 31, 2020 consisted primarily of salaries and related costs for personnel, including non-cash stock-based compensation. Other general and administrative expenses included accounting and legal services, office and facility-related costs.

Total general and administrative expenses for the year ended December 31, 2020 decreased by $1.4 million compared to $20.3 million for the year ended December 31, 2019 primarily due to a decrease in legal expenses.

Investment income

Investment income was $1.2 million for the year ended December 31, 2020 and consisted of interest income earned on cash equivalents and investments.

Unrealized loss on marketable equity securities

We recorded an unrealized loss on marketable equity securities of $3.4 million during the year ended December 31, 2020. Unrealized loss on marketable equity securities consists of changes in the fair value of shares of common stock of Processa held by us, as discussed further in Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Income tax benefit

We recognized a $0.1 million tax benefit for the year ended December 31, 2020 upon the utilization of state research and development tax credits when filing our 2019 Massachusetts state tax return.

Discussion of the year ended December 31, 2019

The following table summarizes our results of operations for the year ended December 31, 2019.

(in thousands)	Year ended December 31, 2019
Revenue:	
License and research and development revenue	$ 1,077
Total revenue	1,077
Operating expenses:	
Research and development	59,816
General and administrative	20,276
Total operating expenses	80,092
Loss from operations	(79,015)
Investment income	2,987
Other income	12
Unrealized loss on marketable equity securities	(2,150)
Net loss	$ (78,166)

License and research and development revenue

License and research and development revenue was $1.1 million for the year ended December 31, 2019. The revenue recognized in 2019 was primarily a result of the Cipla Agreement that we entered into in the first quarter of 2019 with Cipla. We recognized $1.0 million in revenue associated with this arrangement for the year ended December 31, 2019. For additional details related to the Cipla Agreement, see Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

As of December 31, 2019, we had deferred revenue of:

- $7.7 million related to our collaboration with Celgene, consisting of $1.3 million related to the R&D Services Performance Obligation, $0.1 million related to the Supply Performance Obligation and $6.4 million related to the First and Second Discount Performance Obligations; and

- $2.8 million related to a payment received from GSK.

Research and development expenses

The following table summarizes our research and development expenses for the year ended December 31, 2019, with our external research expenses separately classified by program and our internal research expenses separately classified by category.

(in thousands)	Year ended December 31, 2019
CTP-543 external costs	$ 17,388
CTP-692 external costs	14,126
External costs for other programs	3,279
Employee and contractor-related expenses	19,498
Facility and other expenses	5,525
Total research and development expenses	$ 59,816

Research and development expenses were $59.8 million for the year ended December 31, 2019. CTP-543 expenses primarily related to clinical development, including multiple Phase 2 clinical trials. CTP-692 expenses were attributable to the Phase 1 clinical trials completed in 2019 and manufacturing costs to support the advancement of the CTP-692 program into a Phase 2 clinical trial. Employee-related expenses consisted primarily of cash and non-cash stock-based compensation expenses. Facility-related expenses consisted primarily of rent and maintenance of our premises. External costs for other programs includes a $0.5 million payment to the nonprofit organization Fast Forward in the first quarter of 2019 under an existing agreement related to CTP-354 between Fast Forward and us, which was triggered by the upfront payment pursuant to the Cipla Agreement, and costs incurred to develop our research pipeline.

General and administrative expenses

The following table summarizes our general and administrative expenses for the year ended December 31, 2019.

(in thousands)	Year ended December 31, 2019
Employee salaries and benefits	$ 11,000
External professional service and legal expenses	5,173
Facility, technology and other expenses	3,797
Depreciation and amortization	306
Total general and administrative expenses	$ 20,276

General and administrative expenses for the year ended December 31, 2019 consisted primarily of salaries and related costs for personnel, including non-cash stock-based compensation. Other general and administrative expenses included accounting and legal services, office and facility-related costs.

Investment income

Investment income was $3.0 million for the year ended December 31, 2019 and consisted of interest income earned on cash equivalents and investments.

Unrealized loss on marketable equity securities

We recorded an unrealized loss on marketable equity securities of $2.2 million during the year ended December 31, 2019. Unrealized loss on marketable equity securities consists of changes in the fair value of shares of common stock of Processa held by us, as discussed further in Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

LIQUIDITY, CAPITAL RESOURCES AND GOING CONCERN

We have incurred cumulative losses and negative cash flows from operations since our inception in April 2006, and as of December 31, 2020, we had an accumulated deficit of $269.4 million. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through a combination of equity offerings, debt financings, collaboration and licensing arrangements and other sources.

As of December 31, 2020, we had cash, cash equivalents and investments of $130.0 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Currently, our funds are held in U.S. government-backed securities and money market mutual funds consisting of U.S. government-backed securities.

We have financed our operations to date primarily through the public offering and private placement of our equity, debt financing, funding from collaborations and patent assignments, an asset sale and other arrangements. In February 2014, we completed our initial public offering, whereby we sold 6,649,690 shares of common stock at a price to the public of $14.00 per share, raising aggregate net proceeds of $83.1 million. In March 2015, we sold 3,300,000 shares of common stock through an underwritten public offering at a price to the public of $15.15 per share, raising aggregate net proceeds of $46.7 million. In January 2020, we sold 5,735,283 shares of common stock through an underwritten public offering at a price to the public of $9.92 per share. At the same time, we sold to a certain existing investor pre-funded warrants to purchase up to an aggregate of 1,800,000 shares of common stock at a purchase price of $9.919 per pre-funded warrant, which represents the per share public offering price for the common stock less the $0.001 per share exercise price for each pre-funded warrant. The aggregate net proceeds from the January 2020 offering was $70.1 million.

In March 2019, we entered into the ATM Agreement with Jefferies. As of December 31, 2020, we had sold 2,044,364 shares of our common stock pursuant to the ATM Agreement for net proceeds of $23.2 million, after payment of cash commissions of 3.0% of the gross proceeds to Jefferies.

In June 2015, we received a one-time payment of $50.2 million from Auspex Pharmaceuticals, Inc., or Auspex, pursuant to a patent assignment agreement between us and Auspex. We became eligible to receive the payment due to a change of control of Auspex, which was acquired by Teva Pharmaceutical Industries Ltd., or Teva, in May 2015.

In July 2017, we completed the transaction contemplated by the Vertex Agreement, as discussed further in Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. We received $160.0 million in cash upon closing, with $16.0 million initially held in escrow, which was released to us in February 2019.

As of December 31, 2020, we had net working capital of $132.5 million. We have incurred cumulative net losses of $269.4 million since inception and require capital to continue future development activities. We do not have any products approved for sale and have not generated any revenue from product sales. We have financed our operations primarily through the public offering and private placement of our equity, debt financing, funding from collaborations and patent assignments, an asset sale and other arrangements. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials such as the Phase 3 trial of CTP-543 in alopecia areata. For information regarding our recently completed equity financings, see Notes 13-14 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

We are subject to risks common to companies in the biotechnology industry, including, but not limited to, risks of failure or unsatisfactory results of nonclinical studies and clinical trials, the need to obtain additional financing to fund the future development of our pipeline, the need to obtain marketing approval for our product candidates, the need to successfully commercialize and gain market acceptance of our product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from pilot-scale manufacturing to large-scale production of products.

Under ASC Topic 205-40, *Presentation of Financial Statements - Going Concern*, management is required at each reporting period to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists, management evaluates whether the mitigating effect of our plans sufficiently alleviates the substantial doubt about our ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (i) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued and (ii) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about our ability to continue as a going concern within one year after the date that the financial statements are issued. Generally, to be considered probable of being effectively implemented, the plans must have been approved by the our board of directors before the date that the financial statements are issued.

Successful completion of our development programs and, ultimately, the attainment of profitable operations are dependent upon future events, including obtaining adequate financing to support our cost structure and operating plan. Our plans to alleviate our financing requirements include, among other things, pursuing one or more of the following steps to raise additional capital, none of which can be guaranteed or are entirely within our control:

- raise funding through the sale of our common stock;
- raise funding through debt financing; and
- establish collaborations with potential partners to advance our product pipeline.

Based on our current operating plan, we believe that our current cash, cash equivalents and available-for-sale investments will allow us to meet our liquidity requirements through 2021. Our history of significant losses, our negative cash flows from operations, our limited liquidity resources currently on hand and our dependence on our ability to obtain additional financing to fund our operations after the current resources are exhausted, about which there can be no certainty, have resulted in our assessment that there is substantial doubt about our ability to continue as a going concern for a period of at least twelve months from the issuance date of this Annual Report on Form 10-K. The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business, and do not include any adjustments that may result from the outcome of this uncertainty.

If we are unable to raise capital when needed or on acceptable terms, or if we are unable to procure collaboration arrangements to advance our programs, we would be forced to discontinue some of our operations or develop and implement a plan to further extend payables, reduce overhead or scale back our current operating plan until sufficient additional capital is raised to support further operations. There can be no assurance that such a plan would be successful.

Cash flows

The following table sets forth the primary sources and uses of cash for each of the periods presented:

	Year ended December 31,	
(in thousands)	**2020**	**2019**
Net cash (used in) provided by:		
Operating activities	$ (69,037)	$ (48,761)
Investing activities	344	82,583
Financing activities	92,852	1,451
Net increase in cash, cash equivalents and restricted cash	$ 24,159	$ 35,273

Discussion of the years ended December 31, 2020 and 2019

Operating activities. The cash used in operating activities generally approximates our net loss adjusted for non-cash items and changes in operating assets and liabilities. During the year ended December 31, 2020, our operating activities used cash of $69.0 million as compared to cash used by operating activities of $48.8 million during the prior year. The cash used during both 2020 and 2019 was largely driven by our development activities associated with CTP-543 and CTP-692.

During the year ended December 31, 2019, we received $16.0 million that had previously been held in escrow to secure potential indemnity claims related to the Vertex Agreement, as discussed further in Note 12 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.
Investing activities. Net cash provided by investing activities consisted of proceeds from the maturity of investments, purchases of investments and purchases of fixed assets. Net cash used to purchase investments for the years ended December 31, 2020 and 2019 was $156.7 million and $97.8 million, respectively. Net cash provided by maturities of investments for the years ended December 31, 2020 and 2019 was $157.2 million and $181.1 million, respectively. Purchases of fixed assets for the years ended December 31, 2020 and 2019 was $0.2 million and $0.7 million, respectively. The increase in the purchase of investments during the 2020 period is primarily due to the management of funds received from the January 2020 public offering of common stock and pre-funded warrants, as discussed further in Note 14 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Financing activities. During the years ended December 31, 2020 and 2019, our financing activities generated cash of $92.9 million and $1.5 million, respectively. Cash generated during the year ended December 31, 2020 consisted of $70.1 million of net proceeds from the January 2020 public offering of common stock and pre-funded warrants, $22.0 million of proceeds from our at-the-market offering program and $0.8 million of proceeds from the exercise of stock options. Cash generated during the year ended December 31, 2019 consisted of $1.1 million of proceeds from the exercise of stock options and $1.0 million of proceeds from the exercise of warrants, offset by $0.7 million used to pay withholding taxes on behalf of employees in connection with the vesting of restricted stock units, in exchange for the surrender of shares of common stock by such employees.

Operating capital requirements

We do not anticipate commercializing any of our product candidates for several years. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek marketing approvals for, our product candidates, and begin to commercialize any approved products for which we retain commercialization rights. We are subject to all of the risks incident in the development of new drug products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business, as well as additional risks stemming from the unproven nature of deuterated drugs.

To date, we have not generated any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we, or our collaborators, obtain marketing approval of and commercialize one of our current or future product candidates. Because our product candidates are in various stages of development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete development and commercialization of our product candidates or whether or when we will achieve profitability.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration and licensing arrangements and other sources. Except for any obligations of our collaborators to reimburse us for research and development expenses or to make milestone payments under our agreements with them, we do not have any additional committed external sources of funds. Additional capital may not be available on reasonable terms, if at all. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. If we raise additional funds through the issuance of additional equity or debt securities, it could result in dilution to our existing stockholders, increased fixed payment obligations and the issuance of securities with rights senior to those of our common stock. We may become subject to covenants under any future indebtedness that could limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could adversely impact our ability to conduct our business.

Our expectation with respect to the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including those discussed in the "Risk Factors" section in Part I, Item 1A. of this Annual Report on Form 10-K. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

OFF-BALANCE SHEET ARRANGEMENTS

We did not have 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.

ITEM 7A. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required by this Item.

ITEM 8. Financial Statements and Supplementary Data

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Concert Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Concert Pharmaceuticals, Inc. (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2020, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

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

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

Critical Audit Matter

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

Prepaid and Accrued Contract Research and Development Expenses

Description of the Matter

The Company's total accrued expenses were $9.0 million as of December 31, 2020, which included the obligation for contract research and development expenses incurred as of December 31, 2020 but not paid as of that date. In addition, the Company's total prepaid expenses were $7.6 million as of December 31, 2020, which included amounts that were paid in advance of services provided in connection with its contract research and development.

As discussed in Note 2 of the consolidated financial statements, the Company contracts with service providers to conduct research and development on its behalf, and the amount of expense recorded in the consolidated financial statements is based in part on third-party information which includes the services provided and efforts expended under these arrangements. Given the nature and significance of contract research and development expenses, subjective auditor judgement was required to evaluate the evidence obtained to support the amounts accrued and prepaid for costs associated with the services provided.

How We Addressed the Matter in Our Audit

To evaluate the evidence obtained to support the amounts accrued and prepaid for costs associated with services provided for contract research and development as of December 31, 2020, our audit procedures included, among others, testing the accuracy and completeness of the data used to derive the recorded amounts. We also inquired of the Company's research and development personnel overseeing the contract research and development regarding the progress of clinical trials and evaluated the completeness and valuation of the prepaid and accrued contract research and development expenses. We compared invoices received by the Company subsequent to December 31, 2020 to the total costs recognized by the Company as of that date, and we inspected significant contracts, including any pending change orders, between the Company and service providers conducting research and development on its behalf.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2007.
Boston, Massachusetts
February 25, 2021

CONCERT PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS

	December 31,	
	2020	2019
	(Amounts in thousands, except share and per share data)	
Assets		
Current assets:		
Cash and cash equivalents	$ 77,202	$ 53,043
Investments, available for sale	52,766	53,395
Marketable equity securities	1,969	5,375
Interest receivable	145	260
Deferred offering costs	—	143
Accounts receivable	686	72
Income taxes receivable, current	2,346	—
Prepaid expenses and other current assets	7,610	4,567
Total current assets	142,724	116,855
Property and equipment, net	6,363	7,753
Restricted cash	1,157	1,157
Other assets	51	96
Income taxes receivable	—	2,358
Operating lease right-of-use assets, long-term	8,968	9,252
Total assets	$ 159,263	$ 137,471
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 230	$ 881
Accrued expenses and other liabilities	9,017	8,336
Deferred revenue, current portion	—	7,783
Lease liability, current portion	931	268
Total current liabilities	10,178	17,268
Accrued expenses, net of current portion	108	—
Deferred revenue, net of current portion	2,750	2,750
Lease liability, net of current portion	15,065	15,996
Total liabilities	28,101	36,014
Commitments (Note 11)		
Stockholders' equity:		
Preferred stock, $0.001 par value per share; 5,000,000 shares authorized; no shares issued and outstanding as of December 31, 2020 and 2019, respectively	—	—
Common stock, $0.001 par value per share; 100,000,000 shares authorized; 32,062,799 and 24,065,676 shares issued and 31,862,198 and 23,865,075 outstanding as of December 31, 2020 and 2019, respectively	31	24
Additional paid-in capital	400,636	296,145
Accumulated other comprehensive loss	(58)	(31)
Accumulated deficit	(269,447)	(194,681)
Total stockholders' equity	131,162	101,457
Total liabilities and stockholders' equity	$ 159,263	$ 137,471

See accompanying notes.

CONCERT PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Year ended December 31,	
	2020	2019
	(Amounts in thousands, except per share data)	
Revenue:		
License and research and development revenue	$ 7,902	$ 1,077
Total revenue	7,902	1,077
Operating expenses:		
Research and development	61,624	59,816
General and administrative	18,925	20,276
Total operating expenses	80,549	80,092
Loss from operations	(72,647)	(79,015)
Investment income	1,202	2,987
Other income	—	12
Unrealized loss on marketable equity securities	(3,406)	(2,150)
Loss before income taxes	(74,851)	(78,166)
Income tax benefit	85	—
Net loss	$ (74,766)	$ (78,166)
Other comprehensive income:		
Unrealized (loss) gain on investments, available for sale	(27)	106
Comprehensive loss	$ (74,793)	$ (78,060)
Net loss attributable to common stockholders - basic and diluted	$ (74,766)	$ (78,166)
Net loss per share attributable to common stockholders - basic and diluted	$ (2.40)	$ (3.29)
Weighted-average number of common shares used in net loss per share attributable to common stockholders - basic and diluted	31,200	23,740

See accompanying notes.

CONCERT PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock						
	Issued	In Treasury	Amount	Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity
	(in thousands)						
Balance at December 31, 2018	23,519	81	$ 23	$ 284,369	$ (137)	$ (116,515)	$ 167,740
Exercise of stock options	237	58	—	1,076	—	—	1,076
Release of restricted stock units	203	61	1	(741)	—	—	(740)
Unrealized gain on short-term investments	—	—	—	—	106	—	106
Stock-based compensation expense	—	—	—	10,326	—	—	10,326
Exercise of stock warrants	71	—	—	1,000	—	—	1,000
Proceeds from at-the-market offering, net of issuance costs	36	—	—	115	—	—	115
Net loss	—	—	—	—	—	(78,166)	(78,166)
Balance at December 31, 2019	24,066	200	$ 24	$ 296,145	$ (31)	$ (194,681)	$ 101,457
Exercise of stock options	117	—	—	833	—	—	833
Release of restricted stock units	136	—	—	—	—	—	—
Unrealized loss on short-term investments	—	—	—	—	(27)	—	(27)
Stock-based compensation expense	—	—	—	11,113	—	—	11,113
Sale of common stock and pre-funded warrants, net of underwriters' discount and costs	5,735	—	5	70,059	—	—	70,064
Proceeds from at-the-market offering, net of issuance costs	2,008	—	2	22,486	—	—	22,488
Net loss	—	—	—	—	—	(74,766)	(74,766)
Balance at December 31, 2020	32,062	200	$ 31	$ 400,636	$ (58)	$ (269,447)	$ 131,162

See accompanying notes.

CONCERT PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31,	
	2020	**2019**
	(in thousands)	
Operating activities		
Net loss	$ (74,766)	$ (78,166)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,605	1,664
Stock-based compensation expense	11,113	10,326
Accretion of premiums and discounts on investments	48	(1,013)
Non-cash lease expense	284	226
Unrealized loss on marketable equity securities	3,406	2,150
(Gain) loss on disposal of asset	(2)	4
Changes in operating assets and liabilities:		
Accounts receivable	(81)	(57)
Contract asset	—	16,000
Interest receivable	115	296
Prepaid expenses and other current assets	(3,043)	(1,828)
Other assets	45	(96)
Accounts payable	(651)	(217)
Accrued expenses and other liabilities	929	2,984
Income taxes receivable	12	(36)
Income taxes payable	—	(392)
Operating lease liability	(268)	(606)
Deferred revenue	(7,783)	—
Net cash used in operating activities	(69,037)	(48,761)
Investing activities		
Purchases of property and equipment	(210)	(685)
Purchases of investments	(156,671)	(97,837)
Maturities of investments	157,225	181,105
Net cash provided by investing activities	344	82,583
Financing activities		
Proceeds from at-the-market offering, net of issuance costs	21,955	115
Proceeds from exercise of warrants	—	1,000
Repurchase of common stock pursuant to share surrender	—	(740)
Proceeds from exercise of stock options	833	1,076
Proceeds from common stock and pre-funded warrants sold, net of underwriters' discount and costs	70,064	—
Net cash provided by financing activities	92,852	1,451
Net increase in cash, cash equivalents and restricted cash	24,159	35,273
Cash, cash equivalents and restricted cash at beginning of period	54,200	18,927
Cash, cash equivalents and restricted cash at end of period	$ 78,359	$ 54,200
Supplemental cash flow information:		
Cash paid for income taxes	$ —	$ 459
Purchases of property and equipment unpaid at period end	$ 3	$ 4
Public offering costs unpaid at period end	$ —	$ 143
Cash paid included in measurement of lease liabilities	$ 2,406	$ 2,778
Pre-funded warrants issued	$ 16,736	$ —

See accompanying notes.

1. Nature of Business

Concert Pharmaceuticals, Inc., or the Company, was incorporated on April 12, 2006 as a Delaware corporation and has its operations based in Lexington, Massachusetts. The Company is a clinical stage biopharmaceutical company that is developing small molecule drugs that it discovered through the application of its DCE Platform. Selective incorporation of deuterium into known molecules has the potential, on a case-by-case basis, to provide better pharmacokinetic or metabolic properties, thereby enhancing their clinical safety, tolerability or efficacy. The Company's lead product candidate is in late-stage development for the treatment of alopecia areata, a serious autoimmune dermatological condition. The Company is also assessing a number of earlier-stage pipeline candidates.

Liquidity and Going Concern

In February 2014, the Company completed its initial public offering, whereby the Company sold 6,649,690 shares of common stock at a price to the public of $14.00 per share, raising aggregate net proceeds of $83.1 million. In March 2015, the Company sold 3,300,000 shares of common stock through an underwritten public offering at a price to the public of $15.15 per share, raising aggregate net proceeds of $46.7 million. In January 2020, the Company sold 5,735,283 shares of common stock through an underwritten public offering at a price to the public of $9.92 per share. At the same time, the Company sold to a certain existing investor pre-funded warrants to purchase up to an aggregate of 1,800,000 shares of common stock at a purchase price of $9.919 per pre-funded warrant, which represents the per share public offering price for the common stock less the $0.001 per share exercise price for each pre-funded warrant. The aggregate net proceeds the Company received from the January 2020 offering was $70.1 million.

In March 2019, the Company entered into the ATM Agreement with Jefferies. As of December 31, 2020, the Company had sold 2,044,364 shares of its common stock pursuant to the ATM Agreement for net proceeds of $23.2 million, after payment of cash commissions of 3.0% of the gross proceeds to Jefferies. For additional information on the ATM Agreement, see Note 13.

In June 2015, the Company received a one-time payment of $50.2 million from Auspex pursuant to a patent assignment agreement between the Company and Auspex. The Company became eligible to receive the payment due to a change of control of Auspex, which was acquired by Teva in May 2015.

In July 2017, the Company completed the sale of worldwide development and commercialization rights to CTP-656, now known as VX-561, and other assets related to the treatment of cystic fibrosis to Vertex pursuant to the Vertex Agreement. The Company received $160.0 million in cash upon closing, with $16.0 million initially held in escrow, which was released to the Company in February 2019. For additional information concerning the sale of CTP-656, see Note 12.

As of December 31, 2020, the Company had cash, cash equivalents and investments of $130.0 million and net working capital of $132.5 million. The Company has incurred cumulative net losses of $269.4 million since inception and requires capital to continue future development activities. The Company does not have any products approved for sale and has not generated any revenue from product sales. The Company has financed its operations primarily through the public offering and private placement of its equity, debt financing, funding from collaborations and patent assignments, an asset sale and other arrangements. The Company expects its expenses to increase in connection with its ongoing activities, particularly as it conducts clinical trials such as the Phase 3 trial of CTP-543 in alopecia areata. For information regarding the Company's recently completed equity financings, see Notes 13-14.

The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, risks of failure or unsatisfactory results of nonclinical studies and clinical trials, the need to obtain additional financing to fund the future development of its pipeline, the need to obtain marketing approval for its product candidates, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from pilot-scale manufacturing to large-scale production of products.

Under ASC Topic 205-40, *Presentation of Financial Statements - Going Concern*, management is required at each reporting period to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists, management evaluates whether the mitigating effect of its plans sufficiently alleviates the substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (i) it is probable that the

plans will be effectively implemented within one year after the date that the financial statements are issued and (ii) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued. Generally, to be considered probable of being effectively implemented, the plans must have been approved by the Company's board of directors before the date that the financial statements are issued.

Successful completion of the Company’s development program and, ultimately, the attainment of profitable operations are dependent upon future events, including obtaining adequate financing to support the Company’s cost structure and operating plan. Management’s plans to alleviate its financing requirements include, among other things, pursuing one or more of the following steps to raise additional capital, none of which can be guaranteed or are entirely within the Company’s control:

- raise funding through the sale of the Company's common stock;
- raise funding through debt financing; and
- establish collaborations with potential partners to advance the Company’s product pipeline.

Based on the Company’s current operating plan, management believes that its current cash, cash equivalents and available-for-sale investments will allow the Company to meet its liquidity requirements through 2021. The Company's history of significant losses, its negative cash flows from operations, its limited liquidity resources currently on hand and its dependence on its ability to obtain additional financing to fund its operations after the current resources are exhausted, about which there can be no certainty, have resulted in management's assessment that there is substantial doubt about the Company's ability to continue as a going concern for a period of at least twelve months from the issuance date of this Annual Report on Form 10-K. The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business, and do not include any adjustments that may result from the outcome of this uncertainty.

If the Company is unable to raise capital when needed or on acceptable terms, or if it is unable to procure collaboration arrangements to advance its programs, the Company would be forced to discontinue some of its operations or develop and implement a plan to further extend payables, reduce overhead or scale back its current operating plan until sufficient additional capital is raised to support further operations. There can be no assurance that such a plan would be successful.

2. Basis of Presentation and Significant Accounting Policies

Basis of Presentation

The consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America, or GAAP. Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the Chief Executive Officer. The Company and the Chief Executive Officer view the Company's operations and manage its business as one operating segment: the development of pharmaceutical products on its own behalf or in collaboration with others. All material long-lived assets of the Company reside in the United States. The Company does use contract research organizations and research institutions located outside the United States. Some of these expenses are subject to collaboration reimbursement, which is presented as a component of license and research and development revenue in the consolidated statements of operations and comprehensive loss.

The accompanying consolidated financial statements include the accounts of Concert Pharmaceuticals, Inc. and its wholly owned subsidiaries. All intercompany transactions and balances have been eliminated.

The Company considers events or transactions that occur after the balance sheet date but before the financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure.

Unless otherwise indicated, all amounts in the following tables are in thousands except share and per share amounts.

Use of Estimates and Summary of Significant Accounting Policies

The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, equity, revenue, expenses and the disclosure of contingent assets and liabilities and the Company's ability to continue as a going concern. In preparing the consolidated financial statements, management used estimates in the following areas, among others: revenue recognition; prepaid and accrued

research and development expenses; stock-based compensation expense; and the evaluation of the existence of conditions and events that raise substantial doubt regarding the Company's ability to continue as a going concern. Actual results could differ from those estimates.

Cash, Cash Equivalents and Investments

Cash equivalents include all highly liquid investments maturing within 90 days from the date of purchase. Investments consist of securities with original maturities greater than 90 days when purchased. The Company classifies these investments as available for sale and records them at fair value in the accompanying consolidated balance sheets. Unrealized gains or losses are included in accumulated other comprehensive income (loss). Premiums or discounts from par value are amortized to investment income over the life of the underlying investment.

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The Company classifies all investments as current assets, as these assets are readily available for use in current operations. The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses. During 2020 and 2019, there were no realized gains or losses on sales of investments, and no investments were adjusted for other than temporary declines in fair value.

The Company reviews available-for-sale securities for other-than-temporary impairment whenever the fair value of an available-for-sale security is less than the amortized cost and evidence indicates that an available-for-sale security's carrying amount is not recoverable within a reasonable period of time. Other-than-temporary impairments of investments are recognized in the consolidated statements of operations if the Company has experienced a credit loss, has the intent to sell the security or if it is more likely than not that the Company will be required to sell the security before recovery of the amortized cost basis. Evidence considered in this assessment includes reasons for the impairment, compliance with the Company's investment policy, the severity and the duration of the impairment and changes in value subsequent to the end of the period.

Deferred Offering Costs

Costs incurred in the course of preparing for a capital raise, such as legal, accounting and other professional fees, are deferred on the balance sheet as deferred offering costs. At the time of the completion of the offering, the costs are reclassified as a reduction of the proceeds of the capital raise as part of additional paid-in capital. Should the offering be terminated, deferred offering costs are charged to operations during the period in which the offering is terminated.

Marketable Equity Securities

Marketable equity securities consist of the fair value of shares of common stock of Processa held by the Company, as discussed further in Note 12. The Company recognizes the effects of changes in fair value of equity securities within net income.

The Company reviews investments in marketable securities for other-than-temporary impairment whenever the fair value of the investment is less than the cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. To determine whether an impairment is other-than-temporary, the Company considers whether it has an intent to sell, or whether it is more likely than not that the Company will be required to sell, the investment before recovery of the investment's cost basis. Evidence considered in this assessment includes reasons for the impairment, the severity and duration of the impairment and changes in value subsequent to year-end.

Fair Value of Financial Measurements

The Company has certain financial assets and liabilities that are recorded at fair value which have been classified as Level 1, 2 or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements:

- Level 1—quoted prices for identical instruments in active markets;
- Level 2—quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active and model-derived valuations in which all significant inputs and significant value drivers are observable in active markets; and
- Level 3—valuations derived from valuation techniques in which one or more significant value drivers are unobservable.

For additional information related to fair value measurements, see Note 3.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentration of credit risk consist principally of money market funds, investments (including interest receivable) and accounts receivable. The Company's current investment policy is to maintain a diversified investment portfolio in U.S. government-backed securities and money market mutual funds consisting of U.S. government-backed securities. The Company's cash is deposited in and invested through highly rated financial institutions in North America.

The Company has not experienced any credit losses in these accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no foreign exchange contracts, option contracts or other foreign exchange hedging arrangements.

As of December 31, 2020 and 2019, substantially all of the Company’s cash was deposited in accounts at two financial institutions, thus limiting the amount of credit exposure to any one financial institution. These amounts at times may exceed federally insured limits.

Accounts receivable generally represent amounts due from collaboration partners and from sales under the at-the-market offering program discussed in Note 13. The Company monitors economic conditions to identify facts or circumstances that may indicate that any of its accounts receivable are at risk of collection.

Property and Equipment

Property and equipment are recognized at cost and depreciated over their estimated useful lives using the straight-line method. Leasehold improvements are amortized over the shorter of their useful life or the related lease term. Repair and maintenance costs are expensed as incurred, whereas major improvements are capitalized as additions to property and equipment. Potential impairment is assessed when there is evidence that events or circumstances indicate that the carrying amount of an asset may not be recovered. No such impairment losses have been recorded for the year ended December 31, 2020 and 2019.

Rent Expense

Rent expense for the years ended December 31, 2020 and 2019 consists of the Company's facility at 65 Hayden Avenue, Lexington, Massachusetts. The Company's operating lease for its facility at 65 Hayden Avenue in Lexington, Massachusetts provides for scheduled annual rent increases throughout the lease term, which expires on January 1, 2029. Additionally, the Company has received certain lease incentives, which are recognized as a reduction to rent expense over the remaining lease term. For additional details regarding the Company’s operating lease, see Note 11.

Contingencies

The Company records liabilities for legal and other contingencies when information available to the Company indicates that it is probable that a liability has been incurred and the amount of loss can be reasonably estimated. Legal costs in connection with legal and other contingencies are expensed as costs are incurred. No liabilities for legal and other contingencies were accrued as of December 31, 2020 and 2019.

Revenue Recognition

The Company has generated revenue through arrangements with collaborators and nonprofit organizations for the development and commercialization of product candidates, a patent assignment agreement and an asset sale.

The Company accounts for revenue according to the Financial Accounting Standards Board, or FASB, Accounting Standards Update, or ASU, 2014-09, *Revenue from Contracts with Customers*, and all related amendments, which is also referred to as ASC 606. ASC 606 is a single comprehensive model to account for revenue arising from contracts with customers and is based on the principle that an entity should recognize revenue to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To achieve this core principle, the Company applies the following steps: (1) identify the contract(s) with a customer, (2) identify the performance obligations in the contract, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations in the contract and (5) recognize revenue when, or as, the entity satisfies a performance obligation. ASC 606 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts and costs to obtain or fulfill contracts. For additional information, see Note 12.

Research and Development Costs

Research and development costs are expensed as incurred.

Research and development expenses are comprised of costs incurred in providing research and development activities, including salaries and benefits, facilities costs, overhead costs, contract research and development services and other outside costs. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

External research and development expenses associated with the Company's programs include clinical trial site costs, research compounds and clinical manufacturing costs, costs incurred for consultants and other outside services, such as data management and statistical analysis support and materials and supplies used in support of the clinical and nonclinical programs. Internal costs of the Company's clinical program include salaries, benefits, stock-based compensation and an allocation of the Company's facility costs. When third-party service providers' billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those third parties, including clinical trial and pharmaceutical development costs, contractual services costs and costs for supply of its drug candidates, incurred in a given accounting period and record accruals at the end of the period. The Company bases its estimates on its knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the third-party service contract, where applicable.

Accounting for Stock-Based Compensation

The Company issues stock options and restricted stock units, or RSUs, to certain employees, officers and directors. The Company accounts for stock compensation using the fair value method, which results in the recognition of compensation expense over the vesting period of the awards. For additional information, see Note 8.

Income Taxes

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes*, or ASC 740, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. The Company provides deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax assets to the amount that will more likely than not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. The Company evaluates tax positions taken, or expected to be taken, in the course of preparing its tax returns to determine whether the tax positions are "more likely than not" of being sustained by the applicable tax authority. Tax positions not deemed to meet the more-likely-than-not threshold would be recognized as a tax expense. As of December 31, 2020 and 2019, the Company did not have any significant uncertain tax positions.

For additional details regarding the accounting for income taxes, see Note 10.

Guarantees

As permitted under Delaware law, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is, or was, serving at the Company's request in such capacity. The term of the indemnification is for the officer's or director's lifetime. The maximum potential amount of future payments the Company could be required to make is unlimited; however, the Company has directors' and officers' insurance coverage that limits its exposure and enables it to recover a portion of any future amounts paid.

The Company leases office space under a non-cancelable operating lease, which is further described in Note 11. The Company has standard indemnification arrangements under the lease that require it to indemnify the landlord against all costs, expenses, fines, suits, claims, demands, liabilities and actions directly resulting from any breach, violation or non-performance of any covenant or condition of the Company's lease.

Pursuant to the Vertex Agreement, as discussed further in Note 12, the Company agreed to indemnify Vertex for certain matters, including breaches of specified representations and warranties, covenants included in the Vertex Agreement and specified tax claims. Representations and warranties, other than certain fundamental representations and warranties, survived for a period of eighteen months following the closing, and the maximum liability of the Company for claims by Vertex related to the breaches of such representations and warranties, with limited exceptions, was limited to the escrow amount, or $16.0 million. In January 2019, the escrow period expired, and the escrow of $16.0 million was released to the Company in February 2019.

As of December 31, 2020 and 2019, the Company had not experienced any material losses related to these indemnification obligations, and no material claims with respect thereto were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related reserves were established.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions, other events and circumstances from non-owner sources. Comprehensive loss consists of net loss and other comprehensive loss, which includes certain changes in equity that are excluded from net loss. Comprehensive loss has been disclosed in the accompanying consolidated statements of operations and comprehensive loss. Accumulated other comprehensive loss is presented separately on the consolidated balance sheets and consists entirely of unrealized holdings losses on investments as of December 31, 2020 and 2019.

Recently Adopted Accounting Pronouncements

In August 2018, the FASB issued ASU 2018-15, *Intangible-Goodwill and Other Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement that is a Service Contract*. This standard aligns the requirements for capitalizing implementation costs in a cloud computing arrangement service contract with the requirements for capitalizing implementation costs incurred for internal-use software. The new guidance also prescribes the balance sheet, income statement and cash flow classification of the capitalized implementation costs and related amortization expense, and requires additional quantitative and qualitative disclosures. ASU 2018-15 is effective for fiscal years beginning after December 15, 2019, and early adoption is permitted. The Company adopted this standard effective January 1, 2020, on a prospective basis, and it did not have a material effect on the consolidated financial statements and related disclosures.

In December 2019, the FASB issued ASU 2019-12*, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*. This standard includes removal of certain exceptions to the general principles of ASC 740, *Income Taxes*, and simplification in several other areas. ASU 2019-12 is effective for public business entities for annual reporting periods beginning after December 15, 2020, and interim periods within those reporting periods, and early adoption is permitted. The Company adopted this standard effective January 1, 2020, and it did not have a material effect on the consolidated financial statements and related disclosures. For a detailed discussion of the adoption of ASU 2019-12, see Note 10.

Pending Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses*. This standard requires entities to measure all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions and reasonable and supportable forecasts. As a smaller reporting company, ASU 2016-13 will become effective for the Company for fiscal years beginning after December 15, 2022, and early adoption is permitted. The Company is currently evaluating the impact that ASU 2016-13 will have on its financial statements and related disclosures.

3. Fair Value Measurements

The tables below present information about the Company’s financial assets and liabilities that are measured and carried at fair value as of December 31, 2020 and 2019 and indicate the level within the fair value hierarchy where each measurement is classified. The carrying amounts reflected in the consolidated balance sheets for cash, prepaid expenses and other current assets, restricted cash, accounts payable and accrued expenses approximate their fair values due to their short-term nature.

	Level 1	Level 2	Level 3	Total
December 31, 2020				
Cash equivalents:				
Money market funds	$ 69,928	$ —	$ —	$ 69,928
Investments, available for sale:				
U.S. Treasury obligations	25,528	—	—	25,528
Government agency securities	8,737	18,501	—	27,238
Marketable equity securities:				
Corporate equity securities	1,969	—	—	1,969
Total	$ 106,162	$ 18,501	$ —	$ 124,663

	Level 1	Level 2	Level 3	Total
December 31, 2019				
Cash equivalents:				
Money market funds	$ 40,782	$ —	$ —	$ 40,782
Government agency securities	—	2,000	—	2,000
Investments, available for sale:				
U.S. Treasury obligations	34,499	—	—	34,499
Government agency securities	10,997	7,899	—	18,896
Marketable equity securities:				
Corporate equity securities	5,375	—	—	5,375
Total	$ 91,653	$ 9,899	$ —	$ 101,552

4. Cash, Cash Equivalents, Investments and Marketable Equity Securities

Cash, cash equivalents, available-for-sale investments and marketable equity securities consists of the following as of December 31, 2020 and 2019:

	Average maturity	Amortized cost	Unrealized gains	Unrealized losses	Fair value
December 31, 2020					
Cash		$ 7,274	$ —	$ —	$ 7,274
Money market funds		69,928	—	—	69,928
Cash and cash equivalents		$ 77,202	$ —	$ —	$ 77,202
U.S. Treasury obligations	70 days	$ 25,523	$ 5	$ —	$ 25,528
Government agency securities	82 days	27,225	13	—	27,238
Investments, available for sale		$ 52,748	$ 18	$ —	$ 52,766

December 31, 2020	Acquisition value	Unrealized gains	Unrealized losses	Fair value
Marketable equity securities	$ 10,451	$ —	$ (8,482)	$ 1,969

	Average maturity	Amortized cost	Unrealized gains	Unrealized losses	Fair value
December 31, 2019					
Cash		$ 10,261	$ —	$ —	$ 10,261
Money market funds		40,782	—	—	40,782
Government agency securities	8 days	2,000	—	—	2,000
Cash and cash equivalents		$ 53,043	$ —	$ —	$ 53,043
U.S. Treasury obligations	108 days	$ 34,475	$ 24	$ —	$ 34,499
Government agency securities	74 days	18,874	22	—	18,896
Investments, available for sale		$ 53,349	$ 46	$ —	$ 53,395

December 31, 2019	Acquisition value	Unrealized gains	Unrealized losses	Fair value
Marketable equity securities	$ 10,451	$ —	$ (5,076)	$ 5,375

5. Restricted Cash

Restricted cash as of December 31, 2020 and 2019 was held as collateral for stand-by letters of credit issued by the Company to its landlord in connection with the current lease for its principal facilities located at 65 Hayden Avenue, Lexington, Massachusetts. For additional information regarding the Company's lease, see Note 11. Cash, cash equivalents and restricted cash consisted of the following as of December 31, 2020 and 2019:

	December 31, 2020	December 31, 2019
Cash and cash equivalents	$ 77,202	$ 53,043
Restricted cash	1,157	1,157
Total cash, cash equivalents and restricted cash shown in the statements of cash flows	$ 78,359	$ 54,200

6. Property and Equipment

Property and equipment consist of the following as of December 31, 2020 and 2019:

	Estimated useful life (in years)	December 31, 2020	December 31, 2019
Laboratory equipment	5	$ 3,352	$ 3,736
Computer, telephone and office equipment	3	881	891
Software	3	187	122
Leasehold improvements	Lesser of useful life or remaining lease term	5,943	5,929
		10,363	10,678
Less accumulated depreciation and amortization		(4,000)	(2,925)
		$ 6,363	$ 7,753

Depreciation and amortization expense was charged to operations in the amounts of $1.6 million and $1.7 million for the years ended December 31, 2020 and 2019, respectively.

7. Accrued Expenses and Other Liabilities

Accrued expenses and other liabilities consist of the following as of December 31, 2020 and 2019:

	December 31, 2020	December 31, 2019
Accrued professional fees and other	$ 709	$ 862
Employee compensation and benefits	3,690	3,222
Research and development expenses	4,618	4,252
Accrued expenses and other liabilities	$ 9,017	$ 8,336
Employee compensation and benefits, net of current portion	$ 108	$ —
Accrued expenses and other liabilities, net of current portion	$ 108	$ —

8. Stock-Based Compensation

Stock incentive plans

The Company previously sponsored an Amended and Restated 2006 Stock Option and Grant Plan, or the 2006 Plan, which provided for the issuance of shares of common stock in the form of incentive stock options, nonstatutory stock options, awards of stock and direct stock purchase opportunities to directors, officers, employees and consultants of the Company. The 2006 Plan was replaced by the Company's 2014 Stock Incentive Plan, or the 2014 Plan, which became effective in February 2014. The 2014 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. In addition, the 2014 Plan includes an "evergreen provision" that allows for an annual increase in the number of shares of common stock available for issuance under the 2014 Plan. Effective January 1, 2021, 1,274,487 shares were added to the 2014 Plan for future issuance pursuant to this evergreen provision.

The 2006 Plan has no shares remaining available for grant, although existing stock options granted under the 2006 Plan remain outstanding. As of December 31, 2020, 1,159,069 shares were available for future grant under the 2014 Plan.

Stock options

Stock options are granted with an exercise price equal to the closing market price of the Company's common stock on the date of grant. Stock options generally vest ratably over one, three or four years and have contractual terms of ten years. Stock options are valued using the Black-Scholes-Merton option valuation model, and compensation cost is recognized based on such fair value over the period of vesting.

The following table provides certain information related to the Company's outstanding stock options as of December 31, 2020 and 2019:

	Year ended December 31,	
	2020	2019
Weighted-average fair value of options granted, per option	$ 6.53	$ 8.94
Aggregate grant date fair value of options vested during the year	$ 8,506	$ 9,354
Total cash received from exercises of stock options	$ 833	$ 1,076
Total intrinsic market value of stock options exercised	$ 452	$ 1,277

The weighted-average fair value of options granted in the years ended December 31, 2020 and 2019 reflect the following weighted-average assumptions:

	Year ended December 31,	
	2020	2019
Expected volatility	68.60 %	76.83 %
Expected term	6.0 years	6.0 years
Risk-free interest rate	1.31 %	2.16 %
Expected dividend yield	— %	— %

Expected volatility. For the year ended December 31, 2019, expected volatility was estimated using a weighted average of the Company's historical volatility of its common stock and the historical volatility of the common stock of a group of similar companies that were publicly traded. Having accumulated sufficient historical trading data, the Company transitioned to calculating expected volatility for the year ended December 31, 2020 based on the historical volatility of only the Company's common stock.

Expected term. The expected term of awards represents the period of time that the awards are expected to be outstanding. The expected term was determined using the simplified method as prescribed by SAB No. 107, *Share-Based Payment*, as the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees.

Risk-free interest rate. For the years ended December 31, 2020 and 2019, the risk-free interest rate was estimated using an average of treasury bill interest rates over a period commensurate with the expected term of the option at the time of grant.

Expected dividend yield. The expected dividend yield is zero, as the Company has not paid any dividends to date and has no current intention of paying cash dividends.

Forfeiture rate. The Company elected to estimate potential forfeiture of stock grants and adjust compensation cost recorded accordingly. The estimate of forfeitures is adjusted over the requisite service period to the extent that actual forfeitures differ, or are expected to differ, from such estimates. Changes in estimated forfeitures are recognized through a cumulative catch-up in the period of change and impact the amount of stock compensation expense to be recognized in future periods. For the years ended December 31, 2020 and 2019, the Company assumed forfeiture rates of approximately 7%.

The following is a summary of stock option activity for the year ended December 31, 2020:

	Number of Option Shares	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Market Value
Outstanding at December 31, 2019	4,112,609	$ 15.01		
Granted	722,054	$ 10.63		
Exercised	(117,304)	$ 7.11		
Forfeited or expired	(64,489)	$ 18.80		
Outstanding at December 31, 2020	4,652,870	$ 14.48	6.55	$ 5,930
Exercisable at December 31, 2020	3,273,330	$ 14.52	5.81	$ 4,520
Vested and expected to vest at December 31, 2020 (1)	4,546,476	$ 14.52	6.50	$ 5,800

(1) Represents the number of vested stock option shares as of December 31, 2020, plus the number of unvested stock option shares that the Company estimated as of December 31, 2020 would vest, based on the unvested stock option shares as of December 31, 2020 and an estimated forfeiture rate of 7%.

As of December 31, 2020, there was $11.4 million of unrecognized compensation cost related to stock options that are expected to vest. The stock option costs are expected to be recognized over a weighted-average remaining vesting period of 2.1 years.

Restricted stock units

On August 15, 2019, or the 2019 RSU grant date, the Company granted 0.4 million RSUs, or the 2019 RSUs, to certain officers and employees. All of the 2019 RSUs are service-based and vest annually over two years. On the first anniversary of the 2019 RSU grant date, 35% of the RSUs vested. The remainder of the RSUs will vest on the second anniversary of the 2019 RSU grant date.

On February 14, 2020, or the 2020 RSU grant date, the Company granted 0.4 million RSUs, or the 2020 RSUs, to certain officers and employees. All of the 2020 RSUs are service-based and vest ratably over three years, with one third of the 2020 RSUs vesting on each anniversary of the 2020 RSU grant date through February 14, 2023.

RSUs are not included in issued and outstanding common stock until the shares have vested and settled. As of December 31, 2020, 0.1 million of the 2019 RSUs had vested, and none of the 2020 RSUs had vested. The fair value of an RSU is measured based on the market price of the underlying common stock as of the date of grant.

The following is a summary of RSU activity for the year ended December 31, 2020:

	Number of RSUs	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2019	393,629	$ 10.27
Granted	409,295	$ 10.87
Released	(136,339)	$ 10.27
Forfeited	(5,552)	$ 10.38
Outstanding at December 31, 2020	661,033	$ 10.64

As of December 31, 2020, there was $4.8 million of unrecognized compensation cost related to RSUs that are expected to vest. The RSU costs are expected to be recognized over a weighted-average remaining vesting period of 1.6 years.

Stock-based compensation expense

Total stock-based compensation expense related to all stock-based options and awards recognized in the consolidated statements of operations and comprehensive loss is as follows for the years ended December 31, 2020 and 2019:

	For the Year Ended December 31,	
	2020	2019
Research and development	$ 5,800	$ 5,049
General and administrative	5,313	5,277
Total stock-based compensation expense	$ 11,113	$ 10,326

9. Loss Per Share

Basic net loss per common share is calculated by dividing net loss allocable to common stockholders by the weighted-average common shares outstanding during the period, without consideration of stock options and RSUs as common stock equivalents. The weighted-average common shares outstanding as of December 31, 2020 includes pre-funded warrants to purchase up to an aggregate of 1.8 million shares of common stock that were issued in connection with the January 2020 public offering, as discussed in Note 14. For purposes of the diluted net loss per share calculation, common stock equivalents are excluded from the calculation if their effect would be anti-dilutive. As such, basic and diluted net loss per share applicable to common stockholders are the same for periods with a net loss.

The following table illustrates the determination of loss per share for the years ended December 31, 2020 and 2019:

	For the Year Ended December 31,	
	2020	2019
Numerator:		
Net loss applicable to common stockholders - basic and diluted	$ (74,766)	$ (78,166)
Denominator:		
Weighted-average shares outstanding - basic and diluted	31,200	23,740
Net loss per share applicable to common stockholders - basic and diluted	$ (2.40)	$ (3.29)
Anti-dilutive potential common stock equivalents excluded from the calculation of net loss per share*:		
Stock options	4,653	4,113
Restricted stock units	661	394
Warrants	61	61

*For the year ended December 31, 2020, the Company has presented "Anti-dilutive potential common stock equivalents excluded from the calculation of net loss per share" to include all stock equivalents that could potentially dilute basic earnings per share. The Company has corrected the presentation for the year ended December 31, 2019 and has concluded that this change is not material to the current or any prior period financial statements.

10. Income Taxes

During the year ended December 31, 2020, the Company recorded net loss before taxes of $74.9 million and an income tax benefit of $0.1 million, for an effective rate of 0.1%.

On July 25, 2017, the transaction contemplated by the Vertex Agreement was completed, as discussed further in Note 12, and Vertex paid the Company $160.0 million in cash, with $16.0 million initially held in escrow. For income tax purposes, the $16.0 million held in escrow was recognized under the installment method and therefore deferred until the cash was received by the Company in February 2019. Under Section 453A of the U.S. Internal Revenue Code, or the Code, the Company is required to recognize interest on the deferred tax liability with respect to the portion of the installment sale outstanding as of the close of each taxable year that exceeds $5.0 million. As a result, the Company accrued interest of $0.2 million for 2018. The $16.0 million initially held in escrow was released to the Company in February 2019, and the Company recognized no interest for 2019. During 2020, the Company was able to utilize $0.1 million of state research and development tax credits with its Massachusetts state tax return for the year ending December 31, 2019. The Company has established a full valuation allowance against these credits, and as such the Company has booked a discrete benefit of $0.1 million in 2020 for the utilization of these credits against their Massachusetts state liability.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, was signed into law, making several changes to the Code. The changes include, among other things, increasing the limitation on the amount of deductible interest expense, allowing companies to carryback certain net operating losses and increasing the amount of net operating loss carryforwards that companies can use to offset taxable income. The tax law changes in the CARES Act did not have a material impact on the Company’s income tax provision.

The Company adopted ASU 2019-12*, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, effective January 1, 2020. Under ASU 2019-12, the Company, having a full valuation and a loss in continuing operations, will no longer include the impacts of items in other comprehensive income in determining intra-period allocation of tax expense for continuing operations. Under ASU 2019-12, the Company can apply this change to intra-period tax allocation on a prospective basis. For the twelve months ended December 31, 2020, the Company applied the tax allocation rules of ASU 2019-12 to the $27 thousand of unrealized losses on available-for-sale investments recognized in other comprehensive income, which did not have a material impact on the consolidated financial statements or related disclosures.

The Tax Cuts and Jobs Act, or TCJA, repealed the corporate alternative minimum tax, or AMT, for years after 2017. Companies that were previously subject to the AMT and have AMT tax credit carryforwards as of December 31, 2017 are eligible for a refund of these credits for tax years beginning after 2017 and before 2022. The Company was subject to AMT in

the amount of $1.9 million in 2017. Since the AMT paid on its 2017 tax return generated an AMT credit that will be refundable between 2018 and 2022, the Company recorded a $1.9 million income tax receivable rather than a tax expense for 2017. Further, the Company had a deferred tax asset for its AMT credit carryforward related to its AMT liability paid in 2015 in the amount of $0.3 million. This deferred tax asset was previously offset by a full valuation allowance. As a result of the change in law, the Company reclassified the 2015 AMT credit carryforward from deferred tax assets to income tax receivable during 2017. As of December 31, 2020, the Company had a $2.3 million income tax receivable related to AMT taxes in prior years.

The Company's ability to use its operating loss carryforwards and tax credit carryforwards to offset taxable income is subject to restrictions under Sections 382 and 383 of the Code. Net operating loss and tax credit carryforwards are subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Code. Such changes would limit the Company's use of its operating loss and tax credit carryforwards. In such a situation, the Company may be required to pay income taxes, even though significant operating loss and tax credit carryforwards exist. Additionally, any future financing could result in a change in control, as defined by Sections 382 and 383 of the Code, which could further limit the Company's use of its operating loss and tax credit carryforwards.

A reconciliation of the federal statutory income tax rate and the Company's effective income tax rate is as follows for the years ended December 31, 2020 and 2019:

	Year ended December 31,	
	2020	2019
Federal statutory income tax rate	21.0 %	21.0 %
State income taxes	6.6 %	6.8 %
Change in valuation allowance	(30.3)%	(29.8)%
Research and development and other credits	3.5 %	3.2 %
Permanent items	(0.7)%	(1.1)%
Other	— %	(0.1)%
Federal rate change	— %	— %
Effective income tax rate	0.1 %	— %

The significant components of the Company's net deferred tax assets consist of the following as of December 31, 2020 and 2019:

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 57,057	$ 38,544
Deferred revenue	751	2,878
Research and development and other credit carryforwards	21,546	18,573
Lease liability	4,370	4,443
Other	10,585	7,508
	94,309	71,946
Valuation allowance	(90,446)	(67,737)
Total deferred tax assets, net of valuation allowance	$ 3,863	$ 4,209
Deferred tax liabilities:		
Fixed assets	$ 1,413	$ 1,681
Right of use asset	2,450	2,528
Gain deferred under installment method	—	—
Total deferred tax liabilities	$ 3,863	$ 4,209
Net deferred tax assets	$ —	$ —

Subject to the limitations described above and the impacts of the TCJA, as of December 31, 2020, the Company had gross federal net operating loss carryforwards of $220.8 million and state net operating loss carryforwards of $169.3 million available to reduce future taxable income, of which $54.8 million of the gross federal net operating loss carryforwards and $169.3 million of the state net operating loss carryforwards will expire at various dates beginning in 2034. Approximately $165.9 million of

the federal net operating loss carryforwards will be carried forward indefinitely. The Company also had federal and state tax credit carryforwards of $16.8 million and $6.0 million, respectively, available to reduce future tax liabilities, which expire at various dates through 2040.

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the carryforward period. The Company currently has deferred tax assets in excess of its deferred tax liabilities, resulting in the Company having net deferred tax assets. The Company has evaluated the positive and negative evidence bearing upon the realizability of its net deferred tax assets and concluded that it is more likely than not that the Company will not realize the benefit of its net deferred tax assets. As a result, the net deferred tax assets have been fully reserved as of December 31, 2020 and 2019.

As of December 31, 2020, the Company had no unrecognized tax benefits. The Company has not conducted a study of its research and development credit carryforwards. A study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts will be presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credit carryforwards and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheet or statement of operations if an adjustment were required.

Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the statement of operations. As of December 31, 2020, the Company had no accrued interest related to uncertain tax positions.

The Company is currently open to examination under the statute of limitations by the IRS and state jurisdictions for the tax years ended 2017 through 2019. Carryforward tax attributes generated in years prior to 2017 may still be adjusted upon future examination if they have or will be used in a future period. The Company is currently not under examination by the IRS or any other jurisdictions for any tax years. Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available.

11. Commitments

Lease

The Company currently has a lease, or the Lease, for approximately 56,000 square feet of office and laboratory space located at 65 Hayden Avenue, Lexington, Massachusetts, or the Premises. The Lease is classified as an operating lease. The lease term extends ten years following January 1, 2019. The Company is entitled to two five-year options to extend the Lease. The Lease provides for annual base rent of approximately $2.8 million in the first year following January 1, 2019, which increases on a yearly basis by 3.0% (subject to an abatement of base rent of approximately $0.5 million at the beginning of the second year of the lease term). There are no variable payments, exercise purchase options, penalties, fees or residual value guarantees under the Lease. The Company is also obligated to pay the landlord for certain costs, taxes and operating expenses related to the Premises, subject to certain exclusions.

The Company received an improvement allowance from the landlord of approximately $5.0 million for certain permitted costs related to the design of the Company's improvements to the Premises, consisting of normal tenant improvements. The Company is deemed to be the owner of these tenant improvements during the lease term. These $5.0 million of improvements are included in the Company's property, plant and equipment balances in its consolidated balance sheets as of December 31, 2020 and 2019 and are depreciated over the shorter of their useful life or the related lease term.

In February 2016, the FASB issued ASU 2016-02, *Leases* (Topic 842), which is also referred to as ASC 842. ASC 842 requires lessees to recognize assets and liabilities on the balance sheet for the rights and obligations created by all leases with terms of more than 12 months. ASC 842 also requires certain qualitative and quantitative disclosures designed to give financial statement users information on the amount, timing and uncertainty of cash flows arising from leases. The Company adopted ASC 842 effective January 1, 2019.

On January 1, 2019, the Company recorded a right-of-use asset in the amount of $9.5 million, which represented the lease liability of $16.9 million, adjusted for previously accrued rent of $2.9 million and previously recorded unamortized lease incentives in the amount of $4.5 million. The right-of-use asset is amortized over the remaining lease term in an amount equal to the difference between the calculated straight-line expense of the total lease payments less the monthly interest calculated on

the remaining lease liability. As of December 31, 2020 and 2019, the Company had a long-term lease asset of $9.0 million and $9.3 million, respectively, recorded in its consolidated balance sheets.

The Company used an incremental borrowing rate of 13.08% to discount the remaining lease payments over the remaining lease term and recorded a lease liability of $16.9 million on January 1, 2019. This lease liability is amortized over the remaining lease term in an amount equal to the difference between the cash rent paid and the monthly interest calculated on the remaining lease liability. As of December 31, 2020 and 2019, the Company had a current lease liability of $0.9 million and $0.3 million, respectively, and a non-current lease liability of $15.1 million and $16.0 million, respectively, recorded in its consolidated balance sheets.

The Company recognizes lease expense, calculated as the remaining cost of the Lease allocated over the remaining lease term, on a straight-line basis. Lease expense is presented as part of continuing operations in the consolidated statements of operations and comprehensive loss. For each of the years ended December 31, 2020 and 2019, the Company recognized $2.4 million in rent expense.

For the years ended December 31, 2020 and 2019, the Company paid rent of $2.4 million and $2.8 million, respectively. The year ended December 31, 2020 included two months of rent abatement according to the terms of the Lease. As a payment arising from an operating lease, the $2.4 million and $2.8 million is classified within operating activities in the consolidated statements of cash flows for the years ended December 31, 2020 and 2019, respectively.

As of December 31, 2020 and 2019, the discount rate for the Lease was 13.08%, and the remaining lease term for the Premises was eight years and nine years, respectively.

Future minimum lease payments under the Company's non-cancelable operating leases as of December 31, 2020 were as follows:

Maturities of lease liabilities:	For the year ended December 31,
2021	$ 2,969
2022	3,058
2023	3,150
2024	3,244
2025	3,341
Thereafter	10,637
Total lease payments	$ 26,399
Less imputed interest	$ (10,403)
Total	$ 15,996

12. Revenue

The Company's revenue is generated through collaborative licensing agreements, patent assignments and sales of intellectual property. The Company generates its revenue through one segment. The revenue recognized under each of the Company's arrangements during the current and prior periods is described below. The terms of these agreements may contain multiple promised goods or services or optional goods and services, including licenses to product candidates, referred to as exclusive licenses, as well as research and development activities to be performed by the Company on behalf of the collaboration partner related to the licensed product candidates.

Revenue recognition

Revenue is recognized when control of the promised goods or services are transferred to customers in an amount that reflects the consideration the Company expects to be entitled to in exchange for transferring those goods or providing services. The Company accounts for a contract when it has approval and commitment from both parties, the rights of the parties are identified, payment terms are identified, the contract has commercial substance and collectability of consideration is probable.

When determining whether the customer has obtained control of the goods or services, the Company considers the point at which the customer may benefit from the goods or services. For licenses to product candidates, revenue is recognized upon

grant or transfer of the exclusive license, as the Company's licenses are considered functional in nature. For research, development and manufacturing activities, revenue is recognized as the work is performed using either the output or input method.

Performance obligations

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer, and is the unit of account in ASC 606. A contract's transaction price is allocated to each distinct performance obligation and recognized as revenue when, or as, the performance obligation is satisfied. The Company's contracts may contain multiple performance obligations if a promise to transfer goods or services is separately identifiable from other promises in a contract and, therefore, is considered distinct. For contracts with multiple performance obligations, the Company determines the standalone selling price of each performance obligation and allocates the total transaction price using the relative selling price basis. The Company recognizes performance obligations based on their nature.

Significant payment terms

The Company's revenue arrangements include payments to the Company of one or more of the following: a non-refundable, upfront payment; milestone payments; payment of license exercise or option fees with respect to product candidates; fees for research and development services rendered; and royalties on commercial sales of licensed product candidates, if any. To date, the Company has received upfront payments, several milestone payments and certain research and development service payments, but has not received any license exercise or option fees or earned royalty revenue as a result of product sales.

Under ASC 606, the Company estimates the amount of consideration to which it will be entitled in exchange for satisfying performance obligations. Based on the Company's current contracts, variable consideration primarily exists in the following forms: development and regulatory milestones, royalties and sales-based milestones. The Company utilizes the "most likely amount" variable consideration method for estimating development and regulatory milestone consideration to include in the transaction price. The Company only includes an amount of variable consideration in the transaction price to the extent it is probable that a significant reversal in the cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. The Company refers to this as the variable consideration constraint.

Due to the uncertainty associated with the occurrence of the underlying events which would trigger development and regulatory milestone consideration under its revenue arrangements, with the exception of those development and regulatory milestones received to date, the Company has concluded the variable consideration associated with all development and regulatory milestones to be fully constrained as of the ASC 606 transition date and as of December 31, 2020 and 2019, and therefore has not included such consideration in the transaction price for any of its revenue arrangements. The Company will reassess this conclusion at each subsequent reporting period and will only include amounts associated with regulatory or development milestones in the transaction price when, or if, the variable consideration is determined to be released from the constraint.

To date, the Company has not recognized any royalties or sales-based milestones under its licensing and collaboration arrangements. Royalties and sales-based milestones qualify for the sales-and-usage exemption under ASC 606 as (i) royalties are based strictly on the sales-and-usage by the licensee and (ii) a license of intellectual property is the sole or predominant item to which such royalties relate. Based on this exemption, these royalties are earned under the terms of a license agreement in the period the products are sold by the Company's collaborator and the Company has a present right to payment.

In accordance with ASC 606, the Company is required to adjust the transaction price for the effects of the time value of money if the timing of payments agreed to by the parties to the contract, explicitly or implicitly, provides the Company or its customer with a significant benefit of financing the transfer of goods or services. The Company concluded that its licensing and collaboration arrangements do not contain a significant financing component because the payment structure of its agreements arise from reasons other than providing a significant benefit of financing.

Contract assets

The Company did not have a contract asset as of December 31, 2020 or 2019.

Contract liabilities

As of December 31, 2020 and 2019, the Company had $2.8 million and $10.5 million, respectively, in contract liabilities related to unsatisfied performance obligations as well as variable consideration paid in advance, but currently constrained from recognition. Contract liabilities are presented as deferred revenue and classified as current or non-current based on the timing of

when the Company expects to recognize revenue. The $2.8 million in contract liabilities as of December 31, 2020 is related to a payment received from GSK that the Company will not recognize as revenue until all repayment obligations lapse. The $10.5 million in contract liabilities as of December 31, 2019 is related to the $2.8 million GSK payment and $7.7 million associated with the Company's previous collaboration with Celgene.

During the year ended December 31, 2020, the Company recognized $7.7 million in deferred revenue, which consisted of $6.4 million in deferred revenue upon the expiration of two licensing options under the Company's previous collaboration agreement with Celgene and $1.3 million in deferred revenue upon the satisfaction of obligations to perform research and development services and to supply nonclinical and clinical trial material in connection with the termination of the agreement with Celgene. The Company also recognized $78 thousand in patent reimbursement costs in connection with the termination of the agreement with Celgene. As of December 31, 2020, no further performance obligations remain outstanding from the revenue arrangement with Celgene.

Revenue arrangements

Vertex

On July 25, 2017, or the Vertex Closing Date, the Company completed the sale of worldwide development and commercialization rights to CTP-656, now known as VX-561, and other assets related to the treatment of cystic fibrosis to Vertex pursuant to the Vertex Agreement. The Company received $160.0 million in cash on the Vertex Closing Date, with $16.0 million initially held in escrow, which was released to the Company in February 2019. Additionally, upon the achievement of certain milestone events, Vertex has agreed to pay the Company an aggregate of up to $90.0 million.

As of December 31, 2018, the Vertex indemnification variable consideration represented a contract asset to be released from escrow 18 months following the Vertex Closing Date and was classified as a current asset in the accompanying consolidated balance sheet. In February 2019, the $16.0 million that had previously been held in escrow was released to the Company. Additionally, the variable consideration related to the regulatory milestone payments are fully constrained due to the uncertainty associated with the achievement of the respective milestones. Accordingly, no contract asset was recorded as of December 31, 2020 or 2019.

Processa

On October 4, 2017, the Company entered into an Option and License Agreement, or the Option, with Promet Therapeutics, LLC, or Promet, pursuant to which the Company granted Promet an option to obtain an exclusive license to CTP-499, now known as PCS-499, provided certain conditions were met. On October 5, 2017, Promet closed an asset purchase agreement with Heatwurx, Inc., a public company, creating Processa.

On March 19, 2018, the Company entered into an Amendment to the Option, or the Amendment, and a Securities Purchase Agreement with both Promet and Processa. Pursuant to the Amendment, the Company granted Promet, who then assigned to Processa, an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize CTP-499. Upon transfer of the license and as consideration for the license, the Company received 2,090,301 shares of common stock of Processa. In December 2019, Processa implemented a reverse stock split, and the Company now owns 298,615 shares of common stock of Processa.

The Company is also eligible to receive royalties on worldwide net sales.

The Amendment contained one performance obligation: an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize CTP-499. The Company determined that the transaction price was $10.5 million, which was based on the fair value of the non-cash consideration received on March 19, 2018, which consisted of 2,090,301 shares of publicly traded common stock of Processa. The transaction price of $10.5 million was allocated to the single performance obligation. The performance obligation was considered satisfied at contract inception, as the exclusive license transferred control to the customer at this point in time. Accordingly, revenue of $10.5 million was recognized during the first quarter of 2018.

Subsequent changes to the fair value of the underlying securities are recognized as unrealized gains or losses on marketable equity securities within the consolidated statements of operations and comprehensive loss.

The Amendment contains consideration that is variable based on royalties upon the customer's commercial success with the licensed product. The consideration related to royalty payments is considered variable consideration that is fully constrained in

accordance with the royalty recognition constraint. The variable consideration related to royalties will be recognized in the period the products are sold by Processa and the Company has a present right to payment.

For the year ended December 31, 2020, the Company recognized $18 thousand in revenue related to intellectual property cost reimbursements. For the year ended December 31, 2019, the Company recognized $34 thousand in revenue related to intellectual property cost reimbursements.

Cipla

The Company entered into the Cipla Agreement with Cipla on January 16, 2019, or the Cipla Closing Date, pursuant to which the Company granted Cipla an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize CTP-354. As consideration for the license, the Company received an upfront payment of $1.0 million.

The Cipla Agreement also provides Cipla the option to purchase the Company's existing inventory of CTP-354 held as of the Cipla Closing Date, valued in the aggregate at $0.3 million. Additionally, upon the achievement of certain milestone events, Cipla has agreed to pay the Company an aggregate of up to $57.0 million. The first milestone payment the Company may be entitled to receive is $3.0 million when the first IND for the first CTP-354 product goes into effect.

Furthermore, the Company is eligible to receive royalties on worldwide net sales of future product sales at defined percentages ranging from the mid-single to high-single digits.

The Cipla Agreement contained one performance obligation: an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize CTP-354, referred to as the Transfer of License Performance Obligation. The Company concluded that the option to purchase existing inventory did not provide Cipla a material right, and as such, was treated as a separate contract. The transaction price was determined to be $1.0 million based on the upfront consideration received as of the Cipla Closing Date.

As of the Cipla Closing Date, the Transfer of License Performance Obligation was satisfied, as the control of CTP-354 transferred to Cipla, the customer. As a result, the full transaction price was recognized as revenue on the Cipla Closing Date. The sale of existing inventory is recognized as goods are transferred to the customer.

The arrangement with Cipla contains consideration that is variable based on the customer's achievement of certain development and regulatory milestones in addition to royalties upon the customer's commercial success with the licensed product. The next milestone payment the Company may be entitled to receive of $3.0 million related to the first IND for the first CTP-354 product going into effect is considered variable consideration that is fully constrained due to the uncertainty associated with the achievement of the development milestone. The consideration related to royalties is also variable consideration that is fully constrained in accordance with the royalty recognition constraint. The variable consideration related to royalties will be recognized in the period the products are sold by Cipla and the Company has a present right to payment.

The Company did not recognize revenue related to the Cipla Agreement for the year ended December 31, 2020. The Company recognized $1.0 million in revenue associated with the sale of existing inventory and the Transfer of License Performance Obligation for the year ended December 31, 2019.

13. Open Market Sale Agreement

On March 1, 2019, the Company entered into the ATM Agreement with Jefferies with respect to an at-the-market offering program under which the Company may offer and sell, from time to time at its sole discretion, shares of its common stock having an aggregate offering price of up to $50.0 million, referred to as Placement Shares, through Jefferies as its sales agent. The Company will pay Jefferies a commission equal to 3.0% of the gross sales proceeds of any Placement Shares sold through Jefferies under the ATM Agreement, and also has provided Jefferies with customary indemnification and contribution rights. In addition, the Company has agreed to reimburse certain legal expenses and fees incurred by Jefferies in connection with the offering up to a maximum of $50 thousand, in addition to certain ongoing disbursements of Jefferies' counsel.

During the year ended December 31, 2019, the Company sold 36,167 shares of its common stock pursuant to the ATM Agreement for net proceeds of $0.4 million, after payment of cash commissions of 3.0% of the gross proceeds to Jefferies. Additionally, the Company incurred approximately $0.3 million related to legal, accounting and other fees in connection with the ATM Agreement.

On November 5, 2020, the Company entered into an amendment to the ATM Agreement with Jefferies to increase the aggregate offering price of Placement Shares that may be offered and sold pursuant to the ATM Agreement from up to $50.0 million to up to $100.0 million. During the year ended December 31, 2020, the Company sold 2,008,197 shares of its common stock pursuant to the ATM Agreement for net proceeds of $22.8 million, after payment of cash commissions of 3.0% of the gross proceeds to Jefferies. $0.5 million of the net proceeds from the shares sold in 2020 was classified as a receivable as of December 31, 2020. Additionally, the Company incurred approximately $0.3 million related to legal and accounting fees in connection with the ATM Agreement.

Subsequent to December 31, 2020, the Company sold additional shares under the ATM Agreement. For further details, see Note 18.

14. Sale of Common Stock and Pre-Funded Warrants

In January 2020, the Company sold 5,735,283 shares of common stock through an underwritten public offering at a price to the public of $9.92 per share, which included the full exercise of the underwriters' option to purchase 982,863 additional shares of common stock. At the same time, the Company sold to a certain existing investor pre-funded warrants to purchase up to an aggregate of 1,800,000 shares of common stock at a purchase price of $9.919 per pre-funded warrant, which represents the per share public offering price for the common stock less the $0.001 per share exercise price for each pre-funded warrant. The aggregate net proceeds to the Company from this offering was $70.1 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

The pre-funded warrants are exercisable at any time by either (i) payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise or (ii) a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. A holder will not be entitled to exercise any portion of any pre-funded warrant if the holder’s ownership of the Company’s common stock would exceed 19.99% following such exercise.

In the event of certain fundamental transactions, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the pre-funded warrants.

The pre-funded warrants were classified as a component of permanent stockholders’ equity within additional paid-in capital and were recorded at the issuance date using a relative fair value allocation method. The pre-funded warrants are equity classified because they are freestanding financial instruments that are legally detachable and separately exercisable from the equity instruments, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, permit the holders to receive a fixed number of shares of common stock upon exercise, are indexed to the Company’s common stock and meet the equity classification criteria. In addition, such pre-funded warrants do not provide any guarantee of value or return. The Company valued the pre-funded warrants at issuance, concluding that their sales price approximated their fair value, and allocated net proceeds from the sale proportionately to the common stock and pre-funded warrants, of which $16.7 million was allocated to the pre-funded warrants and recorded as a component of additional paid-in capital.

15. 401(k) Retirement Plan

In January 2008, the Company established the Concert Pharmaceuticals 401(k) Retirement Plan, or the 401(k) Plan, in which substantially all of its permanent employees are eligible to contribute a percentage of base wages up to an amount not to exceed an annual statutory maximum. The Company matches 50% of the first 6% of an employee’s contributions, subject to statutory limits.

The Company made matching contributions under the 401(k) Plan of $0.4 million for each of the years ended December 31, 2020 and 2019.

16. Warrants to Purchase Redeemable Securities

On June 8, 2017, the Company entered into a Loan Agreement with Hercules Technology Growth Capital, Inc., or Hercules. In connection with entering into the Loan Agreement, the Company issued warrants, or the Warrants, to certain entities affiliated with Hercules, exercisable for an aggregate of 61,273 shares of the Company’s common stock at an exercise price of $12.24 per share. The Warrants have a five-year term that expires on June 8, 2022 and may be exercised on a cashless basis. The Warrants had a total relative fair value of $0.5 million upon issuance and were recorded as a debt discount.

Pursuant to ASC 480, *Distinguishing Liabilities from Equity*, and ASC 815, *Derivatives and Hedging*, the Warrants were classified as equity and were initially measured at relative fair value. Subsequent changes to fair value will not be recognized so long as the instrument continues to be equity classified. To determine the relative fair value, the Company measured the fair value of the Warrants as of June 8, 2017 using the Black-Scholes-Merton option pricing model. The significant assumptions used in estimating the fair value of the Warrants include the volatility of the stock underlying the Warrants, risk-free interest rate and estimated life of the Warrants. The Company used the following weighted-average assumptions:

Expected volatility	73.71 %
Expected term (in years)	5
Risk-free interest rate	1.75 %
Expected dividend yield	— %

Consistent with the Company's weighted-average assumptions used in determining the fair value of options in 2017, expected volatility was estimated using a weighted average of the Company's historical volatility of its common stock and the historical volatility of the common stock of a group of similar companies that were publicly traded.

17. Quarterly Financial Information (unaudited)

	Three Months Ended			
	March 31, 2020	**June 30, 2020**	**September 30, 2020**	**December 31, 2020**
Revenue	$ 7	$ 6,387	$ 1,501	$ 7
Operating expenses	18,658	19,519	20,861	21,511
Loss from operations	(18,651)	(13,132)	(19,360)	(21,504)
Other (expense) income, net	(1,826)	56	452	(886)
Income tax benefit	—	85	—	—
Net loss	$ (20,477)	$ (12,991)	$ (18,908)	$ (22,390)
Net loss per share - basic and diluted	$ (0.70)	$ (0.41)	$ (0.60)	$ (0.69)

	Three Months Ended			
	March 31, 2019	**June 30, 2019**	**September 30, 2019**	**December 31, 2019**
Revenue	$ 1,005	$ 49	$ 10	$ 13
Operating expenses	21,399	19,474	18,253	20,966
Loss from operations	(20,394)	(19,425)	(18,243)	(20,953)
Other (expense) income, net	(1,432)	757	1,058	466
Net loss	$ (21,826)	$ (18,668)	$ (17,185)	$ (20,487)
Net loss per share - basic and diluted	$ (0.93)	$ (0.78)	$ (0.72)	$ (0.86)

18. Subsequent Events

Subsequent to December 31, 2020, the Company sold an additional 165,323 shares of its common stock pursuant to the ATM Agreement for net proceeds of $2.0 million, after payment of cash commissions of 3.0% of the gross proceeds to Jefferies.

On February 1, 2021, the Company announced that its Phase 2 trial to evaluate CTP-692 as an adjunctive treatment for schizophrenia did not meet the primary endpoint or other secondary endpoints. As a result, the Company has ceased development of CTP-692.

ITEM 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

ITEM 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act refers to controls and procedures 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. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020, the end of the period covered by this Annual Report on Form 10-K. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company's principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of a company's assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that a company's receipts and expenditures are being made only in accordance with authorizations of the company's management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2020 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control—Integrated Framework* (2013 framework). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2020.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the three months 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

None.

Part III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by Item 10 will be included in our definitive proxy statement relating to our 2021 Annual Meeting of Stockholders, to be filed no later than 120 days after December 31, 2020, and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by Item 11 will be included in our definitive proxy statement relating to our 2021 Annual Meeting of Stockholders, to be filed no later than 120 days after December 31, 2020, and is incorporated herein by reference.

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

The information required by Item 12 will be included in our definitive proxy statement relating to our 2021 Annual Meeting of Stockholders, to be filed no later than 120 days after December 31, 2020, and is incorporated herein by reference.

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

The information required by Item 13 will be included in our definitive proxy statement relating to our 2021 Annual Meeting of Stockholders, to be filed no later than 120 days after December 31, 2020, and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by Item 14 will be included in our definitive proxy statement relating to our 2021 Annual Meeting of Stockholders, to be filed no later than 120 days after December 31, 2020, and is incorporated herein by reference.

Part IV

Item 15. Exhibits and Financial Statement Schedules

(1) Financial Statements

Our consolidated financial statements are set forth in Part II, Item 8. of this Annual Report on Form 10-K and are incorporated herein by reference.

(2) Financial Statement Schedules

Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(3) Exhibits

Exhibit number	Description
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on February 20, 2014)
3.2	Amended and Restated By-laws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed on February 20, 2014)
3.3	Amendment to Amended and Restated By-laws of the Registrant (incorporated by reference to Exhibit 3.3 to the Registrant's Annual Report on Form 10-K filed on March 6, 2017)
3.4	Second Amendment to Amended and Restated By-laws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on December 11, 2020)

4.1	Specimen certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1 filed on February 3, 2014)
4.2	Form of Warrant Agreement, dated as of June 8, 2017, issued to Hercules Technology II, L.P. and Hercules Technology III, L.P. (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on June 12, 2017)
4.3	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on January 28, 2020)
4.4	Description of Capital Stock (incorporated by reference to Exhibit 4.4 to the Registrant's Annual Report on Form 10-K filed on February 27, 2020)
10.1 #	Amended and Restated 2006 Stock Option and Grant Plan, as amended (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 filed on January 13, 2014)
10.2 #	Form of Incentive Stock Option Agreement under 2006 Stock Option and Grant Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 filed on January 13, 2014)
10.3 #	Form of Nonstatutory Stock Option Agreement under 2006 Stock Option and Grant Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 filed on January 13, 2014)
10.4 #	2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1 filed on February 3, 2014)
10.5 #	Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1 filed on February 3, 2014)
10.6 #	Form of Nonstatutory Stock Option Agreement under 2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 filed on February 3, 2014)
10.7 #	Form of Restricted Stock Unit Award Agreement under 2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on July 10, 2017)
10.8 #	Employment Agreement, dated as of October 31, 2018, by and between the Registrant and Roger D. Tung (incorporated by reference to Exhibit 10.8 to the Registrant's Annual Report on Form 10-K filed on February 27, 2020)
10.9 #	Form of Employment Agreement by and between the Registrant and each non-CEO executive officer (incorporated by reference to Exhibit 10.9 to the Registrant's Annual Report on Form 10-K filed on February 27, 2020)
10.10 #	Form of Indemnification Agreement by and between the Registrant and each director and executive officer (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 filed on January 13, 2014)
10.11 #	Summary of Executive Bonus Program (incorporated by reference to Exhibit 10.19 to the Registrant's Registration Statement on Form S-1 filed on January 13, 2014)
10.12 #*	Summary of Non-Employee Director Compensation Program
10.13	Indenture of Lease, dated as of December 21, 2017, by and between the Registrant and HCP/King Hayden Campus LLC (incorporated by reference to Exhibit 10.10 to the Registrant's Annual Report on Form 10-K filed on March 1, 2018)
10.14 †	Development and License Agreement, dated as of February 28, 2012, by and between the Registrant and Avanir Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1 filed on February 3, 2014)

10.15	Asset Purchase Agreement, dated as of March 3, 2017, by and among the Registrant, Vertex Pharmaceuticals (Europe) Limited, as Buyer, and Vertex Pharmaceuticals Incorporated, as Guarantor (incorporated by reference to Exhibit 10.12 to the Registrant's Annual Report on Form 10-K filed on March 6, 2017)
21.1 *	Subsidiaries of the Registrant
23.1 *	Consent of Ernst & Young LLP
31.1 *	Principal Executive Officer-Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2 *	Principal Financial Officer-Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1 **	Principal Executive Officer-Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2 **	Principal Financial Officer-Certification 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.

** Furnished herewith.

Management contract or compensatory plan or arrangement.

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

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, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on February 25, 2021.

CONCERT PHARMACEUTICALS, INC.

By: /s/ Roger D. Tung, Ph.D.
Roger D. Tung, Ph.D.
President and Chief Executive Officer

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

Signature	Title	Date
/s/ Roger D. Tung, Ph.D. Roger D. Tung, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	February 25, 2021
/s/ Marc A. Becker Marc A. Becker	Chief Financial Officer (Principal Financial and Accounting Officer)	February 25, 2021
/s/ Richard H. Aldrich Richard H. Aldrich	Chairman of the Board	February 25, 2021
/s/ Thomas G. Auchincloss, Jr. Thomas G. Auchincloss, Jr.	Director	February 25, 2021
/s/ Ronald W. Barrett, Ph.D. Ronald W. Barrett, Ph.D.	Director	February 25, 2021
/s/ Jesper Høiland Jesper Høiland	Director	February 25, 2021
/s/ Peter Barton Hutt Peter Barton Hutt	Director	February 25, 2021
/s/ Wilfred E. Jaeger, M.D. Wilfred E. Jaeger, M.D.	Director	February 25, 2021
/s/ Christine van Heek Christine van Heek	Director	February 25, 2021

Exhibit 10.12

Summary of Non-Employee Director Compensation Program

The Board of Directors (the "Board") of Concert Pharmaceuticals, Inc. (the "Company") has approved the following non-employee director compensation program.

Each non-employee director will receive a cash retainer for service on the Board and for service on each committee of which the director is a member. The Chairman of the Board and the chair of each committee will receive higher retainers for such service. These fees are payable quarterly in arrears. The fees paid to non-employee directors for service on the Board and for service on each committee of the Board of which the director is a member are as follows:

	Member Annual Retainer	Chair Annual Retainer
Board of Directors	40,000	70,000
Audit Committee	10,000	20,000
Compensation Committee	7,500	15,000
Nominating and Corporate Governance Committee	5,000	10,000

Non-employee directors may elect to receive all or a portion of their cash retainer for the one-year period following each annual meeting of stockholders in the form of a stock option award. The option will be granted on the date of the first Board meeting held after the annual meeting of stockholders that marks the beginning of the one-year period. The number of shares subject to the option will be calculated using the fair value of a share of the Company's common stock on the date of grant. Each of these options will vest in equal quarterly installments over a one-year period measured from the date of the annual meeting of stockholders that marks the beginning of the one-year period, subject to the director's continued service as a director, and will become exercisable in full on the date that is one business day prior to the date of the Company's next annual meeting of stockholders (if earlier than the first anniversary of the annual meeting of stockholders that marks the beginning of the one-year period).

In addition, each new non-employee director elected to the Board will receive an option to purchase 25,000 shares of the Company's common stock. Each of these options will vest in equal quarterly installments over a three-year period measured from the date of grant, subject to the director's continued service as a director, and will become exercisable in full upon a change in control of the Company.

Further, on the date of the first Board meeting held after each annual meeting of stockholders, each non-employee director that has served on the Board for at least six months will receive an option to purchase 10,000 shares of the Company's common stock. Each of these options will vest in equal quarterly installments over a one-year period measured from the date of grant, subject to the director's continued service as a director, and will become exercisable in full

(i) on the date that is one business day prior to the date of the Company's next annual meeting of stockholders (if earlier than the first anniversary of the date of grant) and (ii) upon a change in control of the Company.

The exercise price of all options granted to non-employee directors will equal the closing market price of the Company's common stock on the date of grant.

The Company will also reimburse non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending Board and committee meetings.

Exhibit 21.1

Subsidiaries of the Registrant

Name	Jurisdiction of Organization
Concert Pharmaceuticals Securities Corp.	Massachusetts
Concert Pharma U.K. Ltd	United Kingdom
Concert Pharma Ireland Limited	Ireland

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-223334) of Concert Pharmaceuticals, Inc. and the related Prospectus;

(2) Registration Statement (Form S-3 No. 333-249862) of Concert Pharmaceuticals, Inc. and the related Prospectus;

(3) Registration Statement (Form S-8 No. 333-195125) pertaining to the Amended and Restated 2006 Stock Option and Grant Plan and 2014 Stock Incentive Plan of Concert Pharmaceuticals, Inc.;

(4) Registration Statement (Form S-8 No. 333-202453) pertaining to the 2014 Stock Incentive Plan of Concert Pharmaceuticals, Inc.;

(5) Registration Statement (Form S-8 No. 333-209841) pertaining to the 2014 Stock Incentive Plan of Concert Pharmaceuticals, Inc.;

(6) Registration Statement (Form S-8 No. 333-216459) pertaining to the 2014 Stock Incentive Plan of Concert Pharmaceuticals, Inc.;

(7) Registration Statement (Form S-8 No. 333-223335) pertaining to the 2014 Stock Incentive Plan of Concert Pharmaceuticals, Inc.;

(8) Registration Statement (Form S-8 No. 333-229932) pertaining to the 2014 Stock Incentive Plan of Concert Pharmaceuticals, Inc.; and

(9) Registration Statement (Form S-8 No. 333-236679) pertaining to the 2014 Stock Incentive Plan of Concert Pharmaceuticals, Inc.;

of our report dated February 25, 2021, with respect to the consolidated financial statements of Concert Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Concert Pharmaceuticals, Inc. for the year ended December 31, 2020.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 25, 2021

Exhibit 31.1

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

I, Roger D. Tung, certify that:

1 I have reviewed this Annual Report on Form 10-K of Concert Pharmaceuticals, 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

5 The registrant's other certifying officer(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: February 25, 2021

/s/ Roger D. Tung
Roger D. Tung
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

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

I, Marc A. Becker, certify that:

1 I have reviewed this Annual Report on Form 10-K of Concert Pharmaceuticals, 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

5 The registrant's other certifying officer(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: February 25, 2021

/s/ Marc A. Becker
Marc A. Becker
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of Concert Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Roger D. Tung, President and Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

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

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

Dated: February 25, 2021

/s/ Roger D. Tung
Roger D. Tung
President and Chief Executive Officer
(Principal Executive Officer)

A signed original of this written statement required by Section 906 has been provided to Concert Pharmaceuticals, Inc. and will be retained by Concert Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

Exhibit 32.2

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

In connection with the Annual Report on Form 10-K of Concert Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Marc A. Becker, Chief Financial Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

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

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

Dated: February 25, 2021

/s/ Marc A. Becker
Marc A. Becker
Chief Financial Officer
(Principal Financial Officer)

A signed original of this written statement required by Section 906 has been provided to Concert Pharmaceuticals, Inc. and will be retained by Concert Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.