CONCERT PHARMACEUTICALS, INC.
Form 10-K
March 31, 2014
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended: December 31, 2013

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.)**

99 Hayden Avenue, Suite 500

Lexington, Massachusetts 02421

(Address of principal executive offices) (Zip Code)

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

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

Title of each class	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	**The 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 x

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 x

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 x

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes ¨ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of large accelerated filer, accelerated filer, and smaller reporting

company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer x (Do not check if a smaller reporting company)	Smaller reporting company ¨

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

The aggregate market value of the registrant s common stock, par value $0.001 per share (Common Stock), held by non-affiliates of the registrant, based on the last reported sale price of the Common Stock on the NASDAQ Global Market at the close of business on February 13, 2014, was $167,507,049. The registrant has elected to use February 13, 2014, the initial trading date of the registrant s common stock on the NASDAQ Global Market, as the calculation date because on June 28, 2013 (the last business day of the registrant s most recently completed second fiscal quarter), the registrant was not publicly traded. For purposes hereof, shares of Common Stock held by each executive officer and director of the registrant and entities affiliated with such executive officers and directors have been excluded from the foregoing calculation because such persons and entities may be deemed to be affiliates of the registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares outstanding of the registrant s Common Stock as of March 28, 2014: 17,899,585

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References to Concert

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

Forward-Looking Information

This Annual Report on Form 10-K contains forward-looking statements regarding, among other things, our future discovery and development efforts, our future operating results and financial position, our business strategy, and other objectives for our operations. The words anticipate, believe, estimate, expect, intend, may, plan, predict, would and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. You also can identify forward-looking statements by the fact that they do not relate strictly to historical or current facts. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. These risks and uncertainties include those inherent in pharmaceutical research and development, such as adverse results in our drug discovery and clinical development activities, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates, our ability to obtain any necessary financing to conduct our planned activities and other risk factors. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the section entitled Risk Factors in Part I 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 or investments that we may make. Unless required by law, we do not undertake any obligation to publicly update any forward-looking statements.

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PART 1

ITEM 1. **Business**

OVERVIEW

We are a clinical stage biopharmaceutical company applying our extensive knowledge of deuterium chemistry to discover and develop novel small molecule drugs. Our approach starts with approved drugs, advanced clinical candidates or previously studied compounds that we believe can be improved with deuterium substitution to provide better pharmacokinetic or metabolic properties and thereby enhance clinical safety, tolerability or efficacy. We believe our approach may enable drug discovery and clinical development that is more efficient and less expensive than conventional small molecule drug research and development.

We have a robust pipeline, including three clinical-stage candidates and a number of preclinical compounds that we are actively developing. Our clinical programs are CTP-354 for spasticity associated with multiple sclerosis and spinal cord injury, CTP-499 for diabetic kidney disease and AVP-786 for neurologic and psychiatric disorders under our collaboration with Avanir. We also have ongoing collaborations with Celgene, for deuterated compounds including CTP-730, which is in preclinical development for inflammatory diseases, and with Jazz Pharmaceuticals, for JZP-386, a deuterated analog of sodium oxybate, the active ingredient in its marketed drug Xyrem®, which is in preclinical development for narcolepsy. Between our wholly owned and collaboration programs, we expect to have up to five product candidates in clinical development by the end of 2014, including at least two product candidates in Phase 2 clinical trials.

We believe we are the leader in applying deuterium chemistry in drug discovery and development. Deuterium is similar to hydrogen in size and shape. However, deuterium differs from hydrogen in one pharmaceutically important respect deuterium forms a more stable chemical bond with carbon. This increased stability has the potential, through the selective substitution of deuterium for hydrogen, to improve pharmacokinetic and metabolic properties without changing a compound s intrinsic biological activity. We believe that our application of deuterium chemistry, which we refer to as deuteration, is an efficient way to build on existing knowledge to create important new medicines.

We have built a deuterated chemical entity platform, which we refer to as our DCE Platform®. Our platform comprises the proprietary know-how, techniques and information that we have accumulated since our inception in 2006. Our DCE Platform allows us to efficiently identify compounds for deuteration and to design, evaluate, develop and manufacture deuterated compounds.

In our drug discovery and development processes, we build on the significant existing information regarding the corresponding non-deuterated compound. This allows us to efficiently identify lead compounds and, in some cases, shorten the amount of time necessary to initiate clinical trials as compared to conventional small molecule drug research and development. In clinical development, we believe that the Food and Drug Administration, or FDA, and comparable foreign regulatory authorities may allow some of our compounds that are deuterated analogs of approved products, or of compounds for which approval is pending, to follow an expedited development pathway by relying on previous clinical and preclinical data related to the non-deuterated compound. For example, in June 2013, Avanir reported that the FDA agreed to an expedited development pathway for AVP-786, permitting Avanir to reference data from its development of dextromethorphan and quinidine in its investigational new drug application, or IND, and any future New Drug Application, or NDA, for AVP-786.

We are utilizing our DCE Platform to discover and develop product candidates for a variety of indications. CTP-354, CTP-499 and AVP-786 are advancing in clinical trials and we have multiple preclinical candidates, two of which we expect to move into clinical trials in 2014. Our priority programs include:

CTP-354, a novel, potentially first-in-class, non-sedating treatment for spasticity that we are initially developing for use in patients with multiple sclerosis and patients with spinal cord injury to address a

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significant unmet medical need in these markets. CTP-354 is a subtype selective $GABA_A$ receptor modulator. $GABA_A$ receptors are found in the nervous system and, when activated, reduce the transmission of certain nerve signals. Several classes of widely used drugs target $GABA_A$ receptors, including benzodiazepines and some sleep agents, none of which have the receptor subtype selectivity that we believe CTP-354 possesses. We designed CTP-354 to provide therapeutic benefits without the severe side effects and dosing burden that can limit or prevent the use of existing agents in treating spasticity. For example, the strong sedative effects of benzodiazepines severely limit their therapeutic use in spasticity and certain other indications. We completed a 71-subject Phase 1 single ascending dose clinical trial of CTP-354 and the nine-subject first part of a related Phase 1 imaging study. The results from our Phase 1 single ascending dose trial indicate that CTP-354 has a favorable pharmacokinetic profile that supports once-daily dosing. The results also indicate that CTP-354 did not cause sedation at levels of $GABA_A$ receptor occupancy well above the levels achieved by benzodiazepines at doses that are typically prescribed. $GABA_A$ receptor occupancy is a measure of the extent to which CTP-354 binds to $GABA_A$ receptors that we believe may correlate to therapeutic activity. In January 2014, we initiated a multiple ascending dose Phase 1 clinical trial evaluating daily doses of 2 mg and 6 mg of CTP-354 in healthy volunteers and we expect to report top line results in the second half of 2014. Assuming successful completion of the multiple ascending dose Phase 1 clinical trial, we plan to initiate a Phase 2 clinical program for CTP-354 in the second half of 2014. We expect that the Phase 2 clinical program will include one clinical trial for the treatment of spasticity associated with multiple sclerosis and one clinical trial for the treatment of spasticity associated with spinal cord injury. Due to the fact that we did not determine a maximum tolerated dose in our preclinical testing, the FDA has informed us that we may not administer multiple doses of CTP-354 in excess of 6 mg per day in clinical trials without first conducting an additional higher dose preclinical toxicology study. We believe that multiple doses of 6 mg per day would be sufficient for the treatment of spasticity; however we initiated an additional preclinical toxicology study to enable us to evaluate higher doses of CTP-354, if needed in our spasticity trials, as well as to support clinical development in other disease indications.

CTP-499, a novel oral multi-subtype selective inhibitor of phosphodiesterases, or PDEs, which are enzymes that we believe play an important role in type 2 diabetic kidney disease. According to a 2009 article in the American Diabetes Association journal *Diabetes Care*, type 2 diabetes is the leading cause of chronic kidney disease. Type 2 diabetic kidney disease can result in the need for dialysis and renal transplantation. Many patients with this disease continue to experience a decline in renal function despite treatment with standard of care therapies. We are developing CTP-499 as an additive treatment to the current standard of care to further slow progression towards kidney failure. We are currently conducting a three-part Phase 2 clinical trial of CTP-499 in which we have enrolled patients with type 2 diabetic kidney disease and macroalbuminuria. In 2013, we completed the first part of this trial, a 24-week, double-blind, parallel, two-arm, placebo-controlled study in 182 patients. We have also completed dosing in the second part of the trial, a blinded 24-week extension study, which, combined with the data from the first part of the trial, has provided 48 weeks of placebo-controlled data in 123 patients. We did not achieve statistical significance in the primary efficacy endpoint of this trial, which was measured at 24 weeks. However, we believe that the data we have analyzed to date from the first 48 weeks of treatment support the potential of CTP-499 to help protect kidney function in patients with rapidly progressing type 2 diabetic kidney disease. We have conducted preliminary analyses of these 48 weeks of data, but have not yet completed a full analysis. We expect to report the final results for the first 48 weeks of the trial in the second quarter of 2014.

AVP-786, a combination of a deuterium-substituted dextromethorphan analog and an ultra-low dose of quinidine. We have granted Avanir Pharmaceuticals, Inc., or Avanir, an exclusive license to develop and commercialize

deuterated dextromethorphan analogs, including the analog in AVP-786. Avanir is developing AVP-786 for the treatment of neurologic and psychiatric disorders. In February 2013, Avanir reported positive results from a Phase 1 clinical trial of AVP-786. In October 2013, Avanir reported plans to advance AVP-786 into a Phase 2 clinical trial in the second half of 2014 for treatment-resistant major depressive disorder in patients with insufficient response to conventional anti-depressants.

A collaboration with Celgene Corporation and Celgene International Sàrl, which we collectively refer to as Celgene, to research, develop and commercialize certain deuterated compounds for the treatment of cancer

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or inflammation, with an initial focus on a single program. In the initial program, we have selected CTP-730, a product candidate for the treatment of inflammatory diseases, and expect to begin Phase 1 clinical trials in 2014.

A collaboration with Jazz Pharmaceuticals Ireland Limited, or Jazz Pharmaceuticals, to research, develop and commercialize JZP-386, a product candidate containing a deuterated analog of sodium oxybate for potential use in patients with narcolepsy. Sodium oxybate is the active ingredient in the marketed drug Xyrem. In December 2013, an investigational medicinal product dossier, or IMPD, the basis for initiating clinical trials in the European Union, was filed for JZP-386. The IMPD received approval in January 2014. Jazz Pharmaceuticals expects a Phase 1 clinical trial of JZP-386 to be conducted in 2014, following manufacturing of clinical material.

Through December 31, 2013, we had received an aggregate of $106.0 million in upfront and milestone payments, equity investments and research and development funding from current and former collaborations. Under our current collaborations, we have the potential to receive up to $1.6 billion in future milestone payments, including over $1.2 billion in research, development and regulatory milestones, as well as royalties on any future net product sales.

On February 19, 2014, we completed the sale of 6,000,000 shares of common stock in our initial public offering, or IPO, at a price to the public of $14.00 per share, resulting in net proceeds to us of $74.6 million after deducting underwriting discounts and commissions of $5.9 million and offering costs of $3.5 million. On March 3, 2014, we completed the sale of an additional 649,690 shares of common stock at a price to the public of $14.00 per share under the underwriters over-allotment option to purchase additional shares of common stock, resulting in net proceeds to us of $8.5 million after deducting underwriting discounts and commissions.

Our senior management team has extensive experience in drug discovery and development. Collectively, our team has been involved in the research, development or approval of 12 drugs. Dr. Roger D. Tung, our Chief Executive Officer and one of our founders, is an accomplished leader in drug research and development. Prior to founding our company, Dr. Tung was the Vice President of Drug Discovery at Vertex Pharmaceuticals, Inc. At Vertex, he was a co-inventor of two drugs that were approved for the treatment of HIV, amprenavir and fosamprenavir, and oversaw the discovery of two other approved drugs, ivacaftor (Kalydeco®) for cystic fibrosis and telaprevir (Incivek®) for hepatitis C. Dr. Tung conceptualized our DCE Platform approach as a means to accelerate pharmaceutical research and development and create important new medicines. He has invented or co-invented many of the compounds in our pipeline.

OUR STRATEGY

Our strategy is to apply our extensive knowledge of deuterium chemistry to discover, develop and commercialize novel small molecule drugs. Key components of our strategy include:

Rapidly advancing our deuterated product candidates. We seek to reduce the time and cost associated with conventional small molecule drug research and development by capitalizing on the known activity, safety, efficacy or development history of the non-deuterated analogs of our product candidates. Leveraging this knowledge, we have been able in a number of our programs, including CTP-499, to advance compounds from initial synthesis to clinical evaluation in less than two years. We also seek to develop product candidates that may be eligible for an expedited development or regulatory pathway, such as reported by Avanir for AVP-786.

Establishing collaborations to develop and commercialize deuterated product candidates. Our current collaborations are focused on deuterated analogs of one or more of our collaborators proprietary compounds. In these situations, we benefit from our collaborators knowledge and experience with, and rights of reference to regulatory filings for, their corresponding non-deuterated compounds. We may establish similar collaborations in the future and also plan to enter into other collaborations to access the resources of larger biopharmaceutical companies.

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Capitalizing on our DCE Platform to build a robust pipeline of additional deuterated product candidates. Our DCE Platform consists of the proprietary know-how, techniques and information that we have developed over the past seven years. We broadly apply our DCE Platform to approved drugs, advanced clinical candidates or previously studied compounds. We particularly look to initiate development programs in areas of significant medical need and commercial opportunity. We believe we are capable of identifying one to two novel deuterated compounds per year that we can advance into preclinical development while concurrently progressing our existing pipeline.

Retaining commercialization rights on a selective basis and building a specialized commercialization capability in the United States. 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. For 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 other parties for commercialization outside the United States.

Expanding our broad patent estate covering deuterated compounds and related technology. Since our inception in 2006, we have systematically sought, and continue to seek, to identify compounds that can be improved through selective deuterium substitution and to obtain patent protection for deuterated analogs of these compounds with the goal of establishing a broad proprietary position in this field. We hold issued U.S. patents covering the composition of matter of each of our most advanced product candidates. In addition, we own issued patents or patent applications that claim the deuterated analogs of more than 90 non-deuterated compounds.

DEUTERIUM: IMPLICATIONS FOR DRUG RESEARCH AND DEVELOPMENT

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 toxic metabolites, increased formation of desired active metabolites, or a combination of these effects. At the same time, because deuterium closely resembles hydrogen, the substitution of deuterium for hydrogen has generally been found not to materially alter the intrinsic biological activity of a compound.

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Deuterated compounds 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.

OUR DCE PLATFORM

Our DCE Platform consists of the proprietary know-how, techniques and information that we have developed over the past seven years. Deuterated compounds can have an increased half-life in the body and increased systemic exposure as compared to their corresponding non-deuterated analogs, which we believe can lead to benefits such as improved safety, efficacy, tolerability and convenience. Due to our significant experience in deuterium chemistry and pharmaceutical research and development, we believe we are well-positioned to efficiently identify compounds that can benefit from deuterium substitution and create optimally deuterated product candidates.

We believe that our DCE Platform can enable drug discovery and clinical development that is more efficient and less expensive than conventional small molecule drug research and development. Conventional drug discovery and development are lengthy processes with high failure rates. Relatively few molecules identified in drug discovery possess the beneficial pharmacological activity and acceptable tolerability and toxicity required to become clinically useful medicines that address commercially important needs. We believe that our product candidates may have a higher likelihood of becoming useful medicines because we selectively deuterate molecules that are already known to be pharmacologically active *in vivo* and have either been studied in humans or are closely chemically related to such molecules. We believe that our likelihood of success may be even greater in cases in which we have selectively deuterated analogs of approved drugs.

Our DCE Platform includes the following capabilities, which we believe provide us with key competitive advantages:

Selection of attractive compounds for deuteration. We identify candidate compounds for selective deuteration through the efforts of a team that integrates chemistry, biology, medical, regulatory, intellectual property and commercial expertise. We believe our ability to choose appropriate candidate molecules for selective deuteration is an important competitive advantage. We apply our experience and know-how to identify approved drugs, advanced clinical candidates or previously studied compounds that we believe can be improved with deuterium substitution to provide better pharmacokinetic or metabolic properties and thereby enhance clinical safety, tolerability or efficacy. We prioritize candidate compounds based on medical need, commercial opportunity, competitive and patent landscapes and internal strategic fit. We believe that we are capable of identifying one to two novel deuterated compounds per year that we can advance into preclinical development while concurrently progressing our existing pipeline.

Medicinal chemistry and chemical and biological testing of deuterated compounds. We have developed significant proprietary know-how in the design, synthesis, chemical analysis, bioanalytical assessment, preclinical evaluation and clinical development of deuterated compounds. Our know-how includes the ability to:

- synthesize a wide range of chemical compounds that incorporate deuterium selectively at specific positions and accurately analyze deuterium content at those positions;

- identify, through an efficient, iterative process, the deuterated compounds that possess improved *in vitro* or *in vivo* metabolic or pharmacokinetic properties relative to the corresponding non-deuterated compound;

develop and apply bioanalytical methods to identify and measure metabolites formed by the *in vitro* and *in vivo* metabolism of deuterated compounds; and

understand how the effects of selective deuterium substitution may translate from *in vitro* to *in vivo* systems and from non-human models to humans.

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Manufacturing of deuterated compounds. By applying our manufacturing and analytical know-how and capabilities, we are able to reproducibly manufacture deuterated compounds. Our manufacturing capabilities include the ability to:

- manufacture, analyze and formulate deuterated compounds that can be used in early stage clinical trials;
- manufacture low kilogram quantities of deuterated active pharmaceutical ingredients and product candidates suitable for early stage clinical trials;
- transfer our methods to manufacturing vendors that can produce multi-kilogram quantities of clinical trial materials; and
- utilize a supply chain that we have built with multiple vendors that can provide deuterium reagents and intermediates in commercial scale quantities.

Development opportunities using our DCE Platform

We apply our DCE Platform to create deuterated analogs of:

- marketed drugs for their approved indications or compounds in clinical development for their targeted indications;
- marketed drugs for non-approved indications or compounds in clinical development for indications that were not previously targeted; and
- previously studied compounds, or close analogs thereof, that were not, or are no longer being, developed.

Potential advantages of product candidates based on our DCE Platform

We apply our DCE Platform to systematically identify approved drugs, advanced clinical candidates or previously studied compounds for which we believe we can improve or create clinical benefit through deuterium substitution. Potential advantages of our selective deuteration include:

- *Improved metabolic profile.* We have selectively deuterated compounds and compounds produced by metabolism of other compounds, which are called metabolites, to improve their metabolic profiles by reducing the formation of toxic or reactive metabolites or by increasing the formation of desired, active metabolites relative to the corresponding non-deuterated compound. The improved metabolic profile may potentially reduce or eliminate unwanted side effects or undesirable drug interactions. For example, Avanir has reported that, compared to dextromethorphan, the deuterated dextromethorphan in AVP-786 required less quinidine, a metabolic inhibitor, to achieve desired clinical blood levels in a Phase 1 clinical trial.

Improved oral bioavailability. We have selectively deuterated compounds to reduce the extent of undesired metabolism in the wall of the intestines and in the liver, referred to as first-pass metabolism. This resulted in a larger percentage of unmetabolized drug reaching the target site of action. Deuterated compounds with improved bioavailability may be active at lower doses. For example, CTP-354 achieved substantially higher blood levels in *in vivo* preclinical tests than did the corresponding non-deuterated compound at an equivalent dose.

Increased half-life. We have selectively deuterated compounds to prolong their pharamacokinetic profile, which is an increase in the half-life of the compound in the body. This 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. For example, in preclinical *in vivo* testing, JZP-386 demonstrated a prolonged pharmacokinetic profile and reduced variability relative to sodium oxybate.

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Potential for expedited discovery and development of deuterated product candidates

We believe our approach of applying selective deuteration using our DCE Platform has the potential to provide a more efficient and less expensive approach to developing new chemical entity drugs as compared to conventional small molecule drug research and development. Key reasons include:

By building on the known activity, safety or efficacy of approved drugs, advanced clinical candidates or previously studied compounds, we believe we can progress our product candidates through discovery and into clinical development more quickly than in conventional small molecule drug research and development. In a number of cases, including CTP-499, we have advanced compounds from initial synthesis to clinical evaluation in less than two years.

We believe the FDA and comparable foreign regulatory authorities may allow some of our compounds that are deuterated analogs of approved products, or of compounds for which approval is pending, to follow an expedited development pathway by relying on previous clinical data regarding the corresponding non-deuterated compound. For example, our collaborator Avanir reported agreeing with the FDA to an expedited development pathway for AVP-786 that would permit Avanir to reference data from its development of dextromethorphan and quinidine in its IND, and any future NDA, for AVP-786.

OUR PRODUCT CANDIDATES

The following table summarizes key information about our priority programs. All of these product candidates are small molecules designed for oral administration.

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CTP-354

Overview

CTP-354 is a novel, potentially first-in-class, non-sedating treatment for spasticity that we are initially developing for use in patients with multiple sclerosis and patients with spinal cord injury. CTP-354 is a subtype selective $GABA_A$ receptor modulator. $GABA_A$ receptors are found in the nervous system and, when activated, reduce the transmission of certain nerve signals.

$GABA_A$ receptors can possess one of a number of a subunits, including a1, a2, a3 and a5. The pharmacological effects of activating a $GABA_A$ receptor in the nervous system are believed to depend mainly on which type of a subunit the receptor contains. Several classes of widely used drugs target $GABA_A$ receptors, including benzodiazepines such as diazepam (Valium). Benzodiazepines are used for the treatment of anxiety, spasticity, muscle tension, insomnia, acute alcohol withdrawal and seizures. Activation of a1 $GABA_A$ receptors is believed to be mainly responsible for sedation and ataxia, which is a lack of muscle control during voluntary movements, associated with benzodiazepine use, and may also contribute to their amnesiac and habituating effects. Activation of a2, a3 and a5 $GABA_A$ receptors is believed to cause other therapeutic effects of benzodiazepines, including anti-spasticity, muscle relaxation, anti-anxiety, anti-seizure and potentially anti-pain activities. Some sleep agents, such as zolpidem (Ambien®) and zaleplon (Sonata®), also target $GABA_A$ receptors, but activate a1 $GABA_A$ receptors significantly more potently than the other a subtypes, which is believed to cause their pronounced sedative properties. Based on this clinical precedent as well as a variety of preclinical models, we believe that a compound that activates a2, a3 and a5 $GABA_A$ receptors but does not significantly activate a1 $GABA_A$ receptors will have clinical effects similar in a number of important respects to benzodiazepines, including anti-spasticity, muscle relaxant, anti-seizure and potentially anti-pain effects, but without the strong sedative effects of benzodiazepines.

We submitted an IND to the FDA in January 2013 for the development of CTP-354 for spasticity in patients with multiple sclerosis or spinal cord injury. We have completed a single ascending dose Phase 1 clinical trial to evaluate the safety, tolerability and pharmacokinetics of CTP-354 in healthy volunteers. We have also conducted a Phase 1 positron emission tomography, or PET, imaging study to assess the brain $GABA_A$ receptor occupancy of CTP-354 following a single dose of the compound in healthy volunteers.

In January 2014, we initiated a multiple ascending dose Phase 1 clinical trial evaluating daily doses of 2 mg and 6 mg of CTP-354 in healthy volunteers. Assuming successful completion of the multiple ascending dose Phase 1 clinical trial, we plan to initiate a Phase 2 clinical program for CTP-354 in the second half of 2014. We expect that the Phase 2 clinical program will include one clinical trial for the treatment of spasticity associated with multiple sclerosis and one clinical trial for the treatment of spasticity associated with spinal cord injury. In our previous preclinical testing, minimal, if any, toxicity was observed for CTP-354, and a maximum feasible dose or a maximum tolerated dose was not determined. As a result, the FDA has informed us that we may not administer multiple doses of CTP-354 in excess of 6 mg per day in clinical trials without first conducting an additional higher dose preclinical toxicology study. We believe that multiple doses of 6 mg per day would be sufficient for the treatment of spasticity; however, we initiated an additional preclinical toxicology study to enable us to evaluate higher doses of CTP-354, if needed in our spasticity trials, as well as to support clinical development in other disease indications. Based on the well-known efficacy of benzodiazepines and other $GABA_A$ modulators, we believe CTP-354 has potential in a number of other indications, including anxiety, chronic pain, muscle tension and epilepsy.

Background

CTP-354 is a deuterated analog of a compound discovered by Merck & Co. referred to as L-838417. L-838417 was found in preclinical animal studies to possess certain therapeutic benefits of the benzodiazepine class of drugs, but without their predominantly sedative effect. Merck reported that, in *in vitro* testing, L-838417 activated the a2, a3 and a5 $GABA_A$ receptors, which are associated with anti-spasticity, muscle relaxation, anti-anxiety, anti-seizure and, potentially, anti-pain activities, with approximately 40% of the *in vitro* activity of a

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benzodiazepine, with no significant activity at the a1 $GABA_A$ receptors. Moreover, in a number of *in vivo* animal studies, L-838417 provided potent muscle relaxant, anti-anxiety, anti-convulsant and anti-pain activity, without causing apparent sedation or ataxia. In preclinical animal testing, Merck identified pharmacokinetic limitations of L-838417 relating to bioavailability and variability and did not progress the compound into clinical development. We designed CTP-354 to overcome the pharmacokinetic limitations of L-838417 while retaining its attractive pharmacological profile.

Spasticity

Spasticity is a chronic condition characterized by involuntary tightness, stiffness or contraction of muscles that occurs in patients who have damage to the brain or spinal cord. Spasticity can result from a wide range of disorders, including multiple sclerosis, spinal cord injury, cerebral palsy, amyotrophic lateral sclerosis, stroke and hereditary spastic paraplegia. Symptoms can range from mild muscle tightness to more severe symptoms, including crippling and painful inability to move limbs that can result in disability and diminished quality of life. The American Association of Neurological Surgeons estimated in 2006 that there were 12 million patients suffering from spasticity worldwide.

Market

Spasticity in Multiple Sclerosis. Multiple sclerosis is the most common disabling neurological condition affecting young adults, typically developing between the ages of 20 to 40 years. According to a 2008 World Health Organization report, multiple sclerosis affects more than 1.3 million people worldwide, including an estimated 400,000 people in the United States. Spasticity is one of the more common symptoms of multiple sclerosis and can be among the most painful, damaging and debilitating symptoms of multiple sclerosis. According to American Association of Neurological Surgeons, about 80% of people with multiple sclerosis suffer from some degree of spasticity. Of the estimated 400,000 patients diagnosed with multiple sclerosis in the United States, we estimate that at least 34%, or 140,000 patients, suffer from moderate to severe spasticity that impacts daily function in a meaningful way. Spasticity in multiple sclerosis may be as mild as the feeling of tightness of muscles or may be so severe as to produce painful, uncontrollable spasms of extremities, usually of the legs. Spasticity may also produce pain or tightness in and around joints, and can cause low back pain. Although spasticity in multiple sclerosis can occur in the arms and legs, it is much more common in the legs.

Spasticity in Spinal Cord Injury. Spasticity is a significant health issue for many people with spinal cord injury. According to the National Spinal Cord Injury Statistics Center, in 2012, there were approximately 270,000 people in the United States suffering from spinal cord injury with approximately 12,000 new incidences per year. According to a 2011 report of the University of Washington Model Systems Knowledge Translation Center, 65% to 78% of spinal cord injury patients experience some degree of spasticity. Based on articles published in Archives of Physical Medicine and Rehabilitation in 1990 and 1999, we estimate that 28% to 46% of spinal cord injury patients suffer from problematic spasticity that could result in treatment. The most common muscles to be affected by spasticity in connection with spinal cord injury are the flexors, muscles that contract joints such as hips, knees or elbows, or the extensors, muscles that extend such joints. Spasms can occur as an automatic response to painful sensations.

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Limitations of Current Treatments

Spasticity is typically treated with a combination of pharmacotherapy, physical therapy, occupational therapy and, in some severe cases, surgical intervention to sever affected nerves or muscles. The available pharmaceutical treatments for spasticity are frequently limited by either inadequate relief of symptoms or dose-limiting side effects, such as sedation, and based on a 2009 report of WE MOVE, a not-for-profit organization dedicated to improving awareness of movement disorders, we estimate that over 40% of people with spasticity are not satisfied with the management of their disorder or the state of their overall health. First-line treatments for adult use in the United States typically include:

- Oral baclofen, the most commonly prescribed agent for spasticity, which is approved by the FDA for treatment of spasticity resulting from multiple sclerosis and spinal cord injury or spinal cord disease. It is also used extensively, although not approved, for treatment of spasticity in post-stroke and cerebral palsy patients. Baclofen has dose-limiting side effects, including drowsiness, dizziness and ataxia. Sedation resulting from baclofen is particularly problematic and many patients are maintained on sub-therapeutic doses due to lack of more attractive options. In addition, baclofen has a short half-life in the body and, as a result, it is typically dosed three times a day, which is an inconvenience for patients. Moreover, baclofen can result in severe withdrawal symptoms if abruptly discontinued, including hallucinations, seizures and rebound spasticity.

- Tizanidine, which is approved by the FDA for the general management of spasticity. Oral tizanidine is marketed as Zanaflex®. Tizanidine can be highly sedating, has a short half-life in the body and is not as widely used as baclofen for the treatment of spasticity. It is typically reserved for daily activities and times when relief of spasticity is most important. Use of tizanidine can also result in liver injury and the recommended monitoring of liver function imposes a burden on both the patient and the physician.

- Injected botulinum toxin, which is approved by the FDA for treatment of upper limb spasticity in adults, among other indications. Botulinum toxin, which is marketed as Botox®, is also used, although not approved for, treatment of children with cerebral palsy. It is currently in Phase 3 trials for that indication. Botulinum toxin can be very effective for treatment of spasticity in small muscle groups and localized injections of botulinum toxin are commonly used to treat spasticity as a monotherapy or in combination with other therapies. However, more extensive injections of botulinum toxin can result in systemic toxicity that is characterized by swallowing and breathing difficulties that can lead to death.

Other less commonly used treatments include:

- Diazepam, which is approved by the FDA as an oral agent for the treatment of spasticity related to upper motor neuron disorders, including cerebral palsy and paraplegia. Diazepam is marketed as Valium. Diazepam is a benzodiazepine and, like other benzodiazepines, its therapeutic efficacy is limited by side effects and concerns about abuse potential. The most commonly reported side effects of diazepam are drowsiness, fatigue, muscle weakness and ataxia. As a result of these side effects, use of diazepam for the treatment of spasticity is typically reserved for use in small doses at night for patients who have difficulty sleeping.

Dantrolene, which is approved by the FDA as an oral agent for the treatment of spasticity resulting from upper motor neuron disorders such as spinal cord injury, stroke, cerebral palsy or multiple sclerosis, but which is rarely used as it causes severe muscle weakness and can cause liver damage.

Abdominal implantation of a pump that injects baclofen around the spinal cord, referred to as intrathecal administration. Intrathecal administration of baclofen can provide effective relief of spasticity, particularly in lower limbs, but its use is limited by its invasiveness and potentially dangerous complications resulting from spinal fluid leaks, hemorrhage, infection, catheter dislodgement or blockage and pump failure. Abrupt discontinuation, whether as a result of catheter dislodgement, pump failure or another cause, can result in high fever, altered mental status, exaggerated rebound spasticity and, in rare cases, multiple organ-system failure and death.

Surgical intervention, to sever sensory nerves or, more rarely, muscles. The use of surgical intervention is limited due its invasiveness and irreversibility.

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Potential Advantages of CTP-354 for Spasticity

We believe that CTP-354 has the potential to provide therapeutic benefits without the limitations of existing spasticity therapies, which can include severe sedative effects, toxicity, frequent dosing or invasiveness. In our Phase 1 clinical trials, CTP-354 demonstrated highly favorable pharmacokinetics with low variability, dose-proportional exposure, a long half-life in the body and high levels of $GABA_A$ receptor occupancy. We believe these results support once-daily dosing, which would provide a substantial improvement on the three-times-daily dosing required by current standard-of-care oral spasticity medicines. In our Phase 1 clinical trials, CTP-354 provided much higher levels of $GABA_A$ receptor occupancy without causing sedation than benzodiazepines at doses that are typically prescribed, which we believe supports the potential of CTP-354 to be a non-sedating treatment for spasticity.

CTP-354 Clinical Development

Phase 1 Single Ascending Dose Clinical Trial. In August 2013, we completed a randomized, double-blind, placebo-controlled, single ascending dose Phase 1 clinical trial in 71 healthy adult volunteers at a single center in the United States to assess the safety, tolerability and pharmacokinetics of CTP-354. Volunteers were randomized to receive CTP-354 or placebo in a three to one ratio with eight cohorts of eight volunteers each and one cohort of seven volunteers. Six volunteers in each cohort received a single dose of CTP-354 and the remaining subjects received placebo. Doses were administered in oral liquid suspensions ranging from 0.15 mg up to 60 mg.

In the clinical trial, CTP-354 was generally well-tolerated up to 60 mg, the highest dose tested. We did not test higher doses after our concurrently conducted Phase 1 imaging study indicated that high levels of $GABA_A$ receptor occupancy could be achieved at doses lower than 60 mg.

Pharmacokinetic data from our single ascending dose trial indicated that CTP-354 was well-absorbed with low inter-subject variability and a long plasma half-life, potentially supporting once-daily dosing of the compound. The following graph shows the mean plasma concentration over time following administration of single ascending doses of CTP-354 in the six subjects in each cohort of the trial who received CTP-354. As illustrated in the graph, doses of CTP-354 of 20 mg and higher resulted in plasma concentrations in excess of 100 ng/mL, maintained for 24 hours following dosing. Our Phase 1 imaging study indicated that these plasma concentrations corresponded to brain $GABA_A$ receptor occupancy of greater than 50%. We believe that the high $GABA_A$ receptor occupancy of CTP-354 at well-tolerated doses supports its potential as a non-sedating oral treatment for spasticity.

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CTP-354 Mean Plasma Concentration vs. Time

CTP-354 was generally well-tolerated in our Phase 1 single ascending dose trial. No serious adverse events were reported in the trial. The most common adverse events observed in the trial were:

- dizziness, which was experienced by nine of the 54 subjects treated with CTP-354;
- drowsiness, which was experienced by seven of the 54 subjects treated with CTP-354;
- prolonged QTc, an indicator of potential cardiac arrhythmias, which was experienced by four of the 54 subjects treated with CTP-354; and
- pain or muscle tightness, which was experienced by three of the 54 subjects treated with CTP-354 and two of the 17 subjects receiving placebo.

Neurologic adverse effects were more common at higher doses of CTP-354, particularly 40 mg and 60 mg, whereas prolonged QTc and muscular adverse effects did not appear to be dose-dependent. In the clinical judgments of the principal study investigator and an independent medical monitor, no incident of QTc prolongation was considered to have posed a health risk to the subjects in the trial. All adverse events were considered mild with the exception of two incidents of dizziness and drowsiness in the 40 mg group, and one incident of nausea in the 60 mg group, each of which was considered moderate. Each incident of muscular pain or tightness with CTP-354 occurred at least one day after dosing.

Phase 1 Imaging Study. We are currently conducting a Phase 1 imaging clinical trial using PET scanning to measure the extent to which CTP-354 binds to $GABA_A$ receptors in the brain in healthy adult volunteers. For the first part of this imaging study, we evaluated single doses of CTP-354 of 4 mg, 20 mg, 40 mg and 60 mg in a total of nine healthy volunteers. We selected these doses because they did not produce dose-limiting side effects in our single ascending dose clinical trial and with the goal of providing a wide range of $GABA_A$ receptor occupancy. Our objectives in this study were to assess whether CTP-354 could provide similar or higher brain $GABA_A$ receptor occupancy levels than those typically provided by benzodiazepines at doses that do not cause dose-limiting sedation; and to compare the relationship between CTP-354 plasma levels and $GABA_A$ brain receptor occupancy.

In the first part of the imaging study, we observed average $GABA_A$ receptor occupancies of between 34% and 82% in subjects five hours after subjects received a single dose of either 4 mg, 20 mg, 40 mg or 60 mg of CTP-354. For each subject, we conducted a baseline scan in which a small amount of flumazenil, a radiolabeled, positron emitting benzodiazepine, was injected intravenously and the brain was subsequently imaged to show

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flumazenil binding to the $GABA_A$ receptors. The subject was given a single oral dose of CTP-354 within two weeks of the baseline scan. Five hours after CTP-354 dosing, the subject received another injection of radiolabeled flumazenil and the imaging was repeated to provide a second scan. Twenty-four hours after CTP-354 dosing, the subject received another injection of radiolabeled flumazenil and the imaging was repeated to provide a third scan.

The images below were obtained from the two subjects who received a single 20 mg dose of CTP-354. In the images:

- the baseline, or first, scans appear bright due to the presence of radiolabeled flumazenil bound to the $GABA_A$ receptors;
- the second and third scans are not as bright as the first scan due to the binding of CTP-354 to the subjects $GABA_A$ brain receptors, which prevents the radiolabeled flumazenil from binding; and
- the third scan is somewhat brighter than the second scan, showing that less CTP-354 is bound to the $GABA_A$ receptors after 24 hours than after five hours.

Phase 1 Imaging Study: 20 mg of CTP-354

The scans we obtained from the seven other subjects in the first part of the imaging study were consistent with these scans from the subjects receiving the 20 mg dose, with $GABA_A$ receptor occupancy levels increasing with dosing levels between 4 mg and 40 mg, but appearing not to increase significantly between 40 mg and 60 mg.

In the first part of the imaging study, we obtained quantitative measures of $GABA_A$ receptor occupancy for the single doses of CTP-354 that were administered. A single 20 mg dose of CTP-354, a dose at which no sedative or other adverse events were reported in the study, provided $GABA_A$ receptor occupancy levels, at both five hours and 24 hours following dosing, substantially in excess of the 10% to 25% occupancy levels at which benzodiazepines and $GABA_A$ receptor-binding sleep drugs become highly sedative.

The table below shows the average $GABA_A$ receptor occupancy at five hours and 24 hours after dosing in the first part of the imaging study.

CTP-354 Dose	Number of Subjects	Average $GABA_A$ Receptor Occupancy at 5 Hours After Dosing	Average $GABA_A$ Receptor Occupancy at 24 Hours After Dosing
4 mg	2	34%	13%
20 mg	2	63%	60%
40 mg	3	79%(1)	71%
60 mg	2	82%	76%

(1) Reflects data from two of the three subjects. We could not calculate $GABA_A$ receptor occupancy at five hours for the first subject due to a computer error.

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The graph below shows the relationship between plasma concentration and brain $GABA_A$ receptor occupancy for CTP-354 in the first part of the imaging study. The 17 data points on the graph below each represent a single reading in a single subject. These include two readings for each subject, one at five hours and one at 24 hours following dosing, with the exception of one subject for whom we could not calculate $GABA_A$ receptor occupancy at five hours due to a computer error. The graph below shows how $GABA_A$ receptor occupancy increases with increasing plasma concentration. As illustrated in the graph, we observed that plasma concentrations in excess of 100 ng/mL correlated with $GABA_A$ receptor occupancies greater than 50%.

CTP-354 $GABA_A$ Receptor Occupancy vs. Plasma Concentration in Healthy Volunteers

In the Phase 1 imaging study, no drug related adverse events were reported in volunteers receiving 4 mg or 20 mg of CTP-354. At 40 mg, two of three subjects reported mild to moderate dizziness, mild drowsiness and nausea and one subject each reported mild euphoria, loss of balance and lightheadedness. At 60 mg, adverse events included sedation and ataxia, both mild in one subject and both moderate in the other. One subject receiving 60 mg of CTP-354 reported mild lightheadedness, restlessness and irritability and the other reported mild dizziness. All adverse effects had resolved by the following day.

Based on clinical studies of diazepam and other benzodiazepines, we believe that the high and sustained brain $GABA_A$ receptor occupancy levels achieved by CTP-354, at doses that were well-tolerated in our Phase 1 clinical trials, provide evidence of its therapeutic potential. For instance, in our Phase 1 imaging study, a single 20 mg dose of CTP-354 did not cause sedation or ataxia while producing $GABA_A$ receptor occupancy of greater than 50% sustained for 24 hours, which is much higher than the receptor occupancies at which benzodiazepines typically cause sedation. Therefore, we believe that CTP-354 may provide clinical benefit against spasticity similar to that of benzodiazepines without the dose-limiting effects of benzodiazepines. However, while the data we have obtained to date in our Phase 1 imaging study have generally been consistent, due to the relatively small scale of the study we cannot be certain that these data are representative of the data that would be obtained from a larger-scale clinical trial.

We plan to conduct the second part of this Phase 1 imaging study during the first half of 2014 to evaluate $GABA_A$ receptor occupancy after repeated dosing of CTP-354. We expect that repeated dosing will enable us to determine $GABA_A$ receptor occupancy levels after CTP-354 plasma levels are at steady state. We expect that this imaging study will support selection of therapeutically relevant doses for Phase 2 clinical trials.

Partial Clinical Hold

In November 2013, we received notice from the FDA of a partial clinical hold on CTP-354 that prevents us from administering single doses in excess of 60 mg per day and multiple doses in excess of 6 mg per day. In January

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2014, we initiated a multiple ascending dose Phase 1 clinical trial evaluating daily doses of 2 mg and 6 mg of CTP-354 in healthy volunteers. We do not intend to conduct single dose clinical trials of CTP-354 with doses in excess of 60 mg.

In our previous preclinical testing, CTP-354 was associated with minimal, if any, toxicity. However, the FDA notice stated that, since a maximum tolerated dose was not achieved in those studies, preclinical testing at doses higher than those tested in our preclinical studies to date would be needed before we can clinically evaluate multiple doses that exceed 6 mg per day. In December 2013, we had a phone conference with the FDA to discuss the partial clinical hold notice. During the phone conference, the FDA confirmed that we could dose CTP-354 up to 6 mg per day in multiple doses for 28 days. They also stated that to administer CTP-354 in a Phase 2 clinical trial at multiple doses greater than 6 mg per day, the required additional testing could be conducted in only one animal species to determine a maximum tolerated dose or a maximum feasible dose. We estimate that administration of 6 mg per day of CTP-354 in multiple doses may provide brain $GABA_A$ receptor occupancy of about 60%, which is significantly higher than that achieved by typical clinical doses of benzodiazepines. Based on this estimated receptor occupancy level, we believe that multiple doses of 6 mg per day would be sufficient for the treatment of spasticity, the first indication for which we plan to conduct clinical trials. However, we have initiated the additional preclinical toxicology study to enable us to evaluate higher doses of CTP-354, if needed in our spasticity trials, as well as to support clinical development in other disease indications. Based on our dialog with the FDA, we do not believe that the partial clinical hold will affect the timelines of our previously planned Phase 2 clinical trials of CTP-354.

Additional Phase 1 Clinical Trial

In January 2014, we commenced a Phase 1 multiple ascending dose clinical trial to evaluate safety, tolerability and pharmacokinetics of CTP-354 in up to 62 healthy volunteers. We expect to report initial data from this Phase 1 clinical trial in the second half of 2014. We designed this clinical trial to assess multiple doses and formulations of CTP-354 as well as the effects of taking CTP-354 with food as compared to following fasting. As a result of the long half-life of CTP-354, we believe that plasma concentrations of CTP-354 will increase over the course of a number of days when it is administered once daily. Accordingly, in this clinical trial we are evaluating doses of CTP-354 lower than those that resulted in saturation of $GABA_A$ receptor occupancy following a single dose. We currently plan to evaluate daily doses of 2 mg and 6 mg of CTP-354 over 10-day periods, with dosing in a liquid suspension formulation. We may also incorporate into this clinical trial a cross-over to a solid dose formulation for subjects receiving 6 mg. If we are able to lift the partial clinical hold on CTP-354, we plan to evaluate daily doses of CTP-354 that are higher than 6 mg over 10-day periods, with dosing that may be in a liquid suspension or a solid dose formulation.

Planned Phase 2 Clinical Development

Subject to successful completion of our ongoing Phase 1 multiple ascending dose clinical trial and Phase 1 imaging study, we plan to advance CTP-354 into two Phase 2 clinical trials. We expect to commence the Phase 2 clinical development in the second half of 2014 and report initial top-line results in the first half of 2016. We plan to determine dosing levels following completion of the Phase 1 multiple ascending dose clinical trial. We expect that the Phase 2 clinical trials will evaluate the safety and efficacy of CTP-354 for the potential treatment of spasticity associated with both multiple sclerosis and spinal cord injury and will feature two-way cross-over between dosing with CTP-354 and placebo.

CTP-354 Preclinical Development

Our preclinical program included testing of CTP-354 in a neuropathic pain rat model, in which CTP-354 was effective with no apparent sedation or ataxia at the therapeutic doses. Specifically, the effectiveness of CTP-354 in the neuropathic pain rat model at oral doses of between 10 and 100 mg/kg was similar to that of gabapentin, a standard positive control in this model, dosed at 100 mg/kg. In this preclinical test, 30 and 100 mg/kg doses of

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CTP-354 also demonstrated a longer duration of action than gabapentin. Our preclinical program also included studies in rat models in which CTP-354 demonstrated an improved pharmacokinetic profile compared to L-838417. We also conducted a $GABA_A$ receptor occupancy study in rats evaluating doses ranging from 1 mg to 30 mg. The minimally effective dose of CTP-354 in the rat neuropathic pain model was 1 mg/kg, a dose that provided rat brain $GABA_A$ receptor occupancy of about 25%. Higher doses resulted in greater occupancy, with 30 mg/kg resulting in brain $GABA_A$ receptor occupancy of about 80% to 85%.

Our preclinical program also included pharmacokinetic studies in rats comparing CTP-354 to L-838417. CTP-354 and L-838417 were orally dosed at 1 mg/kg in eight male Sprague-Dawley rats. The plasma levels of CTP-354 were significantly greater than those of L-838417. The maximum observed peak plasma concentration for CTP-354 was 4.8 times higher than that of L-838417 and the total exposure to CTP-354 was three times higher as compared to L-838417. Based on this study, we were encouraged to further develop CTP-354. The Phase 1 study that we later conducted showed that CTP-354 has a longer half-life in humans than it does in rats. The graph below shows the comparison of CTP-354 and L-838417 in this rat pharmacokinetic study.

CTP-354 vs. L-838417 Oral Pharmacokinetics in Rats

Fast Forward Sponsored Research Agreement

In February 2012, we entered into a sponsored research agreement with Fast Forward LLC, a subsidiary of the National Multiple Sclerosis Society, to fund the preclinical advancement of CTP-354. Under the Fast Forward agreement, we received a non-refundable upfront payment of $0.2 million, as well as further non-refundable payments of $0.6 million for the achievement of the preclinical development milestones set forth in the agreement. We are obligated to make milestone payments to Fast Forward not in excess of a low-single digit multiple of the funding amount if we commercialize CTP-354 or license the development and commercialization of CTP-354 to a third party.

Potential Additional Indications

Based on the well-known efficacy of benzodiazepines and other $GABA_A$ modulators, we believe CTP-354 has potential in a number of other indications, including anxiety, chronic pain, muscle tension and epilepsy.

CTP-499

Overview

CTP-499 is a novel oral multi-subtype selective inhibitor of PDEs that we are developing to slow the progression of type 2 diabetic kidney disease in patients with macroalbuminuria. We use the term type 2 diabetic kidney

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disease to refer to chronic kidney disease in patients with type 2 diabetes. We are developing CTP-499 as an additive treatment to the current standard of care for type 2 diabetic kidney disease, angiotensin modulation, which is treatment with an ACEi or an ARB. We are currently conducting a three-part Phase 2 clinical trial of CTP-499 in which we have enrolled patients with type 2 diabetic kidney disease and macroalbuminuria who were receiving standard-of-care treatment. We believe that CTP-499, if approved in this indication, will address a substantial commercial market, as despite the protective effect of angiotensin modulators in type 2 diabetic kidney disease, we estimate that each year over 40,000 patients with type 2 diabetes progress to end-stage kidney failure in the United States. We expect that we would conduct any large Phase 3 clinical trial of CTP-499 in type 2 diabetic kidney disease in collaboration with one or more partners.

CTP-499 is a deuterated analog of 1-(S)-5-hydroxyhexyl-3,7-dimethylxanthine, or HDX, an active metabolite of pentoxifylline. Pentoxifylline was approved over three decades ago for the treatment of intermittent claudication, or lower limb pain resulting from obstructed arteries, and has a well-established safety profile. Investigator-sponsored, single site clinical studies have evaluated pentoxifylline in chronic kidney disease patients, including in patients with diabetes, who were also simultaneously treated with an angiotensin modulator. In most of these studies, the investigator reported that patients experienced a reduction in albuminuria. In some of these studies, which were conducted for at least 12 months, the investigator also reported a slowing in decline of kidney function in patients receiving pentoxifylline compared to the decline in patients receiving placebo. We chose to develop CTP-499 because our preclinical research, combined with literature data, indicated that HDX, rather than pentoxifylline, may be responsible for the majority of these observed beneficial effects of pentoxifylline in humans.

Type 2 Diabetic Kidney Disease

Type 2 diabetic kidney disease is a condition in which the kidneys ability to filter blood is impaired and is typically chronic and progressive. The filtering ability of the kidney is measured as glomerular filtration rate, or GFR. Direct measurement of GFR is cumbersome. As a result, it is typically estimated by measuring blood levels of certain waste products, creatinine or cystatin C or both, and then applying a mathematical formula that accounts for additional variables, including age, race and gender, to derive the eGFR. GFR and eGFR are measured in units of milliliters per minute per 1.73 meters squared, which is a typical adult body surface area. An eGFR of 60 to 89 is mild or early stage kidney disease, 30 to 59 is moderate or mid-stage, 15 to 29 is advanced or severe kidney disease and below 15 indicates kidney failure requiring dialysis or kidney transplantation to avoid death.

Urinary excretion of albumin, a common protein in the blood, is believed to indicate kidney damage if sustained for longer than three months. Albumin excretion is typically measured in terms of UACR, a ratio that helps to correct for variability in urine concentrations. UACR is expressed as milligrams of albumin per gram of creatinine. A UACR greater than 300 mg/g is referred to as macroalbuminuria and, when sustained for three months or longer, generally indicates substantial kidney damage. Macroalbuminuria and reduced eGFR are independent indicators of kidney disease. Patients who have both macroalbuminuria and reduced eGFR are at high risk for rapidly advancing disease, death or progression to kidney failure.

Type 2 diabetic kidney disease is a highly complex, multifactorial disease involving inflammatory, oxidative and fibrotic processes. PDEs are a family of enzymes that regulate diverse pathways involved in these processes. Different PDEs, including several which CTP-499 inhibits, have been shown to contribute to kidney damage in preclinical animal models.

Market

According to the Centers for Disease Control, in 2011, approximately 26 million people in the United States had diabetes, with 90% to 95% suffering from type 2 diabetes, commonly referred to as adult-onset diabetes. According to a 2009 article in the American Diabetes Association journal *Diabetes Care*, type 2 diabetes is the leading cause of chronic kidney disease. The United States Renal Data Survey, a national data system that

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collects, analyzes and distributes information about end-stage renal disease, the most severe stage of chronic kidney disease, in the United States, indicates that diabetes is the leading cause of end-stage renal disease in the United States. Patients with type 2 diabetes and chronic kidney disease have a markedly increased mortality rate compared to type 2 diabetics without chronic kidney disease.

Patients with end stage renal disease resulting from chronic kidney disease and other causes impose a significant economic burden on the United States, constituting approximately 1.3% of Medicare beneficiaries but accounting for approximately 8.0% of Medicare expenditures, or $33 billion, according to the 2012 annual report of the United States Renal Data Survey. According to the United States Renal Data Survey, in 2010 in the United States, it cost approximately $60,000 more per year to treat a patient undergoing hemodialysis, treatment in which a machine filters wastes, salts and fluid from the blood, than a patient with chronic kidney disease who did not require hemodialysis. Consequently, we believe that a drug that would delay or prevent the progression of renal disease and the onset of end stage renal disease would have significant pharmacoeconomic benefits.

Limitations of Current Therapies

Current standard of care for type 2 diabetic kidney disease is treatment with angiotensin modulators. These are antihypertensive agents that also have the effect of reducing albuminuria and slowing the decline of renal function. However, despite treatment with these drugs, many type 2 diabetic kidney disease patients continue to experience loss in renal function at a rate that is significantly faster than normal age-related decline. No new disease modifying treatments for type 2 diabetic kidney disease have been approved by the FDA in the last decade and we believe that an agent with a novel mechanism, such as CTP-499, that can complement the effects of angiotensin modulation and further slow the progression toward kidney failure would offer an important medical benefit and present a substantial commercial opportunity.

CTP-499 Phase 2 Clinical Trial

We have completed dosing in the blinded parts of a Phase 2 placebo-controlled clinical trial of CTP-499 in patients with type 2 diabetic kidney disease and macroalbuminuria. All patients enrolled in the clinical trial are being concurrently treated with angiotensin modulators. The clinical trial consists of three parts:

Part 1 a double-blind, parallel, two-arm, placebo-controlled study evaluating the safety and efficacy of 600 mg of CTP-499 twice daily for 24 weeks. We enrolled 182 patients in this first part of the trial, which we completed in 2013.

Part 2 a blinded 24-week extension study in which all patients who completed Part 1 were eligible to continue receiving 600 mg of CTP-499 or placebo twice daily. We enrolled 143 patients in this part of the clinical trial and have completed dosing 123 of the 143 patients that we enrolled in Part 2 of the clinical trial completed Part 2. We have conducted preliminary analyses of the combined 48 weeks of data from Parts 1 and 2 of the clinical trial, but have not yet completed a full analysis of the data from Part 2. We expect to report final results for the first 48 weeks of the trial in the second quarter of 2014.

Part 3 all patients who complete Part 2 are eligible to receive 600 mg of CTP-499 twice daily in a 48 week open-label extension study. We expect the open-label extension study will be completed by the end of 2014.

As of December 31, 2013, 102 patients had enrolled in the open-label extension study.

The primary objective of the trial was to evaluate the safety and efficacy of treatment with CTP-499 administered in twice daily oral doses of 600 mg in a controlled release formulation for a minimum of 24 weeks. The primary endpoint was measurement of changes in UACR at 24 weeks. Key secondary endpoints were changes in serum creatinine, eGFR and UACR, as well as safety, including incidence of adverse events, over 48 weeks.

The key criteria for inclusion of patients in the trial included the following characteristics:

eGFR from 23 to 89 mL/min/1.73 m2, which indicates mild to moderately severe type 2 diabetic kidney disease;

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having been on a stable angiotensin modulation regimen for a minimum of four weeks prior to initiating screening and nine weeks prior to initiating dosing;

blood pressure less than or equal to 145/90 mm Hg;

glycosylated hemoglobin A1c (HbA1c) less than or equal to 10.5%, for the purposes of excluding patients with poorly controlled blood glucose; and

UACR greater than or equal to 200 mg/g in male patients and 300 mg/g in female patients, ratios of albumin to creatinine that are indicative of substantial kidney damage in men and women, but not more than 5,000 mg/g, a ratio indicative of severe kidney disease.

Phase 2 Clinical Trial Results

We believe that the preliminary data we have analyzed to date from the first 48 weeks of treatment support the potential of CTP-499 to help protect kidney function in patients at risk for type 2 diabetic kidney disease progression. As described below, we did not achieve statistical significance in the primary endpoint of the trial at 24 weeks. However, while our Phase 2 clinical trial was not intended to be powered for statistical significance with respect to serum creatinine or eGFR, and 48 weeks is a limited duration for measuring kidney function, our preliminary analyses of these key secondary endpoints at 48 weeks showed potential benefits including a nearly statistically significant impact on serum creatinine levels and a positive trend in eGFR.

Our preliminary 48 week analyses suggest that the serum creatinine levels of patients who received CTP-499 rose less than those of patients who received placebo. Serum creatinine is waste product that is cleared by the kidneys and increasing serum creatinine levels are believed to indicate worsening of kidney function. Our preliminary analyses indicate that the mean serum creatinine level in the 65 patients receiving CTP-499 increased by 0.13 mg/dL over the 48 weeks of treatment, as compared to an increase of 0.21 mg/dL in the 58 patients receiving placebo. The lower value in the case of CTP-499 represents a 38% improvement as compared to placebo ($p = 0.06$ using a two-tailed statistical analysis) at 48 weeks and may indicate a slower decline of kidney function in patients treated with CTP-499 than those who received placebo. A two-tailed analysis is a rigorous statistical test that assesses whether a study drug performs better or worse than placebo, as opposed to a one-tailed analysis that only tests if it is better. The statistical analysis plan for our Phase 2 trial was based on a two-tailed analysis. However, many Phase 2 trials use a one-tailed analysis. If analyzed by a one-tailed analysis, the serum creatinine results would be statistically significant ($p < 0.05$).

Our preliminary analyses of mean eGFR levels in the 65 patients receiving CTP-499 compared to the 58 patients receiving placebo at 48 weeks did not indicate a statistical difference. However, our preliminary analyses indicated a favorable trend, which was not statistically significant, at 48 weeks in reduced incidence of large eGFR declines in patients receiving CTP-499 as compared to placebo. Declining eGFR is believed to indicate worsening of kidney function. In this pre-specified analysis, we compared the number of patients who experienced eGFR declines of at least 30% and 40% after 48 weeks in the CTP-499 group and the placebo group. Our preliminary analyses indicated the following:

Eight out of the 58 patients receiving placebo, or 14%, experienced a 30% or greater decline in eGFR, compared with four out of the 65 patients receiving CTP-499, or 6.2% ($p = 0.11$).

Three out of the 58 patients receiving placebo, or 5.2%, experienced a 40% or greater decline in eGFR, compared with one out of the 65 patients receiving CTP-499, or 1.5% ($p = 0.23$).

In addition, a preliminary post-hoc analysis we conducted also indicated a statistically significant effect, at 48 weeks, in reduced incidence of large increases in serum creatinine levels in patients receiving CTP-499 as compared to placebo. After 48 weeks, six out of the 58 patients receiving placebo, or 10.3%, experienced a 50% or greater increase in serum creatinine levels, compared with one out of the 65 patients receiving CTP-499, or 1.5% ($p < 0.05$). A 50% increase in serum creatinine levels corresponds mathematically to between a 30% and a 40% decline in eGFR.

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We believe that the incidence of large declines in kidney function, measured as decreases in eGFR or increases in serum creatinine, in drug-treated versus placebo-treated patients, may be an acceptable primary endpoint for Phase 3 clinical development of a drug candidate for the treatment of type 2 diabetic kidney disease. Our belief is based on the findings of a December 2012 scientific workshop sponsored by the NKF and the FDA, and subsequent presentations by the NKF and the FDA. We intend to request in mid-2014 an end of Phase 2 meeting with the FDA to discuss endpoints for Phase 3 clinical development of CTP-499.

We have also conducted a preliminary post-hoc analysis of our data at 48 weeks in which we determined that all but one of the incidents of 30% or greater declines in eGFR occurred in patients with initial baseline UACR levels above the trial enrollment median, which was about 850 mg/g. This suggests that we may be able to conduct a subsequent clinical trial designed to measure an eGFR decline of at least 30% with a substantially enriched patient population by enrolling only patients with baseline UACR levels that are substantially higher than the minimum that was required for our Phase 2 clinical trial of CTP-499. A trial with such an enriched patient population would have the potential to provide the same statistical power to detect a difference between placebo and drug treatment as a trial enrolling macroalbuminuric patients with a wider range of UACR levels, but with a considerably smaller number of patients.

We did not observe a statistical difference between patients receiving CTP-499 and patients receiving placebo in change in UACR at 24 weeks, the primary endpoint of the Phase 2 clinical trial. However, our preliminary analyses after 48 weeks of treatment indicated that the mean rise in UACR for the CTP-499 group was 24 mg/g (2.2%) from a baseline mean of 1089 mg/g, compared to a mean rise of 222 mg/g for the placebo group from a baseline mean of 1066 mg/g (20.8%) ($p = 0.13$). While UACR has been commonly used as an indicator of efficacy in Phase 2 trials in type 2 diabetic kidney disease, it is not accepted by the FDA as an endpoint for a Phase 3 clinical trial for the treatment of type 2 diabetic kidney disease.

Treatment with CTP-499 was generally well tolerated in Part 1 of our Phase 2 clinical trial. Overall, incidence of serious adverse events in Part 1 of the trial was balanced between the placebo (15.9%) and CTP-499 (15.7%) groups. None of the serious adverse events were attributed by trial investigators to drug treatment and there were numerically more serious adverse cardiac events in placebo-treated patients (5.7%) than in patients who received CTP-499 (3.4%). Two deaths occurred during Part 1 of the trial. Both deaths occurred in patients in the CTP-499 group; however, neither was attributed by trial investigators to drug treatment. Discontinuations due to adverse events were comparable in the placebo (10.2%) and CTP-499 (10.1%) groups. Adverse events with at least 10% incidence in either treatment group were gastrointestinal disorders (22.7% for placebo and 29.2% for CTP-499); infections (15.9% for placebo and 27.0% for CTP-499); vascular disorders (15.9% for placebo and 9.0% for CTP-499); peripheral edema, fatigue and fever (12.5% for placebo and 11.2% for CTP-499); nervous system disorders (9.1% for placebo and 11.2% for CTP-499); musculoskeletal and connective tissue disorders (6.8% for placebo and 11.2% for CTP-499); respiratory and thoracic disorders (6.8% for placebo and 10.1% for CTP-499); endocrine disorders (4.5% for placebo and 10.1% for CTP-499); and metabolism and nutritional disorders (10.2% for placebo and 3.4% for CTP-499). Our preliminary analyses after 48 weeks of treatment also suggest that levels of serum potassium in patients who received CTP-499 were similar to baseline levels. Elevated levels of serum potassium are considered unsafe and have the potential to limit dosing.

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A summary of the serious adverse events in Part 1 of our Phase 2 clinical trial is shown in the table below.

	Placebo n = 88	CTP-499 n = 89
Serious Adverse Events		
Total serious adverse events	14(15.9%)	14(15.7%)
Cardiac disorders	5(5.7%)	3(3.4%)
Infections	3(3.4%)	5(5.6%)
Vascular disorders	4(4.5%)	1(1.1%)
Neoplasms		2(2.2%)
Psychiatric disorders		2(2.2%)
Blood and lymphatic system disorders		1(1.1%)
Gastrointestinal disorders	1(1.1%)	
Nervous system disorders	1(1.1%)	

Data have been collected with respect to safety and tolerability of CTP-499 in Part 2 of the trial. Our preliminary analyses indicates that for Part 2 of the trial, CTP-499 was generally well-tolerated.

AVP-786

Overview

In February 2012, we granted Avanir an exclusive license to develop and commercialize deuterated dextromethorphan analogs. Avanir is developing AVP-786, which is a combination of a deuterated dextromethorphan analog and an ultra-low dose of quinidine, for the treatment of neurologic and psychiatric disorders. In February 2013, Avanir reported positive results from a Phase 1 clinical trial of AVP-786. In June 2013, Avanir reported that the FDA had agreed to an expedited development pathway for AVP-786. In October 2013, Avanir reported plans to advance AVP-786 into a Phase 2 clinical trial in the second half of 2014 for treatment-resistant major depressive disorder in patients with insufficient response to conventional anti-depressants.

Avanir currently markets a combination of dextromethorphan and quinidine, Nuedexta®, for pseudobulbar affect, which is a neurological condition characterized by involuntary, sudden and sometimes frequent episodes of laughing or crying. The quinidine in Nuedexta inhibits the metabolism of dextromethorphan. Without a metabolic inhibitor such as quinidine, dextromethorphan is rapidly metabolized by most humans, limiting its effectiveness and resulting in the production of metabolites that are harmful in large amounts. However, quinidine can cause heart rhythm changes. As a result, it is preferable to minimize dosing of quinidine.

Planned Development by Avanir

Avanir has stated that it plans to develop AVP-786 for the treatment of neurologic and psychiatric disorders, including pain, behavioral disorders, mood disorders and movement disorders. Avanir has also reported that it plans to integrate its development of AVP-786 into its ongoing clinical development program for AVP-923, a dextromethorphan and quinidine combination product candidate. Avanir reported that AVP-786, which includes a lower dose of quinidine than AVP-923, provided approximately the same pharmacokinetic exposure as AVP-923 in a Phase 1 clinical trial. Avanir has announced conducting Phase 2 or Phase 3 clinical trials of AVP-923 in agitation in Alzheimer s disease; central neuropathic pain in multiple sclerosis; levodopa-induced dyskinesia, a movement disorder caused by the use of levodopa to treat Parkinson s disease; and diabetic peripheral neuropathic pain.

AVP-786 Clinical Development

Phase 1 Clinical Trial. In February 2013, Avanir reported the results of a randomized, double-blind, two-way crossover Phase 1 clinical trial of AVP-786 at a single center in Australia to assess the pharmacokinetic profile,

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safety and tolerability of single and multiple doses of AVP-786 both with and without quinidine. In this Phase 1 clinical trial, Avanir used AVP-923 as a control. The first stage of this study included 36 healthy subjects. Twelve additional subjects were enrolled in the second stage of the study. Avanir reported results indicating that AVP-786 with a reduced dose of quinidine relative to AVP-923 demonstrated a pharmacokinetic profile comparable to AVP-923 with comparable safety and tolerability.

Planned Phase 2 Clinical Trial. In October 2013, Avanir reported that it expects to file its IND for AVP-786 in the second half of 2014. Avanir was not required to file an IND prior to commencement of its Phase 1 clinical trial of AVP-786 because that trial was conducted in Australia. Avanir reported that, subject to the acceptance of this IND, it plans to initiate a Phase 2 randomized, placebo-controlled clinical trial in the second half of 2014 to evaluate the safety and efficacy of AVP-786 in patients with treatment-resistant major depressive disorder. Avanir reported that it expects to enroll patients with major depressive disorder who have insufficient response to conventional anti-depressants. Avanir further reported that treatment with AVP-786 or placebo in the trial is expected to be adjunctive to treatment with other anti-depressants.

Expedited Development Path. Avanir has reported conducting Phase 2 and Phase 3 clinical trials to evaluate AVP-923 and has reported plans to expedite the completion of one of its ongoing AVP-923 clinical trials to guide development of AVP-786. Avanir has stated that it intends to replace AVP-923 with AVP-786 in future clinical evaluation and that the FDA has agreed to an expedited development pathway for AVP-786 that would permit Avanir to reference data generated during its clinical testing of AVP-923 in its IND, and any future NDA, for AVP-786.

CTP-730

In April 2013, we entered into a strategic collaboration with Celgene related to deuterium-substituted compounds for the treatment of cancer or inflammation. We are initially focusing on one program; however, the collaboration has the potential to encompass multiple programs. In the initial program, we have selected CTP-730, a product candidate for the treatment of inflammatory diseases, and expect to begin Phase 1 clinical trials in 2014. We are responsible for development, at our expense, through the completion of single and multiple ascending dose Phase 1 clinical trials.

JZP-386

In February 2013, we licensed to Jazz Pharmaceuticals the commercial rights to deuterated analogs of sodium oxybate, including JZP-386, under an exclusive worldwide license agreement. Sodium oxybate is the active ingredient in Xyrem, a prescription medicine marketed in the United States by Jazz Pharmaceuticals to treat two of the key symptoms of narcolepsy, excessive daytime sleepiness and cataplexy. For 2013, Jazz Pharmaceuticals reported Xyrem annual net sales of $569.1 million as compared to net Xyrem sales of $378.7 million for 2012.

In preclinical *in vivo* testing, JZP-386 demonstrated a prolonged pharmacokinetic profile and reduced variability relative to sodium oxybate. We are responsible for conducting specified preclinical and clinical activities for JZP-386 through and including Phase 1 clinical trials. Jazz Pharmaceuticals is responsible for manufacturing clinical material and reimbursing us for all costs associated with our program-related activities, subject to limitations specified in the agreement, including adherence within a particular percentage to a development budget. Jazz Pharmaceuticals is also responsible for conducting and funding all further development and commercialization of JZP-386.

In December 2013, an IMPD, the basis for initiating clinical trials in the European Union, was filed for JZP-386. The IMPD received approval in January 2014. Jazz Pharmaceuticals has reported that it expects a Phase 1 clinical trial of JZP-386 to be conducted in 2014, following manufacturing of clinical material. JZP-386 is being treated as a Schedule I Controlled Substance by the DEA and being regulated accordingly. See Government Regulations Regulation of

Controlled Substances for additional information.

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C-10068

C-10068 is a novel oral deuterium-substituted analog of dextroethorphan, a compound with preclinical pharmacological activities qualitatively similar to those of dextromethorphan. Dextroethorphan was identified in a collaboration between the National Institutes of Health, or NIH, and Walter Reed Army Institute of Research, or WRAIR, to identify analogs of dextromethorphan with improved therapeutic properties. Similar to dextromethorphan, dextroethorphan forms the undesirable metabolite dextrorphan, but to a lesser degree.

We believe that C-10068 has the potential to treat pain and seizure-generating diseases and injuries, such as epilepsy, ischemic stroke and traumatic brain injury. C-10068 has demonstrated anti-seizure activity in *in vivo* preclinical studies in animals. C-10068 has also shown therapeutic potential for the treatment of pain in *in vivo* models. In addition, we have found that C-10068 forms less dextrorphan than either dextromethorphan or dextroethorphan *in vitro* in human liver microsomes, which are small particles isolated in the laboratory to study metabolism. We have conducted a portion of our preclinical program for C-10068 in collaboration with the National Institute of Neurological Disorders and Stroke and WRAIR. We are conducting further preclinical evaluation of C-10068.

OTHER PRECLINICAL PROGRAMS AND PIPELINE OPPORTUNITIES

We are also conducting a number of other preclinical programs, including deuterated ivacaftor for the potential treatment of cystic fibrosis and chronic obstructive pulmonary disease and deuterated praziquantel in collaboration with the Therapeutics for Rare and Neglected Diseases division of the NIH for the treatment of schistosomiasis and other parasitic diseases.

We have discovered a significant number of additional compounds utilizing our DCE Platform that have potential application in many different therapeutic areas, including oncology, central nervous system disorders, inflammation and antivirals. We are evaluating these programs for possible further development, either by us alone or in collaboration with another party.

COLLABORATIONS

We are party to a number of collaborations for the research, development and commercialization of deuterated compounds. Through December 31, 2013, we had received an aggregate of $106.0 million in upfront and milestone payments, equity investments and research and development funding from current and former collaborations. Under our current collaborations, which are described below, we have the potential to receive up to $1.6 billion in future milestone payments, including over $1.2 billion in research, development and regulatory milestones, as well as royalties on any future net product sales.

Celgene

Overview. In April 2013, we entered into a master development and license agreement with Celgene, which is primarily focused on the research, development and commercialization of specified deuterated compounds targeting cancer or inflammation. The collaboration is initially focused on one program, but has the potential to encompass up to four programs. For the initial program, we granted Celgene an exclusive worldwide license to develop, manufacture and commercialize deuterated analogs of a selected non-deuterated compound and certain close chemical derivatives thereof. We further granted Celgene licenses with respect to two additional programs and an option with respect to a third additional program. We and Celgene have agreed on the non-deuterated compounds for each of the two additional license programs. For the option program, Celgene may select the non-deuterated compound at a later time, which, unless otherwise agreed by us, will be limited to a compound for which Celgene possesses exclusive rights.

With respect to the two additional license programs, we granted Celgene an upfront exclusive worldwide license to develop, manufacture and commercialize deuterated products that contain deuterated analogs of the agreed non-deuterated compounds. Celgene is restricted from utilizing their research, development and commercialization rights under each of the upfront licenses, unless, within seven

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years after the effective date of the agreement, Celgene pays us a license exercise fee. If Celgene does not elect to pay the license exercise fee during the seven year period, the license will expire. With respect to the option program, once a compound is selected, Celgene may exercise its option by paying us an option exercise fee within seven years of the effective date of the agreement, and upon Celgene s exercise of the option we will grant to Celgene an exclusive worldwide license to develop, manufacture and commercialize deuterated products that contain deuterated analogs of the selected non-deuterated compound.

Research Obligations. We are responsible for conducting and funding research and early development activities for the initial program at our own expense pursuant to agreed upon development plans. This includes the completion of single and multiple ascending dose Phase 1 clinical trials and any mutually agreed upon additional Phase 1 clinical trials, as set forth in the development plan and approved by the joint steering committee for the collaboration.

We do not have any obligation to conduct any research or development activities for any of the additional programs unless and until Celgene exercises its rights with respect to such program and pays us the applicable exercise fee. If Celgene exercises its rights with respect to any additional program and pays us the applicable exercise fee, we are responsible for conducting research and development activities at our own expense pursuant to agreed upon development plans until the completion of the first Phase 1 clinical trial, which will be defined in each development plan on a program-by-program basis. In addition, if Celgene exercises its rights with respect to the option program and pays us the applicable exercise fee, we are responsible for seeking to generate a deuterated compound for clinical development in the selected option program at our own expense.

Celgene is responsible for all development costs with respect to the initial program beyond the Phase 1 clinical trials that we conduct. If Celgene exercises its rights with respect to any additional program, Celgene will be solely responsible for all research, development and commercialization costs for such program following the completion of the first Phase 1 clinical trial for such program.

Following its assumption of responsibility for development costs of a product candidate, Celgene is required to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize the product candidate until such time, if any, as Celgene determines in its reasonable discretion based on comparative metrics that that product candidate does not represent a substantial improvement over the corresponding non-deuterated compound.

Governance. Oversight of the development program for each category of licensed products under the agreement is guided by separate joint steering committees. There is likewise a joint patent committee to discuss and guide all matters for any patents owned by or licensed to us relating to the licensed products.

Payments. Under the terms of the agreement, we received a non-refundable upfront payment of $35.0 million. In addition, we are eligible to earn up to $23.0 million in development milestone payments, including $8.0 million related to the completion of a Phase 1 clinical trial, up to $247.5 million in regulatory milestone payments and up to $50.0 million in sales-based milestone payments related to products within the initial program. If Celgene exercises its rights with respect to either of the two additional license programs, we will receive a license exercise fee for the applicable program of $30.0 million and will also be eligible to earn up to $23.0 million in development milestone payments and up to $247.5 million in regulatory milestone payments for that program. Additionally, with respect to one of the additional license programs we are eligible to receive up to $100.0 million in sales-based milestone payments based on net sales of products, and with respect to the other additional license program we are eligible to receive up to $50.0 million in sales-based milestone payments based on net sales of products. If Celgene exercises its option with respect to the option program in respect of a compound to be identified at a later time, we will receive an option exercise fee of $10.0 million and will be eligible to earn up to $23.0 million in development milestone payments and up to $247.5 million in regulatory milestone payments.

In addition, with respect to each program, Celgene is required to pay us royalties on net sales of each licensed product at defined percentages ranging from the mid-single digits to low double digits below 20%, on worldwide

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net product sales of licensed products. The royalty term for each licensed product in each country is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the latest of expiration of specified patent coverage, expiration of regulatory exclusivity or 10 years following commercial launch. The royalty rate is reduced, on a country-by-country basis, during any period within the royalty term when there is no patent claim or regulatory exclusivity covering the licensed product in the particular country.

Exclusivity Restrictions. During the term of the agreement, we may not research, develop or commercialize, or grant or offer to grant a third party a license to research, develop or commercialize, any licensed product, and with respect to the option program, certain products that Celgene has the right to select as an option product, other than pursuant to the agreement.

Term and Termination. The agreement will expire upon the later of the seventh anniversary of the effective date of the agreement and the expiration of all royalty terms with respect to each licensed product in each country. Celgene has the right to terminate the agreement, in whole or only with respect to a particular licensed product, upon 60 days prior written notice to us. The agreement may also be terminated by us in the event of an uncured material breach by Celgene. If the agreement is terminated for any reason, the licenses granted by us to Celgene will terminate and specified rights to licensed products will revert to us.

Avanir

Overview. In February 2012, we entered into a development and license agreement with Avanir under which we granted Avanir an exclusive worldwide license to develop, manufacture and commercialize deuterated dextromethorphan containing products. Avanir is initially focused on developing AVP-786, which is a combination of a deuterated dextromethorphan analog and an ultra-low dose of quinidine, for the treatment of neurologic and psychiatric disorders.

Research Obligations. Under the agreement, upon Avanir s request we are obligated to provide research and development services with respect to licensed products pursuant to an agreed upon research and development plan until the first acceptance of an IND for any licensed product filed by Avanir or its affiliates or sublicensees in the United States, European Union or Japan. We are obligated to use commercially reasonable efforts to conduct and complete the activities assigned to us under the agreement. Avanir is required to use commercially reasonable efforts to develop and commercialize licensed product candidates for specified numbers of indications in the United States, European Union and Japan. Avanir is responsible for funding 100% of our research and development costs incurred under the development plan or for activities conducted at Avanir s request, including pass-through costs and a rate per full-time equivalent, or FTE, year of our employees time, which we mutually agreed to, subject to limitations specified in the agreement. However, Avanir is currently conducting all research and development activities without our services.

Governance. Our collaboration with Avanir is guided by a joint steering committee. There is likewise a joint patent committee to discuss and guide all matters for any patents owned by or licensed to us relating to the licensed products or otherwise filed with respect to certain inventions within the scope of the collaboration.

Payments. Under the agreement, we received a non-refundable upfront payment of $2.0 million and a milestone payment of $2.0 million in 2013. We are also eligible to receive, with respect to licensed products comprising a combination of deuterated dextromethorphan and quinidine, up to $4.0 million in development milestone payments, including $2.0 million related to initiation of dosing in a Phase 2 or Phase 3 clinical trial for AVP-786, up to $37.0 million in regulatory and commercial launch milestone payments and up to $125.0 million in sales-based milestone payments based on net product sales of licensed products. In addition, we are eligible for higher development

milestones, up to an additional $43.0 million, for licensed products that do not require quinidine. Avanir is currently developing deuterated dextromethorphan only in combination with quinidine. Avanir also is required to pay us royalties at defined percentages ranging from the mid-single digits to low double digits below

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20% on worldwide net product sales of licensed products. The royalty term for each licensed product in each country is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the later of expiration of specified patent coverage or 10 years following commercial launch. The royalty rate is reduced, on a country-by-country basis, during any period within the royalty term when there is no patent claim covering the licensed product in the particular country.

Exclusivity Restrictions. During the term of the agreement, neither we nor Avanir may research, develop or commercialize any product that contains deuterated dextromethorphan or grant or offer a license under any deuterated dextromethorphan specific intellectual property, other than pursuant to the agreement. We are also subject to certain additional exclusivity restrictions as set forth in the agreement, including certain restrictions on the development, commercialization and licensing of deuterated dextromethorphan analogs, such as C-10068, for the treatment of pseudobulbar affect or behavioral symptoms in dementia patients.

Term and Termination. The agreement will expire on a licensed product-by-licensed product and country-by-country basis on the date of the expiration of the applicable royalty term with respect to each licensed product in each country. Following the earlier of the completion of a specified Phase 2 clinical trial milestone or the second anniversary of the effective date of the agreement, Avanir has the right to terminate the agreement upon 90 days prior written notice to us. We may terminate the agreement if Avanir ceases to develop or commercialize licensed products and does not recommence development or commercialization efforts following our notice to Avanir. The agreement may also be terminated by either Avanir or us in the event of an uncured material breach by the other party.

If the agreement is terminated for any reason, the licenses granted by us to Avanir will terminate. Further, if the agreement is terminated, other than by Avanir as a result of our material breach of the agreement, specified rights to licensed products will revert to us and Avanir will be required, following our request, to grant us a license under specified intellectual property controlled by Avanir and related to licensed products. If the termination takes place after the completion of a Phase 2 clinical trial for a licensed product, we are required to pay a royalty on our net product sales of licensed products until such time as Avanir has recovered a multiple of the out-of-pocket expenses paid by Avanir to develop the licensed product prior to termination of the agreement. If the termination takes place after Avanir has generated Phase 3 clinical data, we are generally restricted for a specified period of time following termination from marketing any licensed product that is approved by the applicable regulatory authority based on the Phase 3 clinical data generated by Avanir.

Jazz Pharmaceuticals

Overview. In February 2013, we entered into a development and license agreement with Jazz Pharmaceuticals to research, develop and commercialize products containing deuterated sodium oxybate, or D-SXB. We are initially focusing on one analog, designated as JZP-386. Under the terms of the agreement, we granted Jazz Pharmaceuticals an exclusive, worldwide, royalty-bearing license under intellectual property controlled by us to develop, manufacture and commercialize D-SXB products including, but not limited to, JZP-386.

Research Obligations. We, together with Jazz Pharmaceuticals, are conducting certain development activities for a Phase 1 clinical trial with respect to JZP-386 pursuant to an agreed upon development plan. We are responsible under the development plan for conducting a Phase 1 clinical trial with respect to JZP-386. Thereafter, our obligations to conduct further development activities are subject to mutual agreement. Jazz Pharmaceuticals has assumed all manufacturing responsibilities. Pursuant to the agreement, our costs for activities under the development plan, including pass-through costs and the costs of our employees time at a rate per full-time equivalent year of our employees time, which we mutually agreed to, are reimbursed by Jazz Pharmaceuticals. This reimbursement is subject to limitations specified in the agreement, including adherence within a particular percentage to the development

budget. Under the agreement, Jazz Pharmaceuticals is subject to specified diligence obligations regarding the development and commercialization of licensed products.

Governance. Our collaboration with Jazz Pharmaceuticals is guided by a joint steering committee and a joint patent committee.

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Payments. Under the agreement, we received a non-refundable upfront payment of $4.0 million and we are eligible to receive an aggregate of up to $8.0 million in development milestone payments, up to $35.0 million in regulatory milestone payments and up to $70.0 million in sales milestone payments based on net product sales of licensed products. In addition, Jazz Pharmaceuticals is required to pay us royalties at defined percentages ranging from the mid-single digits to low double digits below 20%, on a country-by-country and licensed product-by-licensed product basis, on worldwide net product sales of licensed products. The royalty term for each licensed product in each country is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the later of the expiration of specified patent coverage or 10 years following commercial launch. The royalty rate is lowered, on a country by country basis, under certain circumstances as specified in the agreement.

Exclusivity Restrictions. During the term of the agreement, subject to exceptions specified in the agreement, we may not grant or offer a license or other rights to a third party with respect to, or research, develop, manufacture or commercialize, D-SXB compounds, licensed products, sodium oxybate or any compounds that are structurally similar to and have substantially similar biological activity to D-SXB.

Term and Termination. The agreement will expire on a licensed product-by-licensed product and country-by-country basis on the date of the expiration of the applicable royalty term with respect to each licensed product in each country. Jazz Pharmaceuticals may terminate the agreement, on a country-by-country basis or in its entirety, upon 90 days prior written notice to us. We may terminate the agreement upon written notice to Jazz Pharmaceuticals if Jazz Pharmaceuticals decides to permanently cease development and commercialization of all licensed products. We may also terminate the agreement if Jazz Pharmaceuticals has abandoned development or commercialization activities for licensed products and following notice from us does not resume development or commercialization activities. The agreement may also be terminated by either party in the event of an uncured material breach by the other party.

If the agreement is terminated for any reason, the licenses granted by us to Jazz Pharmaceuticals with respect to D-SXB products will terminate and specified rights to licensed products will revert to us. In addition, at our request, both parties will enter into good faith negotiations to agree upon commercially reasonable royalties payable by us for a non-exclusive license under intellectual property controlled by Jazz Pharmaceuticals, and made in the course of developing licensed products, to develop, manufacture and commercialize licensed products.

Following termination of the agreement with respect to a country or countries, but not in its entirety, by Jazz Pharmaceuticals for Jazz Pharmaceuticals convenience, Jazz Pharmaceuticals may provide us written notice that it desires to continue or recommence development and commercialization of licensed products in such country or countries, in which event Jazz Pharmaceuticals license with respect to D-SXB products in such country or countries and corresponding payment obligations under the agreement will be reinstated except in specified circumstances in which we have previously notified Jazz Pharmaceuticals of our intent to develop or commercialize licensed products in such country or countries either directly or through a third party licensee.

INTELLECTUAL PROPERTY

We protect our product candidates through the use of patents, trade secrets and careful monitoring of our proprietary know-how. As of February 28, 2014, we held more than 100 issued patents worldwide, including 50 issued patents in the United States. Our patents and patent applications, if they issue as patents, for our lead programs expire between 2028 and 2034.

CTP-354

We hold U.S. patents covering the composition of matter of CTP-354 and related compounds. These patents expire in 2029. We also have a pending U.S. patent application claiming compositions and methods covering CTP-354. We have corresponding issued patents in Europe and Japan that expire in 2029. We have retained all of the CTP-354 patent rights.

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CTP-499

We hold a U.S. patent that covers the composition of matter of CTP-499 and related compounds. This patent expires in 2029. We also have pending U.S. patent applications that cover CTP-499 and related compounds. We have two patent applications for CTP-499 in Europe and two issued patents in Japan that cover the composition of matter of CTP-499. Patents that issue from the European patent applications would expire in 2029 and 2030. The issued Japanese patents expire in 2029 and 2030. We have retained all of the CTP-499 patent rights.

AVP-786

We hold U.S. patents covering the composition of matter and methods of use of the deuterated dextromethorphan analog that comprises AVP-786. These patents have expirations from 2028 to 2030. We also have a pending U.S. patent application covering methods of use of certain other dextromethorphan compounds. We have corresponding issued patents in Europe and Japan that expire in 2028. We have granted exclusive licenses under these patent rights to Avanir.

Celgene Collaboration

We hold U.S. patents and a U.S. patent application covering the composition of matter of deuterated analogs of one of the compounds that we have exclusively licensed to Celgene and U.S. patent applications covering other compounds that we have exclusively licensed to Celgene. The patents expire in 2030 and the patent applications, if issued as patents, would expire between 2029 and 2034. We also have provisional U.S. patent applications for compounds that we have exclusively licensed to Celgene. We have issued patents in Europe and Japan for compounds that we have exclusively licensed to Celgene that expire between 2029 and 2034.

JZP-386

We hold a U.S. patent covering the composition of matter of deuterated analogs of sodium oxybate, including JZP-386, and their methods of use for treating certain diseases and disorders, including narcolepsy, as well as a corresponding U.S. continuing application. The expiration of this patent and this application occur in 2030. We hold a corresponding European patent that expires in 2030. We also have patent applications in the United States, Europe and Japan that cover JZP-386 and related compounds and their methods of use for treating certain diseases and disorders, including narcolepsy that, if issued, would expire in 2032. We have granted exclusive licenses under these patent rights to Jazz Pharmaceuticals.

C-10068

We have allowed U.S. patent claims for the composition of matter of C-10068, and methods of use for treating certain diseases and disorders. The expiration of a patent issuing from these patent applications would be in 2029. We have a corresponding issued patent in Europe expiring in 2029 and a patent application in Japan that, if issued as a patent, would expire in 2029. We have retained all of the C-10068 patent rights.

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 more than 90 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 U.S. Patent and Trademark Office to act in a timely manner. The patent term of a patent that covers an FDA-

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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 Act permits 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, such as:

- our methods of evaluating candidate compounds for deuteration;
- our bioanalytical methods for identifying and measuring metabolites formed by the *in vitro* and *in vivo* metabolism of deuterated compounds;
- our analytical methods for evaluating how selective deuterium substitution affects different pharmacokinetic and metabolic parameters in *in vitro* and *in vivo* systems; and
- our methods to determine the degree of deuterium substitution in compounds we manufacture.

MANUFACTURING AND SUPPLY

We have developed the internal capability to manufacture up to low kilogram quantities of deuterated active pharmaceutical ingredients for use in Phase 1 clinical trials. Our manufacturing facility occupies approximately 700 square feet at our facility in Lexington, Massachusetts.

While our manufacturing capabilities can support Phase 1 clinical trials, we currently rely, and expect to continue to rely, on third parties for the manufacture of product candidates for our clinical trials, including the ongoing clinical trials of CTP-354 and, potentially, of CTP-499. 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 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.

We have successfully transferred the methods we use in our internal manufacturing to our third party manufacturers, allowing them to produce multi-kilogram quantities of clinical trial materials with similar efficiency as we manufacture compounds internally. If any of our third party manufacturers should become unavailable to us for any reason, we believe that there are a number of potential replacements, although we might incur some delay in identifying and qualifying such replacements.

We believe that all of the deuterium that we use in manufacturing our product candidates is currently derived, directly or indirectly, from deuterium oxide. For most of our deuterium supply we rely on bulk supplies of deuterium oxide, which we currently source from two suppliers, one located in the United States and one located abroad, which is affiliated with a foreign government. We may establish deuterium oxide supply arrangements with an additional supplier, which is located outside of the United States and is affiliated with a foreign government. It is also possible that our current U.S. supplier of deuterium oxide relies on our current foreign supplier, as well as our potential future foreign supplier, for its supply of deuterium oxide, although we are not familiar with its procurement processes. In order to internationally transport any deuterium oxide that we purchase from either of these two foreign suppliers, we, or our U.S. supplier, may be required to obtain an export

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license from the country of origin and we may be required to obtain an International Import Certificate from the country of destination. We are also required to obtain an export license from the Nuclear Regulatory Commission before shipping deuterium oxide from the United States to any contract manufacturer in another country. Each of these documents specifies the maximum amount of deuterium oxide that we, or our suppliers, are permitted to either import or export. In particular, in order to obtain additional supplies of deuterium oxide from the foreign-government affiliated supplier from which we have purchased deuterium oxide, we will be required to obtain an additional export license from the country of origin and a U.S. import certificate. While we have obtained similar licenses and certificates in the past, we may not be able to obtain them in the future in a timely manner or at all.

Certain of our manufacturing processes for our product candidates incorporate deuterium by using deuterated chemical intermediates or reagents that are derived from deuterium oxide. For the deuterated chemical intermediates and reagents, we are not subject to the license requirements applicable to deuterium oxide. However, the manufacturer of the deuterated chemical intermediate or reagent may themselves be required to obtain deuterium oxide under applicable licensing requirements. Most of the manufacturers of these deuterated chemical intermediates and reagents are not located in countries that produce bulk quantities of deuterium oxide. Therefore, our ability to source these deuterated chemical intermediates or reagents will depend on the ability of these manufacturers to obtain deuterium oxide from other countries.

We purchase our raw materials on a purchase order basis and have not entered into long-term 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 biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. 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 spasticity, kidney disease, neurologic disorders, cancer and inflammation, the key indications for our priority programs. Several large pharmaceutical and biotechnology companies have also begun to cover deuterated analogs of their product candidates in patent

applications and may choose to develop these deuterated compounds. In addition, we know of one biotechnology company, Auspex Pharmaceuticals, Inc., and possibly two others, DeutRx LLC and

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Berolina innovative Research and Development Services Pharma GmbH, that are developing product candidates based on deuterium substitution. Potential competitors also include academic institutions, government agencies and other public and private research organizations.

Many of our existing and potential future competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory 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.

The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, product labeling, side effect profiles, safety, convenience, price, particularly if there is generic competition, differentiation from their corresponding non-deuterated compounds when applicable, and the availability of reimbursement from government and other third party payors.

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

In addition, we anticipate that some of the product candidates that we or our collaborators may develop will be deuterated analogs of approved drugs, some of which are or will then be available on a generic basis. If such deuterated analogs are approved, we expect that they will compete against branded and generic non-deuterated compounds in the same indications based on enhanced efficacy, safety or convenience of dosing. If physicians do not believe that a product that we or our collaborators develop offers substantial advantages over the corresponding non-deuterated compound, or that the advantages offered by our product as compared to the corresponding non-deuterated compound are not sufficient to merit the increased price over the corresponding non-deuterated compound that we or our collaborators would seek, physicians might not prescribe our product.

If the product candidates for our priority programs are approved for the indications for which we or our collaborators are currently undertaking clinical trials, they will compete with the therapies discussed below and will likely compete with other therapies that are currently in development.

CTP-354

We are initially developing CTP-354 for the treatment of spasticity associated with multiple sclerosis and spinal cord injury. Current first-line treatment for spasticity includes oral and local agents and physical and occupational therapy. Four oral drugs have been approved in the United States for the treatment of spasticity: baclofen (Lioresal), tizanidine (Zanaflex), diazepam (Valium) and dantrolene (Dantrium), each of which is available on a generic basis. Spasticity is also treated through localized injections of botulinum toxin. In addition, there are several potentially competitive product candidates in Phase 3 clinical development being pursued by pharmaceutical and biotechnology companies, including GW Pharmaceuticals plc and Osmotica Pharmaceuticals Corp.

CTP-499

The current standard of care for type 2 diabetic kidney disease in patients with macroalbuminuria is treatment with angiotensin modulators. Angiotensin modulators are available on a generic basis. We are developing CTP-

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499 as an additive treatment to this current standard of care. If CTP-499 receives marketing approval, it may also face competition from a number of product candidates that are currently in clinical development, including potentially competitive product candidates in Phase 3 clinical development being pursued by AbbVie Inc., Janssen Research & Development LLC and NephroGenex, Inc.

AVP-786

Avanir is developing AVP-786 for the treatment of neurologic and psychiatric disorders. There are a number of marketed drugs and product candidates in clinical development for these indications.

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 statutes and regulations and other regulatory authorities, 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. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant 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, 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 preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA s good laboratory practice, or GLP, regulations;

- submission to the FDA of an IND, which allows human clinical trials to begin unless the FDA objects within 30 days;

- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;

performance of adequate and well-controlled human clinical trials in accordance with the FDA s current Good Clinical Practices, or cGCPs, to establish the safety and efficacy of the proposed drug product for each indication;

preparation and submission to the FDA of an NDA;

satisfactory 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 ingredients thereof, are produced to assess compliance with current good manufacturing practices and to assure that the facilities, methods and controls are adequate to ensure the product s identity, strength, quality and purity;

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payment of user fees and securing FDA approval of the NDA; and

compliance with any post-approval requirements, including REMS and post-approval studies required by the FDA.

Preclinical Studies and an IND

Preclinical studies can include *in vitro* and animal studies to assess the potential for adverse events and, in some cases, to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. 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 preclinical tests, 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 preclinical 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. 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 cGCP requirements, 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 NIH for public dissemination on their ClinicalTrials.gov website.

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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 optimal dosage.

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 more frequently if serious adverse events occur. 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. The FDA will typically inspect one or more clinical sites in late-stage clinical trials to assure compliance with cGCP and the integrity of the clinical data submitted.

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 submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA s previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the 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 preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) 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.

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Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical 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 an application user fee, currently exceeding $2.1 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding $104,000 per product and $554,600 per establishment. These fees are typically increased annually.

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 cGMP requirements 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 cGCP.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to mitigate any identified or suspected serious risks. The REMS plan 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 is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

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, 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

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approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If 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 REMS, which can materially affect the potential market and profitability of the 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.

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 are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, 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 cGMP requirements. 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 cGMP 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 cGMP compliance.

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 program. Other potential consequences include, among other things:

restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;

fines, warning letters or holds on post-approval clinical trials;

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refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;

product seizure or detention, or refusal to permit the import or export of products; or

injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates 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 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 preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD. 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 RLD 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 RLD 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 RLD 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 RLD 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 RLD. 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 RLD has expired. The FDCA provides a period of five years of data exclusivity for new drug containing a new chemical entity. 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,

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.

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Hatch-Waxman Patent Certification and the 30 Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the 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, a 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. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the 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.

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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 approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, 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 Drug Price Competition and Patent Term Restoration Act of 1984 (commonly referred to as 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 a NDA, plus the time between the submission date of a 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 U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Regulation of Controlled Substances

We handle a product that is treated as a controlled substance under the Controlled Substances Act of 1970, or CSA. The CSA authorizes the U.S. Drug Enforcement Agency, or DEA, to regulate the registration, procurement, manufacturing, production, possession, labeling and distribution of controlled substances. Controlled substances are classified as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk.

Our product candidate JZP-386, which we have licensed to Jazz Pharmaceuticals, is a deuterium substituted analog of sodium oxybate. Sodium oxybate is regulated as a chemical by the DEA as a Schedule I controlled substance. However, when formulated into Xyrem, the drug product is regulated as a Schedule III substance. Because of the Schedule I classification of sodium oxybate, JZP-386 is regulated by the DEA as a Schedule I controlled substance. If JZP-386 becomes approved as the active pharmaceutical ingredient in a drug product, the DEA may decide to regulate the drug product as a Schedule III controlled substance, similar to Xyrem.

The manufacture, shipment, storage, sale and use of Schedule I substances are subject to a high degree of regulation. Every person who manufactures, distributes, dispenses, imports or exports any controlled substance must register with the DEA, unless they are exempt. Moreover, for Schedule I substances, the CSA authorizes the DEA to establish aggregate production quotas for all manufacturers, individual production quotas for specific registered manufactures

and individual production quotas for registrants who have not manufactured controlled substances during one or more proceeding years.

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We expect our product candidate CTP-354 to be classified as a Schedule IV substance under the CSA. The CSA also places significant restrictions on substances which have been classified in Schedules III and IV. While these restrictions are not as severe as those governing substances in Schedules I and II, they nonetheless establish strict limitations on the manufacture, sale and distribution of Schedule III and IV substances. For example, prescriptions for controlled substances that are prescription drugs in such schedules may only be filled or refilled by pharmacists up to five times within six months after the date on which the prescription was issued, unless the prescribing practitioner renews the prescription.

The failure to maintain compliance with applicable requirements under the CSA can result in enforcement action that could have a material adverse effect on our business, results of operations and financial condition. The DEA may inspect facilities, seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal proceedings. Individual states also regulate controlled substances, and we and our contract manufacturers are subject to state regulation on distribution of these products.

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 our 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 EMA is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the

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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.

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, including a draft summary of product characteristics, and draft labeling and package leaflet, 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 of 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 test, preclinical 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 the costs of the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. 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 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.

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The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

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, 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 health care 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.

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 health care 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 from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

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

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding 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 transparency requirements under the Health Care Reform Law will require manufacturers of drugs, devices, drugs and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and

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

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care 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.

Regulation of Deuterium Oxide

We believe that all of the deuterium that we use in manufacturing our product candidates is currently derived, directly or indirectly, from deuterium oxide. For most of our deuterium supply we rely on bulk supplies of deuterium oxide, which we currently source from two suppliers, one located in the United States and one located abroad, which is affiliated with a foreign government. We may establish deuterium oxide supply arrangements with an additional supplier, which is located outside of the United States and is affiliated with a foreign government. In order to internationally transport any deuterium oxide that we purchase from either of these two foreign suppliers, we, or our U.S. supplier, may be required to obtain an export license from the country of origin and we may be required to obtain an International Import Certificate from the country of destination. We are also required to obtain an export license from the Nuclear Regulatory Commission before shipping deuterium oxide from the United States to any contract

manufacturer in another country. Each of these documents specifies the maximum amount of deuterium oxide that we, or our suppliers, are permitted to either import or export. We have obtained two export licenses from the Nuclear Regulatory Commission, each for the export of 20,000 kilograms of heavy water over the life of the license, which are valid until December 2015 and January 2019, respectively. However, in order to obtain additional supplies of deuterium oxide from the foreign-government affiliated supplier from which we have purchased deuterium oxide, we will be required to obtain an additional export license from the country of origin and a U.S. import certificate. While we have obtained similar licenses and certificates in the past, we may not be able to obtain them in the future in a timely manner or at all. We have not obtained an export license from the country in which our potential future foreign supplier is located. In addition, if any of our product candidates is approved by the FDA, then the FDA will also have regulatory jurisdiction over the manufacture and use of deuterium oxide in such product.

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EMPLOYEES

As of February 28, 2014, we had 45 employees, 26 of whom were primarily engaged in research and product development activities. A total of 17 employees have Ph.D. degrees. None of our employees are represented by a labor union and we believe our relations with our employees are good.

FACILITIES

Our offices are located in Lexington, Massachusetts, consisting of approximately 45,000 square feet of leased office and laboratory space. The term of the lease expires in September 2015.

LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

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, which we refer to as the Exchange Act. You can find, copy and inspect information we file at the SEC s public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC s public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC s web site at http://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 99 Hayden Avenue, Suite 500, Lexington, Massachusetts, 02421, and our telephone number is (781) 860-0045. Our Internet website is http://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, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled Investor Relations, 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.

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Item 1A. Risk Factors

Our business is subject to numerous risks. The following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Annual Report on Form 10-K and other filings with the Securities and Exchange Commission, or 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 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.

We have incurred significant annual net operating losses in every year since our inception. Our net loss was $11.3 million for the year ended December 31, 2011, $20.4 million for the year ended December 31, 2012 and $6.1 million for the year ended December 31, 2013. As of December 31, 2013, we had an accumulated deficit of $113.6 million. We have not generated any revenues from product sales and have financed our operations to date primarily through the public offering of our common stock, and private placements of our preferred stock, debt financings and funding from collaborations. We have not completed development of any product candidate and have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical development programs. 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 (deficit) and working capital.

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

- continue to develop and conduct clinical trials with respect to CTP-354;
- initiate and continue research, preclinical and clinical development efforts for our other product candidates and potential product candidates;
- seek to identify 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;

hire additional personnel, such as clinical, quality control and scientific personnel;

add operational, financial and management information systems and personnel, including personnel to support our product development and personnel and infrastructure necessary to help us comply with our obligations as a public company; and

add equipment and physical infrastructure to support our research and development.

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 obtain marketing approval for, and successfully commercialize, one or more of our product candidates. This 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

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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.

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 the second quarter of 2006. Our operations to date have been limited to financing and staffing our company, developing our technology and product candidates and establishing collaborations. We have not yet demonstrated an ability to successfully conduct a multi-center international clinical trial, conduct a large-scale pivotal clinical trial, obtain marketing approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful 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.

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 product development programs or commercialization efforts.

Developing pharmaceutical products, including conducting preclinical 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 preclinical development efforts for and seek marketing approval for, our 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. To our knowledge, no deuterated drug has ever been successfully commercialized. Manufacturing a deuterated drug at commercial scale may require expensive and specialized facilities, processes and materials. In addition, relative to previous years when we operated as a private company, we expect to incur significant additional costs in 2014 and future years 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 attractive terms, we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We plan to use our current cash and cash equivalents and investments, including the net proceeds of our recent initial public offering, primarily to fund our ongoing research and development efforts. We will be required to expend significant funds in order to advance the development of CTP-354 and our other product candidates. In addition, while may seek one or more collaborators for future development of CTP-499 and expect that we would conduct any large Phase 3 clinical trial of CTP-499 in type 2 diabetic kidney disease in collaboration with one or more partners that would pay most of the associated costs, we may not be able to enter into a collaboration for CTP-499 on suitable terms or at all. In any event, our existing cash and cash equivalents and investments, including the net proceeds of our recent initial public offering, 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 public or private equity offerings, debt financings, collaborations and licensing arrangements or other

sources. Adequate additional financing may not be available

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to us on acceptable terms, or at all. Our ability to obtain debt financing may be limited by covenants we have made under our loan and security agreement with Hercules Technology Growth Capital, Inc., or Hercules, and our pledge to Hercules of substantially all of our assets, other than our intellectual property, as collateral. The negative pledge in favor of Hercules with respect to our intellectual property under the loan and security agreement could further limit our ability to obtain additional debt financing. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We believe our existing cash and cash equivalents and investments as of December 31, 2013 combined with the proceeds from our recent intial public offering, will enable us to fund our operating expenses, debt service and capital expenditure requirements into the first half of 2016, without giving effect to potential milestone payments that we may receive under existing collaboration agreements. This estimate assumes we either enter into a collaboration agreement pursuant to which a partner funds further development of CTP-499 or we do not otherwise expend significant funds for further development of this product candidate. Our estimate as to how long we expect our existing cash and 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 preclinical development efforts for, our product candidates and potential product candidates, including current and future clinical trials;
- our ability to identify a collaborator for CTP-499 and the terms and timing of any collaboration agreement that we may establish for the development and commercialization of CTP-499;
- our current collaboration agreements remaining in effect and achievement of milestones under these agreements;
- our ability to enter into and the terms and timing of any additional collaborations, licensing 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 regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval, to the extent such costs are not the responsibility of one of our collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;

subject to receipt of marketing approval, revenue, if any, received from commercial sales of our product candidates;

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; and

the costs of operating as a public company.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our 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 public or private equity offerings, debt financings and additional collaborations and licensing arrangements. We do not have any committed external source of funds, other than potential milestone payments and royalties under our collaborations with Celgene, Avanir and Jazz Pharmaceuticals, each of which

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is subject to the achievement of development, regulatory 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. For example, our debt facility with Hercules contains restrictive covenants that, among other things and subject to certain exceptions, prohibit us from transferring any of our material assets, merging with or acquiring another entity, entering into a transaction that would result in a change of control, incurring additional indebtedness, creating any lien on our property, making investments in third parties or redeeming stock or paying dividends. Future debt securities or other financing arrangements could contain similar or more restrictive negative covenants. In addition, securing additional financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management s ability to oversee the development of our product candidates.

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.

Our existing and any future indebtedness could adversely affect our ability to operate our business.

As of December 31, 2013, we had $15.1 million of outstanding borrowings under our loan and security agreement with Hercules, which we are required to repay in monthly installments through October 2015. We could in the future incur additional indebtedness beyond our borrowings from Hercules.

Our outstanding indebtedness combined with our other financial obligations and contractual commitments, including any additional indebtedness beyond our borrowings from Hercules, 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.

In addition, although the rate of interest that we are required to pay under the loan and security agreement is capped, our indebtedness under the loan and security agreement bears interest at a variable rate below that cap, making us vulnerable to increases in the market rate of interest. If the market rate of interest increases substantially, we will have to pay additional interest on this indebtedness, which would reduce cash available for our other business needs.

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We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents and investments and funds from external sources. However, we may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under our existing debt instruments. Failure to make payments or comply with other covenants under our existing debt instruments could result in an event of default and acceleration of amounts due. Under our loan and security agreement with Hercules, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets or condition is an event of default. If an event of default occurs and the lender accelerates the amounts due, we may not be able to make accelerated payments, and the lender could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all of our assets other than our intellectual property. In addition, the covenants under our existing debt instruments, the pledge of our assets as collateral and the negative pledge with respect to our intellectual property could limit our ability to obtain additional debt financing.

RISKS RELATED TO THE DISCOVERY, DEVELOPMENT AND COMMERCIALIZATION OF OUR PRODUCT CANDIDATES

Our approach to the discovery and development of product candidates based on selective deuteration is unproven, and we do not know whether we will be able to develop any products of commercial value.

We are focused on discovering and developing novel small molecule drugs that have improved metabolic or pharmacokinetic characteristics as a result of our selective substitution of deuterium for hydrogen. We apply our proprietary platform to systematically identify approved drugs, advanced clinical candidates or previously studied compounds that we believe can be improved with deuterium substitution to provide better pharmacokinetic or metabolic properties and thereby enhance clinical safety, tolerability or efficacy. To our knowledge, no deuterated drug has ever been approved for sale in the United States. While we believe that selective deuteration can produce compounds that possess favorable pharmaceutical properties, and preclinical studies and early-stage clinical trials have indicated that certain of our product candidates may possess these properties, we have not yet succeeded and may not succeed in demonstrating efficacy and safety for any of our product candidates in later stage clinical trials or in obtaining marketing approval thereafter. For example, although we have discovered and evaluated numerous deuterated compounds, we have not yet advanced a compound beyond Phase 2 clinical development.

We are particularly dependent on the success of our product candidate, CTP-354, and our ability to develop, obtain marketing approval for and successfully commercialize CTP-354. CTP-354 is currently subject to a partial clinical hold that prevents us from administering doses in excess of 60 mg per day in single dose clinical trials and 6 mg per day in multiple dose clinical trials without an additional preclinical study. If we are unable to develop, obtain marketing approval for or successfully commercialize CTP-354, either alone 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 and are investing a significant portion of our efforts and financial resources in the development of CTP-354 for the treatment of spasticity. Our prospects are substantially dependent on our ability, or that of any future partner, to develop, obtain marketing approval for and successfully commercialize CTP-354.

In November 2013, we received notice from the FDA of a partial clinical hold on CTP-354 that prevents us from administering single doses in excess of 60 mg per day and multiple doses in excess of 6 mg per day and the FDA subsequently informed us that we may not administer multiple doses of CTP-354 in excess of 6 mg per day in clinical trials without first conducting an additional higher dose preclinical study. We do not intend to conduct single dose clinical trials of CTP-354 with doses in excess of 60 mg. While we believe that multiple doses of 6 mg per day would be sufficient for the treatment of spasticity, we are conducting the additional preclinical toxicology study to enable us

to evaluate higher doses of CTP-354, if needed in our spasticity trials, as well as to support clinical development in other disease indications. If we are required to perform additional preclinical

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studies to support the lifting of the partial clinical hold, it will increase our expected development costs and could delay the clinical development of CTP-354. If we are delayed in addressing, or unable to address, the FDA s concerns, we could be delayed, or prevented, from studying higher doses of CTP-354, which higher doses may be necessary to show efficacy. If these higher doses are necessary to show efficacy, we could be delayed or prevented from obtaining marketing approval of CTP-354.

The success of CTP-354 will depend on several factors, including the following:

- successful completion of clinical trials, which could require lifting of the partial clinical hold on CTP-354 or agreement by the FDA that the dosing protocols necessary to support successful completion of clinical trials are not subject to the partial clinical hold;
- receipt of marketing approvals from applicable regulatory authorities;
- our ability to develop a solid dose formulation of CTP-354;
- the performance of our future collaborators for CTP-354, if any;
- 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;
- 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 and regulatory exclusivity, both in the United States and internationally;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales if and when approved;
- a continued acceptable safety profile of CTP-354 following any marketing approval;
- commercial acceptance, if and when approved, by patients, the medical community and third party payors; and

competition with other therapies, including baclofen, tizanidine, benzodiazepines and injected botulinum toxin. If we are unable to develop, receive marketing approval for, or successfully commercialize CTP-354, or experience delays as a result of any of these factors or otherwise, our business could be materially harmed.

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 studies 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 population of patients, the occurrence of severe or medically or commercially unacceptable adverse events, failure to comply with protocols or applicable regulatory requirements and determination 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.

While we believe that our DCE Platform may enable drug discovery and clinical development that is more efficient and less expensive than conventional small molecule drug research and development, we may not be

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able to realize the advantages that we expect. In addition, while a key element of our drug discovery and development strategy involves utilizing existing information regarding non-deuterated compounds to assist the discovery and development of deuterated analogs of those compounds, not all of the product candidates that we develop are based on drugs or drug candidates that progressed into advanced clinical development. Particularly in these situations, existing information regarding the corresponding non-deuterated compound may not be sufficient to mitigate drug development risks. For example, we have pursued clinical development of CTP-499 for the potential treatment of type 2 diabetic kidney disease in patients with macroalbuminuria. CTP-499 is a deuterated analog of a metabolite of a drug that was not approved for this indication. CTP-499 failed to achieve statistical significance in the primary efficacy endpoint of urinary albumin to creatinine ratio at 24 weeks for a Phase 2 clinical trial. CTP-354 is subject to development risks normally inherent in clinical development because no corresponding non-deuterated compound has been clinically evaluated. While Merck & Co. reported that the non-deuterated analog of CTP-354 activated the a2, a3 and a5 $GABA_A$ receptors, which are associated with anti-spasticity, muscle relaxation, anti-anxiety, anti-seizure and, potentially, anti-pain activities, with approximately 40% of the *in vitro* activity of a benzodiazepine, we do not know if the pharmacological profile of CTP-354 will be clinically effective for treating spasticity at doses of CTP-354 that are well tolerated.

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.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial, such as the results of our preliminary analyses of data from our Phase 2 clinical trial of CTP-499 that are presented in this Annual Report on Form 10-K, do not necessarily predict final results. For example, although Phase 1 clinical trials of CTP-499 supported advancement into Phase 2 clinical trials, CTP-499 failed to achieve statistical significance in the primary efficacy endpoint of urinary albumin to creatinine ratio in the Phase 2 clinical trial. However, we believe that the incidence of large declines in kidney function, measured as decreases in eGFR or increases in serum creatinine in drug-treated versus placebo-treated patients, could become the primary efficacy endpoint required by the FDA for Phase 3 clinical development of a drug candidate for the treatment of type 2 diabetic kidney disease. While incidence of large declines in eGFR was a secondary endpoint of our ongoing Phase 2 clinical trial, preliminary analyses of our current data from the trial indicate that we have not achieved a statistically significant result in this endpoint. Even if our Phase 2 clinical trial of CTP-499 ultimately demonstrates positive results with respect to this metric as a secondary endpoint, any such results may not be indicative of the results that we may achieve in Phase 3 clinical trials. Furthermore, the FDA has not yet approved incidence of large declines in eGFR as an acceptable endpoint for a Phase 3 clinical trial for the treatment of type 2 diabetic kidney disease. If the endpoints approved by the FDA for Phase 3 clinical trials in this indication differ from the endpoints of the clinical trials we have conducted of CTP-499, we may need to conduct additional clinical trials of CTP-499 to support entry into Phase 3 clinical evaluation.

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. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. 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.

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In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. For example, while we have conducted Phase 1 clinical trials to evaluate the safety and tolerability of single doses of CTP-354, we have not yet evaluated the safety or efficacy of CTP-354 administered in multiple doses or in the intended patient population, each of which will be required for FDA approval, and the FDA has placed a partial clinical hold on CTP-354 that prevents us from administering doses in excess of 60 mg per day in single dose clinical trials and 6 mg per day in multiple dose clinical trials. Any Phase 2, Phase 3 or other clinical trials that we, or our collaborators, may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates.

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, and our collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Comparable foreign regulatory authorities, such as the European Medicines Agency, or EMA, impose similar restrictions. We, and our collaborators, may never receive such approvals. We, and our collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we, or they, will be able to obtain these approvals. For example, as described above, the FDA has placed a partial clinical hold on CTP-354 that prevents us from administering doses in excess of 60 mg per day in single dose clinical trials and 6 mg per day in multiple dose clinical trials. If we are delayed in addressing, or unable to address, the FDA s concerns, we could be delayed, or prevented, from studying higher doses of CTP-354, which higher doses may be necessary to show efficacy. If these higher doses are necessary to show efficacy, we could be delayed or prevented from obtaining marketing approval of CTP-354.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We, and our collaborators, have not previously submitted an NDA to the FDA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates.

Any inability to successfully complete preclinical 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 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.

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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:

clinical trials of our product candidates may produce unfavorable or inconclusive results, such as with Part 1 of our Phase 2 clinical trial for CTP-499;

we, or our collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon product 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;

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 from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial s duration;

we, or our collaborators, may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;

regulators or institutional review boards 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 preclinical studies and clinical trials;

the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we, or our collaborators, enter into agreements for clinical and commercial supplies;

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; 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

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trials and prepare for possible commercialization of our product candidates. We, and our collaborators, do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical 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.

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

We, or our collaborators, may not be able to initiate or continue clinical trials for CTP-354 or any of our other 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 EMA. 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 proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians and patients perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved 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.

We believe we, or our collaborators, may in some instances be able to secure clearances from the FDA or comparable foreign regulatory authorities to use expedited development pathways. If unable to obtain such clearances, we, or they, may be required to conduct additional preclinical studies or clinical trials beyond those that we, or they, contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals.

The deuterated compounds that we produce and seek to develop can have similar pharmacological properties as their corresponding non-deuterated compounds. Therefore, we believe that we, or our collaborators, may, in some instances, be able to obtain clearance from the FDA or comparable foreign regulatory authorities to follow expedited development programs for some deuterated compounds that reference and rely on findings previously

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obtained from prior preclinical studies or clinical trials of the corresponding non-deuterated compounds. For example, our collaborator Avanir reported in June 2013 that the FDA has agreed to an expedited development pathway for AVP-786, a product candidate Avanir is developing that includes our licensed deuterated dextromethorphan compound, permitting Avanir to reference data from its development of dextromethorphan and quinidine in its IND, and any future NDA, for AVP-786.

While we anticipate that following an expedited development pathway may be possible for some of our current and future product candidates, we cannot be certain that we, or our collaborators, will be able to secure clearance to follow such expedited development pathways from the FDA or comparable foreign regulatory authorities. In addition, if we follow, or one of our collaborators follows, such an expedited regulatory pathway and the FDA or comparable foreign regulatory authorities are not satisfied with the results of our having done so, such as might be the case if a deuterated compound is found to have undesirable side effects or other undesirable properties that were not anticipated based on the corresponding non-deuterated compound, the FDA or foreign regulatory authorities may be unwilling to grant clearance to follow expedited development pathways for other deuterated compounds.

Consequently, we, or our collaborators, may be required to pursue full development programs with respect to any product candidates that we, or they, previously anticipated would be able to follow an expedited development pathway, including conducting a full range of preclinical and clinical studies to attempt to establish the safety and efficacy of these product candidates. A need to conduct a full range of development activities would significantly increase the costs of development and length of time required before we, or our collaborators, could seek marketing approval of such a product candidate as compared to the costs and timing that we or they anticipate. While we have been able to reference, for purposes of some of our IND-enabling studies, data generated during development of the corresponding non-deuterated compound, we have not ourselves obtained clearance from the FDA or any comparable foreign regulatory authority to reference such data in connection with more advanced stages of development.

Serious adverse events or undesirable side effects or other unexpected properties of CTP-354 or any of our other 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.

Serious adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, one of our collaborators, an institutional review board or regulatory authorities to interrupt, 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 increased 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 other 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.

For CTP-354, we are seeking to achieve $GABA_A$ receptor occupancy levels that are well above those attained by other $GABA_A$ modulators, such as benzodiazepines, and we do not know what adverse effects may be associated with such high $GABA_A$ receptor occupancy. In our clinical trials of CTP-354, moderate adverse events have been reported including dizziness, drowsiness and nausea at single doses. Additional or more serious adverse events, undesirable

side effects or other unexpected properties of CTP-354 or any of our other product candidates

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could arise or become known either during further clinical development or, if approved, after the approved product has been marketed. If such an event occurs during development, clinical trials for our product candidates could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us or our collaborators to cease further development, require us to conduct additional clinical trials or other tests or studies or deny approval of the applicable product candidate.

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.

We have never commercialized a product. Even if CTP-354 or any of our other 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 and others in the medical community. 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.

Efforts to educate the medical community 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 CTP-354 or any of our other 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, contained in the product s approved labeling;
- our ability, or the ability of our collaborators, to offer the product for sale at competitive 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;

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;

availability and amount of reimbursement from government payors, managed care plans and other third party payors;

adverse publicity about the product or favorable publicity about competitive products; and

potential product liability claims.

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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 effective than previously believed or causes undesirable side effects that were not previously identified, 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 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 or seize the drug;
- we, or our collaborators, may be required 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;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;
- we, or our collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or our collaborators, could be sued and held liable for harm caused to patients;
- the drug may become less competitive; and

our reputation may suffer.

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 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 plan 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

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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 we could otherwise develop and commercialize the product independently.

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 commercialize our product candidates outside the United States through collaboration, licensing and distribution arrangements with third parties. 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.

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.

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 CTP-354 and any other of 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 the key indications of our priority programs, including spasticity, neurologic disorders, cancer and inflammation. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, 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, which could render our product candidates obsolete and noncompetitive.

We are initially developing CTP-354 for the treatment of spasticity in multiple sclerosis and spinal cord injury. Current first-line treatment for spasticity includes oral and local agents and physical and occupational therapy. Four oral drugs have been approved in the United States for the treatment of spasticity: baclofen (Lioresal®), tizanidine (Zanaflex®), diazepam (Valium) and dantrolene (Dantrium®), each of which is available on a generic basis. Spasticity is also treated through localized injections of botulinum toxin. In addition, there are several potentially competitive product candidates in Phase 3 clinical development being pursued by pharmaceutical and biotechnology companies, including GW Pharmaceuticals plc and Osmotica Pharmaceuticals Corp.

We are developing CTP-499 for the treatment of type 2 diabetic kidney disease in patients with macroalbuminuria. The current standard of care in this indication is angiotensin modulation, which is treatment with an angiotensin converting enzyme inhibitor, which we refer to as an ACEi, or an angiotensin receptor blocker, which we refer to as

an ARB. Both of these types of drugs are available on a generic basis. We are developing CTP-499 for administration in combination with these drugs. These drugs are well established therapies that are widely accepted by physicians, patients and third party payors. Physicians, patients and third party payors may not accept the addition of CTP-499 to their current treatment regimens for a variety of potential reasons, including a desire not to incur the additional cost of CTP-499 or a perception that the addition of CTP-

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499 would be poorly tolerated or of limited benefit. If CTP-499 receives marketing approval, it may also face competition from a number of product candidates that are currently in clinical development including potentially competitive product candidates in Phase 3 clinical development being pursued by AbbVie Inc., Janssen Research & Development LLC and NephroGenex, Inc.

Avanir has reported that it plans to develop AVP-786 for the treatment of neurologic and psychiatric disorders. There are a number of marketed drugs and product candidates in clinical development for these indications.

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 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, preclinical 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.

We also face competition in the development of deuterated compounds.

Several large pharmaceutical and biotechnology companies have begun to cover deuterated analogs of their product candidates in patent applications and may choose to develop these deuterated compounds. These large pharmaceutical and biotechnology companies may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. In addition, we know of one biotechnology company, Auspex Pharmaceuticals, Inc., and possibly two others, DeutRx LLC and Berolina innovative Research and Development Services Pharma GmbH, that are developing product candidates based on deuterium substitution. These competitors may be more successful than us in developing deuterated compounds. 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.

If our competitors in the development of deuterated compounds are able to grow their intellectual property estates and create new and successful deuterated compounds more effectively than us, our ability to identify additional compounds for preclinical and clinical development and obtain product revenues in future periods could be compromised, which could result in significant harm to our operations and financial position.

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 abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical

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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 may be 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 Federal Food, Drug, and Cosmetic Act, or 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 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, our products will likely 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 in the same indications. 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.

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.

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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. 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.

Our ability, and the ability of our collaborators, to commercialize CTP-354 or any other product candidate will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. 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 the prices for our products, if any, decrease or if governmental and other third party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including 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 and are 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

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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 our 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.

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

A significant portion of the research that we are conducting involves the development of new deuterated compounds using our DCE Platform. The drug discovery that we are conducting using our DCE Platform may not be successful in creating compounds that have commercial value or therapeutic utility beyond the corresponding non-deuterated compound, or at all. Our research programs may initially show promise in creating potential product candidates, yet fail to yield viable product candidates for clinical development for a number of reasons, including:

- deuterated analogs of existing non-deuterated compounds or newly designed deuterated compounds may not demonstrate satisfactory efficacy or other benefits, such as convenience of dosing, increased tolerability, enhanced formation of desirable active metabolites or reduced formation of toxic metabolites;

- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance; or

- pharmaceutical companies have begun to claim deuterated analogs of their compounds in patent filings, resulting in otherwise promising deuterated product candidates already being covered by patents or patent applications.

Our research programs to identify new product candidates will require substantial technical, financial and human resources. We may be unsuccessful in our efforts to identify new potential product candidates. In addition, we may focus our efforts and resources on one or more potential product candidates that ultimately prove to be unsuccessful.

If we are unable to identify suitable additional compounds for preclinical 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.

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. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result

in:

- decreased demand for 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 resulting litigation;

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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;

reduced resources of our management to pursue our business strategy; and

the inability to commercialize any products that we may develop.

Although we maintain general liability insurance of $2 million in the aggregate and clinical trial liability insurance of $5 million in the aggregate, this insurance 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.

JZP-386 is a deuterated analog of a Schedule I controlled substance and will likely be classified as a Schedule I or Schedule III controlled substance, which could substantially limit our ability to obtain the quantities of JZP-386 needed to conduct clinical trials and the ability of our collaborator to market and sell JZP-386 if it receives marketing approval. We also expect CTP-354 to be classified as a Schedule IV controlled substance, which would result in restrictions on the sale and distribution of that product if it receives marketing approval.

The placement of drugs or other substances into schedules under the Controlled Substances Act of 1970, the CSA, is based upon the substance s medical use, potential for abuse and safety or dependence liability. Under the CSA, every person who manufactures, distributes, dispenses, imports or exports any controlled substance must register with the U.S. Drug Enforcement Agency, or DEA, unless exempt. Our product candidate JZP-386, which we have licensed to Jazz Pharmaceuticals, is a deuterium-substituted analog of sodium oxybate. Sodium oxybate is regulated as a chemical by the DEA as a Schedule I controlled substance. Because of the Schedule I classification of sodium oxybate, JZP-386 is regulated by the DEA as a Schedule I controlled substance. As a result, we or Jazz Pharmaceuticals will be required to obtain a license to ship the chemical intermediate that we are using as the precursor to JZP-386, which may delay or prevent the manufacturing of JZP-386 for clinical trials.

Specifically, the DEA limits the quantity of certain Schedule I controlled substances that may be produced in the United States in any year through a quota system. If our contract manufacturers for JZP-386, or those for Jazz Pharmaceuticals, manufacture JZP-386 in the United States, they will be required to obtain separate DEA quotas to supply us or Jazz Pharmaceuticals with JZP-386 for the conduct of clinical trials. Different, but potentially no less burdensome regulations, may apply if we or Jazz Pharmaceuticals choose to contract for the manufacture of JZP-386 outside of the United States.

The process of obtaining the quotas needed to conduct the planned clinical trials of JZP-386 may involve lengthy legal and other efforts and we or Jazz Pharmaceuticals, or suppliers or manufacturers for us or Jazz Pharmaceuticals, may not be able to obtain sufficient quotas from the DEA. If we or Jazz Pharmaceuticals, or suppliers or manufacturers for us or Jazz Pharmaceuticals, cannot obtain the quotas that are needed on a timely basis, or at all, we and Jazz Pharmaceuticals may not be able to conduct, on a timely basis or at all, the clinical trials of JZP-386 that are planned, including the Phase 1 clinical trial that we will be responsible for conducting, and our business, financial condition, results of operations and growth prospects could be adversely affected.

If JZP-386 is approved for marketing in the United States, we believe that the commercial drug containing JZP-386 will remain subject to the CSA as a Schedule III controlled substance. Those restrictions could limit the

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marketing and distribution of the commercial drug containing JZP-386. We also expect our product candidate, CTP-354, to be classified as a Schedule IV controlled substance under the CSA. Although the CSA s restrictions governing substances in Schedule IV are not as stringent as those for substances in Schedule III, they too could limit our ability to market and sell CTP-354, if it is approved for marketing.

In addition, failure to maintain compliance with applicable requirements under the CSA, particularly as manifested in loss or diversion of regulated substances, can result in enforcement action that could include civil penalties, refusal to renew registrations or quotas, revocation of registrations or quotas or criminal proceedings, any of which could have a material adverse effect on our business, results of operations and financial condition. Individual states also regulate controlled substances, and we and Jazz Pharmaceuticals, and contract manufacturers for us and Jazz Pharmaceuticals, will be subject to state regulation on distribution of these products.

RISKS RELATED TO OUR DEPENDENCE ON THIRD PARTIES

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 with Celgene, Avanir and Jazz Pharmaceuticals 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. 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 the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of 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 such as occurred in a prior collaboration we had with Glaxo Group Limited, or GSK;
- 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;

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;

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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. For example, conducting pivotal Phase 3 clinical trials of CTP-499 in patients with type 2 diabetic kidney disease with macroalbuminuria will likely involve significant cost and we expect that we would conduct any large Phase 3 clinical trial of CTP-499 in type 2 diabetic kidney disease in collaboration with one or more partners. A key element of our business strategy is the development of deuterated product candidates based on approved drugs, advanced clinical candidates or previously studied compounds. Our likely collaborators for these product candidates in many cases will include the pharmaceutical companies that developed the corresponding non-deuterated compounds. In addition, likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator s evaluation of a number of factors. Those factors may include the potential differentiation of our product 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 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 for similar indications that may be available for collaboration and whether such a 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 on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to

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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 preclinical or clinical studies of the corresponding non-deuterated compound.

We rely on third parties to conduct our clinical trials. If they 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. Any of these third parties may terminate their engagements with us under certain circumstances. If we need to enter into alternative arrangements, it could delay our product development activities.

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, regulatory 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 standards, commonly referred to as current Good Clinical Practices, or cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these cGCPs 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 cGCPs, 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 cGCPs. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with 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, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with 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 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.

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Because there are limited sources of deuterium, we, and our collaborators, are exposed to a number of risks and uncertainties associated with our deuterium supply.

We believe that all of the deuterium that we use in manufacturing our product candidates is currently derived, directly or indirectly, from deuterium oxide. For most of our deuterium supply we rely on bulk supplies of deuterium oxide, which we currently source from two suppliers, one located in the United States and one located abroad, which is affiliated with a foreign government. We may establish a deuterium oxide supply arrangement with an additional supplier, which is located outside of the United States and is affiliated with a foreign government. It is also possible that our current U.S. supplier of deuterium oxide relies on our current foreign supplier, as well as our potential future foreign supplier, for its supply of deuterium oxide, although we are not familiar with its procurement practices.

We estimate that our current source of deuterium oxide will be sufficient to meet our anticipated requirements through at least 2015. However, we do not have long-term agreements with our current suppliers. If we are not able to establish or maintain supply arrangements with the foreign government-affiliated suppliers from which we have purchased and believe we may be able to purchase additional deuterium oxide, or the relevant foreign governments decide to withhold any authorization for the export of deuterium oxide that we seek, we may be unable to secure alternative sources. If we are unable to obtain sufficient supplies of deuterium oxide from our current suppliers or our potential future foreign supplier, we would be forced to either seek alternative suppliers of deuterium oxide, likely in other countries, or alternative sources of deuterium. Such alternative supplies may not be available to us on acceptable terms or at all.

In order to internationally transport any deuterium oxide that we purchase from either of these two foreign suppliers, we, or our U.S. supplier, may be required to obtain an export license from the country of origin and we may be required to obtain an International Import Certificate from the country of destination. We are also required to obtain an export license from the Nuclear Regulatory Commission before shipping deuterium oxide from the United States to any contract manufacturer in another country. Each of these documents specifies the maximum amount of deuterium oxide that we, or our suppliers, are permitted to either import or export. In particular, in order to obtain additional supplies of deuterium oxide from the foreign-government affiliated supplier from which we have purchased deuterium oxide, we will be required to obtain an additional export license from the country of origin and a U.S. import certificate. While we have obtained similar licenses and certificates in the past, we may not be able to obtain them in the future in a timely manner or at all. We have not obtained an export license from the country in which our potential future foreign supplier is located and may not be able to do so in a timely fashion or at all. In addition, our current U.S. export licenses may be insufficient to meet our future requirements and we may not be able to obtain further licenses in a timely manner or at all.

Certain of our manufacturing processes for our product candidates incorporate deuterium by using deuterated chemical intermediates or reagents that are derived from deuterium oxide. For the deuterated chemical intermediates and reagents, we are not subject to the license requirements applicable to deuterium oxide; however the manufacturer of the deuterated chemical intermediate or reagent may themselves be required to obtain deuterium oxide under applicable licensing requirements. Most of the manufacturers of these deuterated chemical intermediates and reagents are not located in countries that produce bulk quantities of deuterium oxide. Therefore, our ability to source these deuterated chemical intermediates will depend on the ability of these manufacturers to obtain deuterium oxide from other countries. In the future we may arrange for supplies of deuterated chemical intermediates or reagents from manufacturers located in countries from which they can source deuterium oxide in bulk. However, contract manufacturers in these countries may not represent a viable alternative to our current suppliers. We do not have long-term agreements with our suppliers of deuterated chemical intermediates or reagents and we obtain some of these deuterated chemical intermediates or reagents from single sources, putting us at risk of uncontrolled cost increases or supply interruptions if we cannot establish alternative sourcing arrangements. Deuterated chemical intermediates may

be expensive or difficult to obtain or may be produced by specialized techniques that are not widely practiced and we may not be able to enter into arrangements for larger scale supply of deuterated chemical intermediates on acceptable terms, or at all.

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If we are unable to obtain sufficient supplies of deuterium, our ability to produce our product candidates would be impeded and our business, financial condition and prospects could be harmed. In particular, certain of our manufacturing processes, including those for CTP-499 and certain other of our product candidates, are projected to require particularly large quantities of deuterium for late-stage clinical trials and for commercialization. Consequently, any adverse impact on our ability to obtain deuterium oxide from our current suppliers, import deuterium oxide into the United States or export deuterium oxide to our contract manufacturers could have a particularly severe impact on our ability to develop or commercialize those product candidates.

Similarly, to develop and commercialize any of our licensed product candidates, our collaborators will need to obtain supplies of deuterium and will be subject to risks and requirements in connection with sourcing deuterium that are similar to the ones that we face. In addition, if any of our product candidates is approved by the FDA, then the FDA will also have regulatory jurisdiction over the manufacture and use of deuterium oxide and deuterated chemical intermediates or reagents in such products. Any adverse impact on our, or our collaborators , ability to obtain deuterium could delay or prevent the development or commercialization of our product candidates, which could have a material adverse effect on our business.

We contract with third parties for the manufacture and distribution of our product candidates for clinical trials 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, which could delay, prevent or impair our development or commercialization efforts.

We currently have only very limited internal capabilities to manufacture our product candidates. We currently rely, and expect to continue to rely, on third party contractors to manufacture preclinical 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, 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 if our third party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the possible termination or nonrenewal of agreements by our third party contractors at a time that is costly or inconvenient for us;
- the possible breach by the third party contractors of our agreements with them;
- the failure of third party contractors to comply with applicable regulatory requirements;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;

the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and

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

We currently rely on a small number of third party contract manufacturers to supply the majority of our required finished product for our preclinical studies and clinical trials. We do not have long-term agreements with any of these third parties. If any of our existing manufacturers should become unavailable to us for any reason, we may incur some delay in identifying or qualifying replacements.

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,

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especially if the manufacturer believes it is uniquely suited to use our deuterium chemistry manufacturing processes 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 current good manufacturing practices, or 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 approved 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 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 cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate.

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.

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 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 compounds are 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.

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

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similar compounds. 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 limit, in part or in whole, our ability to seek and obtain patent protection for new product candidates based on deuterium modification of compounds. It may also limit in part or in whole, our ability to develop new product candidates based on deuterium modification of such compounds without obtaining a license from those patent holders.

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. Moreover, we may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, inter partes review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such 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 which 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 United States 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. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against

competing products or processes sufficient to achieve our business objectives.

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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 U.S. Patent and Trademark Office post-grant review procedures. 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.

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.

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. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent s claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there

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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 sued for infringing intellectual property rights of third parties, 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 and use our DCE Platform without infringing the intellectual property and other proprietary rights of third parties. Numerous third party U.S. and non-U.S. issued patents and pending applications exist for compounds and methods of use for the treatment of spasticity, kidney disease, neurologic disorders, cancer and inflammation, the key indications for our priority programs. In addition, some of the non-deuterated compounds on which our product candidates are, or future product candidates may be, based 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. 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.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our products candidates, including interference proceedings before the U.S. Patent and Trademark Office. 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 pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the 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 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. However, we are not aware of any judicial proceedings addressing the question of whether our product would be outside the scope of such a patent claim. 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. 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

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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.

RISKS RELATED TO REGULATORY APPROVAL AND OTHER LEGAL COMPLIANCE

MATTERS

Even if we complete the necessary preclinical and clinical studies, the marketing approval process is expensive, time consuming and uncertain and may prevent us or our collaborators from obtaining 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. We, and our collaborators, are not permitted to market our product candidates in the United States or in other countries until we, or they, receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside the United States. 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 conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the 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.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we, 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, and 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

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approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. 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 Risk Evaluation and Mitigation Strategy, or REMS.

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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 health care 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 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;
- 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.

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. We expect that current laws, as well as other healthcare reform measures that be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or our collaborators, may receive for any approved products.

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 and could decrease the coverage and price that we, or our collaborators, may 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.

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More recently, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the 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

United States 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 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. These include the following:

Anti-Kickback Statute. The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or

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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 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, currently set at $5,500 to $11,000 per false claim;

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters, 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 laws require applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals;

Controlled Substances Act. The CSA regulates the handling of controlled substances such as JZP-386 and, potentially, CTP-354; and

Analogous State and Foreign Laws. Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws can apply to sales or marketing arrangements and claims involving healthcare items or services and are generally broad and are enforced by many different federal and state agencies as well as through private actions.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. 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.

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 and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we

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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. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental 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.

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.

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 medical 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

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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.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug manufacturing, regulatory affairs and sales, 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. Our inability to effectively manage the expansion of our operations may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

RISKS RELATED TO OUR COMMON STOCK

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

Our stock price may be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the prices they paid for it. The market price for our common stock may be influenced by many factors, including:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials of CTP-354 and CTP-499 and any other product candidate;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our development programs;

results of clinical trials of product candidates of our competitors;

regulatory or legal developments in the United States and other countries;

developments or disputes concerning patent applications, issued patents or other proprietary rights;

the recruitment or departure of key personnel;

the level of expenses related to any of our product candidates or clinical development programs;

the results of our efforts to 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;

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sales of our common stock by us, our insiders or other stockholders;

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, if any, that cover our stock;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors;

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 will have 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 an emerging growth company, and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act, and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor s report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute

payments not previously approved. In this Annual Report on Form 10-K, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. 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.

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

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We are currently incurring and expect to continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a newly public company, we are incurring and expect to incur additional significant legal, accounting and other expenses that we did not incur as a private company. We expect that these expenses will further increase after we are no longer an emerging growth company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that we will need to hire additional accounting, finance and other personnel to comply with the requirements of being a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to SOX Section 404 we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the SEC. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, 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 is restricted from immediate resale but 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. Of the 17,249,895 shares of our common stock outstanding as of February 28, 2014, 11,695,895 shares are currently subject to restrictions on transfer under 180-day lock-up arrangements with either the underwriters for our initial public offering or under stock option agreements entered into between us and the holders of those shares. These restrictions are due to expire on August 11, 2014, resulting in these shares becoming eligible for public sale on August 12, 2014 if they are registered under the

Securities Act of 1933, as amended, which we refer to as the Securities Act, or if they qualify for an exemption from registration under the Securities Act, including under Rules 144 or 701.

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Moreover, holders of an aggregate of 9,919,821 shares of our common stock, have rights, subject to conditions, to require us to file registration statements covering their shares or, along with the holder of a warrant to purchase 70,796 shares of common stock, to include their shares in registration statements that we may file for ourselves or other stockholders. We also plan to register all 4,159,374 shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates and the lock-up arrangements described above.

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, the terms of our debt facility with Hercules preclude us from paying dividends, and any future debt agreements may also 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.

As of February 28, 2014, our executive officers and directors, combined with our stockholders who owned more than 5% of our outstanding common stock, and their affiliates, in the aggregate, beneficially owned shares representing approximately 49.9% 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.

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 bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which 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 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;

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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 stockholder meetings;

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 bylaws.

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.

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 would likely 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.

ITEM 1B. Unresolved Staff Comments

None

ITEM 2. Properties

We lease our principal facilities, which consist of approximately 45,000 square feet of office, research and laboratory space located at 99 Hayden Avenue, Lexington, Massachusetts. The leases covering this space expire on September 30, 2015. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

ITEM 3. Legal Proceedings

We are not currently a party to any material legal proceedings.

ITEM 4. Mine Safety Disclosures

Not applicable.

ITEM 5. Market for Registrant s Common Equity, Related Stockholder Matters and Issuers 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. Prior to that time, there was no public market for our common stock. As a result, we have not set forth quarterly information with respect to the high and low prices for our common stock for the two most recent fiscal years.

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HOLDERS

As of March 28, 2014, there were 55 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. Our ability to pay dividends on our common stock is prohibited by the covenants of our debt facility with Hercules and may be further restricted by the terms of any of our future indebtedness.

RECENT SALES OF UNREGISTERED SECURITIES

Set forth below is information regarding shares of common stock issued, and options granted, by us during 2013 that were not registered under the Securities Act of 1933, as amended, or the Securities Act. Included is the consideration, if any, we received for such shares, options and warrants and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, or the SEC, under which exemption from registration was claimed. No underwriters were involved in any such issuances.

During 2013, we granted options to purchase an aggregate of 81,057 shares of common stock, each at an exercise price of $3.73 per share, to employees pursuant to our 2006 Stock Option and Grant Plan. During 2013, we issued an aggregate of 8,062 shares of common stock upon the exercise of options for aggregate consideration of $32,169.

The stock options and the common stock issuable upon the exercise of such options described above were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

PURCHASE OF EQUITY SECURITIES

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

USE OF PROCEEDS FROM REGISTERED SECURITIES

We effected the initial public offering, or IPO, of our common stock through a Registration Statement on Form S-1 (File No. 333-193335) that was declared effective by the Securities and Exchange Commission on February 12, 2014, and a registration statement on Form S-1 (File No. 333-193920) filed pursuant to Rule 462(b) of the Securities Act that became effective on February 12, 2014. On February 19, 2014, we completed the sale of 6,000,000 shares of common stock in our IPO at a price to the public of $14.00 per share, resulting in net proceeds to us of $74.6 million after deducting underwriting discounts and commissions of $5.9 million and offering costs of $3.5 million. In addition, we granted the underwriters a 30-day option to purchase up to 900,000 additional shares of common stock at the IPO price to cover over allotments, if any. On March 3, 2014, we completed the additional sale of 649,690 shares of common stock under this option at a price to the public of $14.00 per share, resulting in net proceeds to us of $8.5 million after deducting underwriting discounts and commissions of $0.6 million. The offering commenced on February 12, 2014 and terminated before the sale of all of the securities registered in the offering. None of the

underwriting discounts and commissions or other offering expenses were paid to directors or officers of ours or their associates or to persons owning 10 percent or more of our common stock or to any affiliates of ours. UBS Securities LLC and Wells Fargo Securities, LLC

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acted as joint book-running managers of the offering and as representatives of the underwriters. JMP Securities LLC acted as lead manager and Roth Capital Partners, LLC acted as co-manager for the offering. There were no selling stockholders in the offering.

As of March 21, 2014, we estimate that we have used approximately $5.2 million of the net proceeds primarily to fund the development of CTP-354, to advance and expand the research and preclinical development of additional product candidates and for working capital, capital expenditures and other general corporate purposes. None of the net proceeds were paid directly or indirectly to directors or officers of ours or their associates or to persons owning 10 percent or more of our common stock or to any affiliates of ours, other than payments in the ordinary course of business to officers for salaries and to non-employee directors as compensation for board or board committee service. We have invested the balance of the net proceeds from the offering in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities. There has been no material change in our planned use of the balance of the net proceeds from the offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act.

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ITEM 6. Selected Financial Data

You should read the following selected consolidated financial data together with our consolidated financial statements and accompanying notes appearing elsewhere in this Annual Report on Form 10-K and the Management s Discussion and Analysis of Financial Condition and Results of Operations section of this Annual Report on Form 10-K. We have derived the statement of operations data for the years ended December 31, 2011, 2012 and 2013 and the balance sheet data as of December 31, 2012 and 2013 from our audited financial statements included in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of the results that may be expected in any future period.

(in thousands, except per share data)	2011	2012	2013
Revenue:			
License and research and development revenue	$ 13,967	$ 11,349	$ 23,408
Milestone revenue	5,500	1,500	2,000
Total revenue	19,467	12,849	25,408
Operating expenses:			
Research and development	$ 23,436	$ 24,193	$ 21,790
General and administrative	7,377	7,266	8,028
Total operating expenses	30,813	31,459	29,818
Loss from operations	(11,346)	(18,610)	(4,410)
Investment income	44	22	21
Interest and other expense	(18)	(1,856)	(1,667)
Net loss	$ (11,320)	$ (20,444)	$ (6,056)
Accretion on redeemable convertible preferred stock	(1,069)	(388)	(396)
Net loss applicable to common stockholders basic and diluted	$ (12,389)	$ (20,832)	$ (6,452)
Net loss per share applicable to common stockholders basic and diluted	$ (9.66)	$ (16.15)	$ (4.99)
Weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted	1,283	1,290	1,292

	As of December 31,		
Consolidated balance sheet data: (in thousands)	**2011**	**2012**	**2013**
Cash and cash equivalents	$ 22,949	$ 7,490	$ 9,638
Short-term investments, available for sale	19,705	20,067	23,039
Working capital	33,861	20,940	18,128

Total assets	49,403	33,129	39,773
Deferred revenue	11,022	2,750	19,631
Loan payable, net of discount	7,135	19,731	14,919
Redeemable convertible preferred stock	111,460	111,848	112,244
Total stockholders deficit	$ (86,718)	$ (106,687)	$ (112,104)

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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 risks and uncertainties. You should read the Risk Factors section in Part 1 Item 1A. of this report for a discussion of important factors that could cause 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 applying our extensive knowledge of deuterium chemistry to discover and develop novel small molecule drugs. Our approach starts with approved drugs, advanced clinical candidates or previously studied compounds that we believe can be improved with deuterium substitution, a process we refer to as deuteration, to provide better pharmacokinetic or metabolic properties and thereby enhance clinical safety, tolerability or efficacy. We believe this approach may enable drug discovery and clinical development that is more efficient and less expensive than conventional small molecule drug research and development.

We are utilizing our DCE Platform to discover and develop product candidates for a variety of indications. CTP-354 and AVP-786 are advancing in clinical trials and we have multiple preclinical candidates, two of which we expect to move into clinical trials in 2014. Our priority programs include:

- CTP-354 for spasticity associated with multiple sclerosis and spinal cord injury, which is in Phase 1 clinical trials;
- CTP-499 for type 2 diabetic kidney disease, which is in a Phase 2 clinical trial;
- AVP-786 for neurologic and psychiatric disorders, which has completed a Phase 1 clinical trial under our collaboration with Avanir;
- CTP-730 for inflammatory diseases, which is in preclinical development under our collaboration with Celgene; and
- JZP-386 for narcolepsy, which is in preclinical development under our collaboration with Jazz Pharmaceuticals.

Since our inception in 2006, we have devoted substantially all of our resources to our research and development efforts relating to our product candidates, including activities to: develop our DCE Platform and our core capabilities in deuterium chemistry, identify potential product candidates, undertake preclinical studies and clinical trials, manufacture product in compliance with current good manufacturing practices, provide general and administrative support for these operations and establish our intellectual property. We have generated an accumulated deficit of $113.6 million since inception through December 31, 2013 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 funded our operations primarily through the public offering and private placement of our equity, debt financing and funding from collaborations. Since inception through December 31, 2013, we have raised an aggregate of $222.3 million to fund our operations, of which $89.3 million was through upfront license fees, milestone payments, reimbursement of research and development costs and other payments under our current and former collaborations, $113.0 million in gross proceeds from the sale of convertible preferred stock, which includes an equity premium of $3.9 million, and $20.0 million was from the gross proceeds of a secured debt financing and the related issuance of a warrant to purchase preferred stock.

On February 19, 2014, we completed the sale of 6,000,000 shares of common stock in our initial public offering, or IPO, at a price to the public of $14.00 per share, resulting in net proceeds to us of $74.6 million after

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deducting underwriting discounts and commissions of $5.9 million and offering costs of $3.5 million. On March 3, 2014, we completed the sale of an additional 649,690 shares of common stock at a price to the public of $14.00 per share under the underwriters over-allotment option to purchase additional shares of common stock, resulting in net proceeds to us of $8.5 million after deducting underwriting discounts and commissions.

We have incurred net losses in each year from our inception in 2006 through 2013. Our net losses were $11.3 million, $20.4 million and $6.1 million for the years ended December 31, 2011, 2012 and 2013, respectively. We do not expect to be profitable for the year ending December 31, 2014. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

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 to develop and conduct clinical trials and additional preclinical studies with respect to CTP-354;
- initiate and continue research, preclinical and clinical development efforts for our other product candidates and potential product candidates;
- seek to identify 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;
- hire additional personnel, such as clinical, quality control and scientific personnel;
- add equipment and physical infrastructure to support our research and development; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and personnel and infrastructure necessary to help us comply with our obligations as a

public company.

We do not expect to generate revenue from product sales unless and until we, or our collaborators, successfully complete development and 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. We have developed the internal capability to manufacture up to low kilogram quantities of deuterated active pharmaceutical ingredients for use in Phase 1 clinical trials. However, to date, almost all of our manufacturing activities have been performed by third parties. Additionally, we currently utilize third-party contract research organizations to carry out our clinical development activities and we do not yet have a sales organization. If we obtain or believe that we are likely to obtain, marketing approval for any of our product candidates for which we retain commercialization rights, 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 and additional collaborations and licensing arrangements 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

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specific development programs and our DCE Platform. They also have provided us with access to the considerable scientific, development, regulatory and commercial capabilities of our collaborators. 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 to seek an expedited development or regulatory pathway by relying on previous clinical data regarding their corresponding non-deuterated compound. For example, our collaborator Avanir reported agreeing with the FDA to an expedited development pathway for AVP-786. We believe that our collaborations have contributed to our ability to progress our product candidates and build our DCE Platform. We have established the following key collaborations:

Celgene. In April 2013, we entered into a master development and license agreement with Celgene, which is primarily focused on the research, development and commercialization of specified deuterated compounds targeting cancer or inflammation. The collaboration is initially focused on one program, but has the potential to encompass up to four programs. For the initial program, we granted Celgene an exclusive worldwide license to develop, manufacture and commercialize deuterated analogs of a selected non-deuterated compound and several close chemical derivatives thereof. We further granted Celgene licenses with respect to two additional programs and an option with respect to a third additional program. We and Celgene have agreed on the non-deuterated compound for each of the two additional license programs. For the option program, Celgene may select the non-deuterated compound at a later time, which, unless otherwise agreed by us, will be limited to a compound for which Celgene possesses exclusive rights. With respect to the two additional license programs, we granted Celgene an upfront exclusive worldwide license to develop, manufacture and commercialize deuterated products that contain deuterated analogs of the agreed upon non-deuterated compounds. Celgene is restricted from utilizing their research, development and commercialization rights under each of the upfront licenses, unless, within seven years after the effective date of the agreement, Celgene pays us a license exercise fee. If Celgene does not elect to pay the license exercise fee during the seven year period, the license will expire. With respect to the option program, once a compound is selected, Celgene may exercise its option by paying us an option exercise fee within seven years of the effective date of the agreement, and upon Celgene s exercise of the option we will grant to Celgene an exclusive worldwide license to develop, manufacture and commercialize deuterated products that contain deuterated analogs of the selected non-deuterated compound.

Under the Celgene agreement, we received a non-refundable upfront payment of $35.0 million in April 2013. During the year ended December 31, 2013, we recognized $17.0 million of revenue upon the delivery of a license for the initial program and $1.3 million of revenue related to research and development services performed on the initial program. In addition, we are eligible to earn up to $23.0 million in development milestone payments, including $8.0 million related to the completion of a Phase 1 clinical trial, up to $247.5 million in regulatory milestone payments and up to $50.0 million in sales-based milestone payments related to products within the initial program. If Celgene exercises its rights with respect to either of the two additional license programs, we will receive a license exercise fee for the applicable program of $30.0 million and will also be eligible to earn up to $23.0 million in development milestone payments and up to $247.5 million in regulatory milestone payments for that program. Additionally, with respect to one of the additional license programs we are eligible to receive up to $100.0 million in sales-based milestone payments based on net sales of products, and with respect to the other additional license program we are eligible to receive up to $50.0 million in sales-based milestone payments based on net sales of products. If Celgene exercises its option with respect to the option program in respect of a compound to be identified at a later time, we will receive an option exercise fee of $10.0 million and will be eligible to earn up to $23.0 million in development milestone payments and up to $247.5 million in regulatory milestone payments. In addition, with respect to each program, Celgene is required to pay us royalties on net sales of each licensed product at defined percentages ranging from the mid-single digits to low double digits below 20%, on worldwide net product sales of licensed products. The royalty rate is reduced on a country-by-country basis during any period within the royalty term when there is no patent

claim or regulatory exclusivity covering the licensed product in the particular country.

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Under the Celgene agreement, we are responsible for conducting and funding research and development activities for the initial program at our own expense pursuant to agreed upon development plans. These activities consist of the completion of single and multiple ascending dose Phase 1 clinical trials and any mutually agreed upon additional Phase 1 clinical trials. If Celgene exercises its rights with respect to any additional program and pays us the applicable exercise fee, we are responsible for conducting research and development activities at our own expense pursuant to agreed upon development plans until the completion of the first Phase 1 clinical trial, which will be defined in each development plan on a program-by-program basis. In addition, if Celgene exercises its rights with respect to the option program and pays us the applicable exercise fee, we are responsible for seeking to generate a deuterated compound for clinical development in the selected option program at our own expense.

Avanir. In February 2012, we entered into a development and license agreement with Avanir under which we granted Avanir an exclusive worldwide license to develop, manufacture and commercialize deuterated dextromethorphan containing products. Avanir is initially focused on developing AVP-786, which is a combination of a deuterated dextromethorphan analog and an ultra-low dose of quinidine, for the treatment of neurologic and psychiatric disorders.

Under the Avanir agreement, we received a non-refundable upfront payment of $2.0 million in February 2012 and a milestone payment of $2.0 million in April 2013. We are also eligible to receive, with respect to licensed products comprising a combination of deuterated dextromethorphan and quinidine, up to $4.0 million in development milestone payments, including $2.0 million related to initiation of dosing in a Phase 2 or Phase 3 clinical trial for AVP-786, up to $37.0 million in regulatory and commercial launch milestone payments and up to $125.0 million in sales-based milestone payments based on net product sales of licensed products. In addition, we are eligible for higher development milestones, up to an additional $43.0 million, for licensed products that do not require quinidine. Avanir is currently developing deuterated dextromethorphan only in combination with quinidine. Avanir also is required to pay us royalties at defined percentages ranging from the mid-single digits to low double digits below 20% on worldwide net product sales of licensed products. The royalty rate is reduced, on a country-by-country basis, during any period within the royalty term when there is no patent claim covering the licensed product in the particular country.

Avanir is responsible for funding 100% of our research and development costs incurred under the development plan or for activities conducted at Avanir s request, subject to limitations specified in the agreement. However, Avanir is currently conducting all research and development activities without our services.

Jazz Pharmaceuticals. In February 2013, we entered into a development and license agreement with Jazz Pharmaceuticals to research, develop and commercialize products containing deuterated sodium oxybate, or D-SXB. We are initially focusing on one analog, designated as JZP-386. Under the terms of the agreement, we granted Jazz Pharmaceuticals an exclusive, worldwide, royalty-bearing license under intellectual property controlled by us to develop, manufacture and commercialize D-SXB products including JZP-386.

Under the Jazz Pharmaceuticals agreement, we received a non-refundable upfront payment of $4.0 million in February 2013. We are also eligible to receive up to $8.0 million in development milestone payments, up to $35.0 million in regulatory milestone payments and up to $70.0 million in sales milestone payments based on net product sales of licensed products. In addition, Jazz Pharmaceuticals is required to pay us royalties at defined percentages ranging from the mid-single digits to low double digits below 20%, on a country-by-country and licensed product-by-licensed product basis, on worldwide net product sales of licensed products. The royalty rate is lowered, on a country-by-country basis, under certain circumstances as specified in the agreement.

We are currently conducting certain development activities for a Phase 1 clinical trial with respect to JZP-386 pursuant to an agreed upon development plan, and we have supplied a deuterated intermediate for making clinical trial material for a Phase 1 clinical trial. Thereafter, our obligations to conduct further development activities are subject to mutual agreement. Jazz Pharmaceuticals has assumed all manufacturing responsibilities. Pursuant to the agreement, our costs for activities under the development

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plan, including pass-through costs and the costs of our employees time at a rate per full-time equivalent year of our employees time, which we mutually agreed to, are reimbursed by Jazz Pharmaceuticals. This reimbursement is subject to limitations in the agreement, including adherence within a particular percentage to the development budget.

Following termination of the agreement with respect to a country or countries, but not in its entirety, by Jazz Pharmaceuticals for Jazz Pharmaceuticals convenience, Jazz Pharmaceuticals may provide us written notice that it desires to continue or recommence development and commercialization of licensed products in such country or countries, in which event Jazz Pharmaceuticals license with respect to D-SXB products in such country or countries and corresponding payment obligations under the agreement will be reinstated except in specified circumstances in which we have previously notified Jazz Pharmaceuticals of our intent to develop or commercialize licensed products in such country or countries either directly or through a third party licensee.

In addition to these collaborations, in February 2012, we entered into a sponsored research agreement with Fast Forward LLC, or Fast Forward, a subsidiary of the National Multiple Sclerosis Society, to fund the preclinical advancement of CTP-354. Under the Fast Forward agreement, we received a non-refundable upfront payment of $0.2 million, as well as further non-refundable payments of $0.6 million for the achievement of the preclinical development milestones set forth in the agreement. We are obligated to make milestone payments to Fast Forward not in excess of a low-single digit multiple of the funding amount if we commercialize CTP-354 or license the development and commercialization of CTP-354 to a third party.

In May 2009, we entered into a research and development collaboration and license agreement with Glaxo Group Limited, or GSK to research, develop and commercialize multiple products containing deuterated compounds, including CTP-499 and, ultimately, CTP-298, which was developed pursuant to the agreement for the treatment of HIV. Our agreement with GSK, as subsequently amended, expired in May 2012 after GSK opted out of further development under the agreement. The rights to the product candidates developed under the agreement have reverted to us and we are free to pursue them without further obligation to GSK other than to repay GSK an amount of up to $2.75 million, if we commercialize CTP-499 or if, prior to a specified date in 2018, we re-license or transfer rights to CTP-499.

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.

The terms of these agreements include one or more of the following types of payments: non-refundable license fees, payments for research and development activities, payments based upon 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 and certain research and development service revenues. 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, milestone payments and royalties on future product sales in connection with our current collaborations with Celgene, Avanir and Jazz Pharmaceuticals, or other collaborations we may enter into.

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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 consist of 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 preclinical 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.

The following summarizes our development programs.

- *CTP-354*, a novel, potentially first-in-class, non-sedating treatment for spasticity that we are initially developing for use in patients with multiple sclerosis and patients with spinal cord injury to address a significant unmet medical need in these markets. We recently completed a 71-subject Phase 1 single ascending dose clinical trial of CTP-354 and the nine-subject first part of a related Phase 1 imaging study. In January 2014, we initiated a multiple ascending dose Phase 1 clinical trial evaluating daily doses of 2 mg and 6 mg of CTP-354 in healthy volunteers. Assuming successful completion of the multiple ascending dose Phase 1 clinical trial, we plan to initiate a Phase 2 clinical program for CTP-354 in the second half of 2014. We expect that the Phase 2 clinical program will include one clinical trial for the treatment of spasticity associated with multiple sclerosis and one clinical trial for the treatment of spasticity associated with spinal cord injury. Due to the fact that we did not determine a maximum tolerated dose in our preclinical testing,

the FDA has informed us that we may not administer multiple doses of CTP-354 in excess of 6 mg per day in clinical trials without first conducting an additional higher dose preclinical toxicology study. We believe that multiple doses of 6 mg per day would be sufficient for the treatment of spasticity; however, we have initiated the additional preclinical toxicology study to enable us to evaluate higher doses of CTP-354, if needed, in our spasticity trials, as well as to support clinical development in other disease indications.

CTP-499, a novel, potentially first-in-class, treatment for type 2 diabetic kidney disease that we are developing as an additive treatment to the current standard of care. We are currently conducting a three-part Phase 2 clinical trial of CTP-499 in which we have enrolled patients with type 2 diabetic kidney disease and macroalbuminuria. In 2013, we completed the first part of this trial, a 24-week, double-blind, parallel, two-arm, placebo-controlled study in 182 patients. We have also completed dosing in the second part of the trial, a blinded 24-week extension study, which, combined with the data from the first part of the trial, has provided 48 weeks of placebo-controlled data in 123 patients. We did not achieve statistical significance in the primary efficacy endpoint of this trial, which was measured at 24 weeks. However, we believe that the data we have analyzed to date from the first 48 weeks of treatment support the potential of CTP-499 to help protect kidney function in patients with rapidly progressing type 2 diabetic kidney disease. We have conducted preliminary analyses of these 48 weeks of data, but have not yet completed a full analysis. We expect to report the final results for the first 48 weeks of the trial in the second quarter of 2014.

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AVP-786, a combination of a deuterium-substituted dextromethorphan analog and an ultra-low dose of quinidine. We have granted Avanir an exclusive license to develop and commercialize deuterated dextromethorphan analogs, including the analog in AVP-786. Avanir is developing AVP-786 for the treatment of neurologic and psychiatric disorders. In February 2013, Avanir reported positive results from a Phase 1 clinical trial of AVP-786. In October 2013, Avanir reported plans to advance AVP-786 into a Phase 2 clinical trial in the second half of 2014 for treatment-resistant major depressive disorder in patients with insufficient response to conventional anti-depressants.

A collaboration with Celgene to research, develop and commercialize certain deuterated compounds for the treatment of cancer or inflammation, with an initial focus on a single program. In the initial program, we have selected CTP-730, a product candidate for the treatment of inflammatory diseases, and expect to begin clinical trials in 2014.

A collaboration with Jazz Pharmaceuticals to research, develop and commercialize JZP-386, a product candidate containing a deuterated analog of sodium oxybate for potential use in patients with narcolepsy. Sodium oxybate is the active ingredient in the marketed drug Xyrem. In December 2013, an investigational medicinal product dossier, or IMPD, the basis for initiating clinical trials in the European Union, was filed for JZP-386. The IMPD received approval in January 2014. Jazz Pharmaceuticals expects a Phase 1 clinical trial of JZP-386 to be conducted in 2014, following manufacturing of clinical material.

C-10068, a novel oral deuterium-substituted analog of dextroethorphan, a compound with preclinical pharmacological activities qualitatively similar to those of dextromethorphan, that we are investigating for the potential treatment of pain and seizures. We are conducting further preclinical evaluation of C-10068.

We are also conducting a number of other preclinical programs, including deuterated ivacaftor for the potential treatment of cystic fibrosis and chronic obstructive pulmonary disease.

We plan to continue to seek to identify compounds that can be improved through selective deuterium substitution and believe we are capable of identifying one to two novel deuterated compounds per year that we can advance into preclinical development while concurrently progressing our existing pipeline.

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 regulatory 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;

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 regulatory approvals;

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- the performance of our collaborators;
- our ability to manufacture, market, commercialize and achieve market acceptance for 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.

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 costs 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, including as a result of the partial clinical hold on CTP-354 that prevents us from administering doses in excess of 6 mg per day in multiple dose clinical trials, 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, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our product candidate development programs progress. However, 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 clinical 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.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development of our product candidates. We also anticipate increased expenses associated with being a public company, including costs for audit, legal, regulatory and tax-related services, director and officer insurance premiums, and investor relations costs. Additionally, if and when we believe a regulatory 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 and marketing of our product candidates.

Investment income

Investment income consists of interest income earned on cash equivalents and short-term and long-term investments.

Interest and other expense

Interest and other expense consists primarily of interest expense on amounts outstanding under our debt facility with Hercules, amortization of debt discount and the re-measurement gain or loss associated with the change in the fair value of the preferred stock warrant liability.

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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 under different assumptions or conditions. 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 the following accounting policies used in the preparation of our financial statements require the most significant judgments and estimates.

Revenue recognition

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

Collaboration revenue

The terms of our collaboration and license agreements have typically contained multiple elements, or deliverables, which have included licenses, or options to obtain licenses, to product candidates, referred to as exclusive licenses, as well as research and development activities to be performed by us on behalf of the collaborator related to the licensed product candidates. Payments that we may receive under these agreements include non-refundable upfront license fees, payment for research and development activities, payments based upon achievement of specified milestones, payment upon exercise of license rights or options to license product candidates and royalties on any resulting product sales.

Multiple-Element Arrangements. Our collaborations primarily represent multiple-element arrangements. We analyze multiple-element arrangements based on the guidance in Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605-25, *Revenue Recognition-Multiple-Element Arrangements*, or ASC 605-25. Pursuant to the guidance in ASC 605-25, we evaluate multiple-element arrangements to determine the deliverables included in the arrangement and whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires us to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (1) the delivered item(s) has value to the customer on a standalone basis and (2) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in our control. In assessing whether a delivered item(s) has standalone value, we consider whether the collaboration partner can use the delivered item(s) for its intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s) and whether there are other vendors that can provide the undelivered element(s). In making these assessments, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. The terms of our collaboration and licensing arrangements do not contain general rights of return that would preclude recognition of

revenue.

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. We determine the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, we determine the estimated selling price for units

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of accounting within each arrangement using vendor-specific objective evidence of selling price, if available, third-party evidence of selling price if vendor-specific objective evidence is not available, or best estimate of selling price if neither vendor-specific objective evidence nor third-party evidence is available. We typically use best estimate of selling price to estimate the selling price for exclusive licenses and research and development services, since we generally do not have vendor-specific objective evidence or third-party evidence of selling price for these items. Determining the best estimate of selling price for a unit of accounting requires significant judgment. In developing the best estimate of selling price for a unit of accounting, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. We validate the best estimate of selling price for units of accounting by evaluating whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

Our multiple-element revenue arrangements may include the following:

Option Arrangements. An option to obtain an exclusive license is considered substantive if, at the inception of the arrangement, we are at risk as to whether the collaboration partner will choose to exercise the option. Factors that we consider in evaluating whether an option is substantive include the overall objective of the arrangement, the benefit the collaborator might obtain from the arrangement without exercising the option, the cost to exercise the option and the likelihood that the option will be exercised. For arrangements under which an option is considered substantive, we do not consider the item underlying the option to be a deliverable at the inception of the arrangement and the associated option fees are not included in allocable arrangement consideration, assuming the option is not priced at a significant and incremental discount. Conversely, for arrangements under which an option is not considered substantive, we would consider the item underlying the option to be a deliverable at the inception of the arrangement and a corresponding amount would be included in the allocable arrangement consideration. A significant and incremental discount included in an otherwise substantive option is considered to be a separate deliverable at the inception of the arrangement.

Exclusive Licenses. We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria included in ASC Topic 605 *Revenue Recognition* are satisfied for that particular unit of accounting. We will recognize as revenue arrangement consideration attributed to exclusive licenses that have standalone value from the other deliverables to be provided in an arrangement upon delivery. We will recognize as revenue arrangement consideration attributed to exclusive licenses that do not have standalone value from the other deliverables to be provided in an arrangement over our estimated performance period as the arrangement would be accounted for as a single, combined unit of accounting.

Research and Development Services. We recognize revenue associated with research and development services ratably over the associated period of performance. If there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, then we recognize revenue on a straight-line basis over the period we are expected to complete our performance obligations. Conversely, if the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then we recognize revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned as of the period ending date.

Milestone Revenue. At the inception of an arrangement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether:

the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from our performance to achieve the milestone;

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the consideration relates solely to past performance; and

the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement.

We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. We have concluded that all of the development and regulatory milestones included in our current collaboration arrangements are substantive. Accordingly, in accordance with FASB ASC Topic 605-28, *Revenue Recognition-Milestone Method*, revenue from development and regulatory milestone payments will be recognized in their entirety upon successful accomplishment of the milestone, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive would be recognized as revenue over the remaining period of performance, assuming all other revenue recognition criteria are met. Revenue from sales-based milestone payments will be accounted for as royalties and recognized as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Royalty Revenue. We will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and we have no remaining performance obligations, assuming all other revenue recognition criteria are met.

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 preclinical 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.

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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 has been no material differences from our estimates to the amount actually incurred.

Stock-Based Compensation

Since our inception in May 2006, we have applied the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification Topic 718, *Compensation-Stock Compensation*, which we refer to as ASC 718, to account for all stock-based compensation. We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant. Stock compensation related to non-employee awards is remeasured at each reporting period until the awards are vested. Described below is the methodology we have utilized in measuring stock-based compensation expense.

Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock-based awards as of their grant date. We recognize stock-based compensation expense ratably over the requisite service period, which in most cases is the vesting period of the award. Calculating the fair value of stock-based awards requires that we make highly subjective assumptions. We use the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that we make assumptions as to the volatility of our common stock, the fair value of our common stock on the grant date for the period prior to our IPO, the expected term of our stock options, the risk free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. Because there had been no public market for our common stock prior to our IPO, we believe that we have insufficient data from our limited public trading history to appropriately utilize company-specific historical and implied volatility information. Accordingly, we utilize data from a representative group of publicly traded companies to estimate expected stock price volatility. We selected representative companies from the biopharmaceutical industry with similar characteristics as us, including stage of product development and therapeutic focus. We use the simplified method as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin 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. For non-employee grants, we use an expected term equal to the remaining contractual term of the award. 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 used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

Under ASC 718, we are also required to estimate the level of forfeitures expected to occur and record compensation expense only for those awards that we ultimately expect will vest. We have performed an historical analysis of option awards that were forfeited prior to vesting and recorded total stock option expense that reflected this estimated forfeiture rate. Stock-based compensation expense requires certain estimates by management. We cannot currently predict the total amount of stock-based compensation expense to be recognized in any future period because such amounts will depend on levels of stock-based payments granted in the future as well as the portion of the awards that actually vest. ASC 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. During the years ended December 31, 2011, 2012 and 2013 our estimated annual forfeiture rate was 5%.

Total compensation cost recognized for all stock-based compensation awards in the consolidated statements of operations and comprehensive loss as follows:

	Year ended December 31,		
(in thousands)	**2011**	**2012**	**2013**
Research and development	$ 572	$ 564	$ 583
General and administrative	331	304	420
Total	$ 903	$ 868	$ 1,003

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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,		
	2011	2012	2013
Expected volatility	78.1%	72.8%	70.1%
Expected term (in years)	6.0	6.0	6.0
Risk-free interest rate	1.09%	0.95%	1.69%
Expected dividend yield	%	%	%

The following table presents the grant dates, numbers of underlying shares of common stock and the per share exercise prices of stock options that we granted from January 1, 2011 through December 31, 2013, along with the fair value per share utilized to calculate stock-based compensation expense:

Date of grant	Number of shares of common stock underlying options granted	Option exercise price	Estimated common stock fair value per share on grant date
3/24/2011	150,441	$ 3.79	$ 3.79
6/23/2011	15,043	3.79	3.79
9/22/2011	44,951	3.50	3.50
11/1/2011	12,387	3.50	3.50
12/12/2011	107,625	3.50	3.50
12/15/2011	173,442	3.50	3.50
1/26/2012	884	3.50	3.50
3/22/2012	4,955	3.50	3.50
11/12/2012	32,650	2.88	8.76(1)
5/3/2013	15,572	3.73	13.00(1)
5/28/2013	65,485	3.73	16.89(1)

(1) The common stock fair value per share on grant date was adjusted in connection with a retrospective fair value assessment for financial reporting purposes.

The estimated fair value per share of common stock for each date of grant in the table above represents the determination by our board of directors of the fair value of our common stock as of that date. Due to the absence of an active market for our common stock as of those dates, each of which was prior to the commencement of trading of our common stock on the NASDAQ Global Market on February 13, 2014 in connection with our IPO, the fair value of our common stock was determined in good faith by our board of directors, in both contemporaneous and retrospective valuations of our common stock, consistent with the methodologies outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, referred to as the AICPA Practice Aid, with the assistance and upon the recommendations of management and based on objective and subjective factors including:

the prices of our preferred stock sold to outside investors in arm s length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;

our results of operations, financial position and the status of research and development efforts;

the composition of, and changes to, our management team and board of directors;

the lack of liquidity of our common stock as a private company;

our stage of development and business strategy and the material risks related to our business and industry;

the achievement of enterprise milestones, including entering into collaboration and license agreements;

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the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;

any external market conditions affecting the life sciences and biotechnology industry sectors;

the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering or a sale of our company, given prevailing market conditions; and

the state of the initial public offering market for similarly situated privately held biotechnology companies.

Since our IPO, the exercise price per share of all option grants has been set at the closing price of our common stock on The NASDAQ Global Market on the applicable date of grant.

We recorded non-cash stock-based compensation expense of $0.9 million, $0.9 million and $1.0 million for the years ended December 31, 2011, 2012 and 2013, respectively. At December 31, 2013, we had $1.5 million of total unrecognized stock-based compensation expense, net of estimated forfeitures, related to stock option plan that will be recognized over a weighted-average period of 2.0 years. We expect to continue to grant stock options in the future, and to the extent that we do, our actual stock-based compensation expense recognized in future periods will likely increase.

There were significant judgments and estimates inherent in the determinations of fair value of our common stock described above. These judgments and estimates included assumptions regarding our future operating performance, the time to completing an initial public offering or other liquidity event and the determinations of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net (loss) income and net (loss) income per common share could have been significantly different.

RECENTLY ADOPTED ACCOUNTING PRONOUNCEMENTS

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by us as of the specified effective date. Unless otherwise discussed, we believe that the impact of recently issued standards that are not yet effective will not have a material effect on our financial position or results of operations upon adoption.

RESULTS OF OPERATIONS

Comparison of the years ended December 31, 2012 and 2013

The following table summarizes our results of operations for the years ended December 31, 2012 and 2013, together with the changes in those items in dollars.

(in thousands)	Year ended December 31, 2012	2013	Increase (Decrease)
Revenue:			
License and research and development revenue	$ 11,349	$ 23,408	$ 12,059

Milestone revenue	1,500	2,000	500
Total revenue	12,849	25,408	12,559
Operating expenses:			
Research and development	24,193	21,790	(2,403)
General and administrative	7,266	8,028	762
Total operating expenses	31,459	29,818	(1,641)
Loss from operations	(18,610)	(4,410)	14,200
Investment income	22	21	(1)
Interest and other expense	(1,856)	(1,667)	189
Net loss	$ (20,444)	$ (6,056)	$ 14,388

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Revenue

Revenue was $25.4 million for the year ended December 31, 2013, compared to $12.8 million for the year ended December 31, 2012, an increase of $12.6 million. The increase in revenue was primarily due to license revenue recognized for the year ended December 31, 2013 of $17.0 million under our collaboration with Celgene and $3.7 million under our collaboration with Jazz Pharmaceuticals, in connection with our grant of licenses under these collaborations, as well as $2.0 million of milestone revenue recognized for the year ended December 31, 2013 based on positive data from Avanir s Phase 1 clinical trial of AVP-786. In comparison, we recognized revenue for the year ended December 31, 2012 comprised primarily of $8.3 million of research and development revenue and $1.5 million of milestone revenue under our collaboration with GSK, which ended in 2012. We recognized license revenue of $2.0 million in the year ended December 31, 2012 relating to the license grant to Avanir for deuterated dextromethorphan. In addition, an increase of $1.7 million in revenue recognized for services performed under our collaborations contributed to the overall increase in revenue for the year ended December 31, 2013 as compared to the prior year, of which $1.4 million was related to services performed under our collaboration with Celgene.

As of December 31, 2013, we had deferred revenue of:

- $16.7 million related to our collaboration with Celgene, $4.2 million of which is classified as current and $12.5 million of which is classified as long-term, on our consolidated balance sheet;
- $0.2 million related to our collaboration with Jazz Pharmaceuticals and associated with research and development services to be performed and recognized as revenue over the estimated remaining performance period of 36 months; and
- $2.8 million related to a payment received from GSK that we will not recognize as revenue until all repayment obligations lapse.

Research and development expenses

The following table summarizes our external research and development expenses, by program, for the years ended December 31, 2012 and 2013, with our internal research expenses separately classified by category. Because Avanir is conducting the clinical development of AVP-786 at its expense, we made minimal investment in the program during these periods.

	Year ended December 31,	
(in thousands)	**2012**	**2013**
Direct research and development expenses:		
CTP-499	$ 5,967	$ 3,903
CTP-354	1,091	1,771
CTP-730	19	455
JZP-386	53	253
CTP-298[(1)]	1,478	4

Total direct research and development expenses	8,608	6,386
Employee and contractor-related expenses	9,031	10,723
Platform-related lab expenses	3,198	1,391
Facility expenses	2,833	2,802
Other expenses	523	488
Personnel and other expenses	15,585	15,404
Total research and development expenses	$ 24,193	$ 21,790

(1) We were developing CTP-298 for the treatment of HIV prior to the termination of our collaboration with GSK.

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Research and development expenses were $21.8 million for the year ended December 31, 2013, compared to $24.2 million for the year ended December 31, 2012, a decrease of $2.4 million. The decrease was primarily due to a $2.1 million decrease in CTP-499 expenses due to the completion of a preclinical toxicology study in August 2012 and subjects completing the Phase 2 clinical trial during the year ended December 31, 2013, a $1.8 million decrease in platform-related laboratory expenses and a $1.5 million decrease in CTP-298 expenses due to the completion of a Phase 1 clinical trial in May 2012. These decreases were partially offset by a $1.7 million increase in employee and contractor-related expenses that were primarily a result of $0.9 million increase for employee bonuses earned, $0.4 million increase for severance obligations due to a former employee and $0.3 million increase due to greater engagement of clinical consultants during the year ended December 31, 2013. In addition, the decreases were further offset by a $0.7 million increase in CTP-354 expenses upon the initiation of Phase 1 clinical trials, $0.4 million increase in CTP-730 expense under our collaboration with Celgene and a $0.2 million increase in JZP-386 expense under our collaboration with Jazz Pharmaceuticals during the year ended December 31, 2013.

General and administrative expenses

General and administrative expenses were $8.0 million for the year ended December 31, 2013, compared to general and administrative expenses of $7.3 million for the year ended December 31, 2012. The increase was primarily due to a $0.4 million increase in compensation expense relating to employee bonuses and $0.3 million increase in professional fees primarily related to market research for our product candidates.

We expect that our general and administrative expenses will increase in future periods as we expand our operations and incur additional costs in connection with being a public company. We anticipate that these increases will likely include legal, auditing and filing fees, additional insurance premiums and general compliance and consulting expenses.

Interest and other expense

Interest and other expense was an expense of $1.7 million for the year ended December 31, 2013, which was comparable to an expense of $1.9 million for the year ended December 31, 2012. Expense recognized in connection with the re-measurement of the fair value of the redeemable convertible preferred stock warrant that we issued to Hercules in connection with draws under our debt facility decreased by $0.3 million for the year ended December 31, 2013 compared to the prior period. The decrease was offset by an increase of $0.1 million in interest expense associated with $12.5 million of principal that we drew under our debt facility with Hercules in March 2012.

Comparison of the years ended December 31, 2011 and 2012

The following table summarizes our results of operations for the years ended December 31, 2011 and 2012, together with the changes in those items in dollars.

(in thousands)	Year ended December 31, 2011	2012	Increase (Decrease)
Revenue:			
License and research and development revenue	$ 13,967	$ 11,349	$ (2,618)
Milestone revenue	5,500	1,500	(4,000)
Total revenue	19,467	12,849	(6,618)

Operating expenses:			
Research and development	23,436	24,193	757
General and administrative	7,377	7,266	(111)
Total operating expenses	30,813	31,459	646
Loss from operations	(11,346)	(18,610)	7,264
Investment income	44	22	(22)
Interest and other expense	(18)	(1,856)	1,838
Net loss	$ (11,320)	$ (20,444)	$ 9,124

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Revenue

Revenue was $12.8 million for the year ended December 31, 2012 compared to $19.5 million for the year ended December 31, 2011, a decrease of $6.6 million. The decrease in revenue was primarily due to decreases of $5.7 million in research and development revenue and $4.0 million in milestone revenue under our collaboration with GSK, which were partially offset by $2.0 million of license revenue relating to the license grant to Avanir for deuterated dextromethorphan analogs and $0.4 million of research and development revenue under our Avanir collaboration as well as $0.7 million of research and development revenue relating to our sponsored research agreement with Fast Forward. Revenue under our collaboration with GSK constituted substantially all of our revenue for the year ended December 31, 2011 and related to CTP-298.

Research and development expenses

The following table summarizes our external research and development expenses, by program, for the years ended December 31, 2011 and 2012, with our internal research expenses separately classified by category. Because Avanir is conducting the clinical development of AVP-786 at its expense, we made minimal investment in the program during these periods.

	Year ended December 31,	
(in thousands)	**2011**	**2012**
Direct research and development expenses:		
CTP-499	$ 5,942	$ 5,967
CTP-354	359	1,091
CTP-298[(1)]	2,778	1,478
Total direct research and development expenses	9,079	8,536
Employee and contractor-related expenses	9,411	9,031
Platform-related lab expenses	1,564	3,270
Facility expenses	2,911	2,833
Other expenses	471	523
Personnel and other expenses	14,357	15,657
Total research and development expenses	$ 23,436	$ 24,193

(1) We were developing CTP-298 for the treatment of HIV prior to the termination of our collaboration with GSK.

Research and development expenses were $24.2 million for the year ended December 31, 2012, compared to $23.4 million for the year ended December 31, 2011, an increase of $0.8 million. The increase was primarily due to $1.7 million of increased expenses relating to preclinical programs that are now covered by our collaboration with Celgene and $0.7 million of increased expenses relating to our CTP-354 program associated with IND-enabling toxicology studies. These increases were partially offset by $1.3 million of decreased expenses with respect to CTP-298 and a $0.3 million decrease in employee compensation expense.

General and administrative expenses

General and administrative expenses were $7.3 million for the year ended December 31, 2012, which was comparable to general and administrative expenses of $7.4 million for the year ended December 31, 2011.

Interest and other expense

Interest and other expense was an expense of $1.9 million for the year ended December 31, 2012, compared to an expense of $18 thousand for the year ended December 31, 2011, an increase in expense of $1.9 million. The

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increase was primarily due to interest expense on $7.5 million of principal that we drew under our debt facility with Hercules in December 2011 and $12.5 million of principal that we drew under our debt facility with Hercules in March 2012.

LIQUIDITY AND CAPITAL RESOURCES

We have incurred cumulative losses and negative cash flows from operations since our inception in April 2006, and as of December 31, 2013, we had an accumulated deficit of $113.6 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 and additional collaborations and licensing arrangements.

We have financed our operations to date primarily through the public offering and private placement of our equity, debt financing and funding from collaborations. As of December 31, 2013, we had cash and cash equivalents and investments of $32.7 million. We subsequently raised net proceeds of $83.1 million from the sale of 6,649,690 shares of common stock in our IPO in the first quarter of 2014.

Cash flows

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

	Year ended December 31,		
(in thousands)	**2011**	**2012**	**2013**
Net cash provided by (used in):			
Operating activities	$ (18,085)	$ (26,427)	$ 13,018
Investing activities	22,901	(1,200)	(3,637)
Financing activities	6,985	12,168	(7,233)
Net increase (decrease) in cash and cash equivalents	$ 11,801	$ (15,459)	$ 2,148

Operating activities. Net cash provided by operating activities was $13.0 million during the year ended December 31, 2013 compared to net cash used in operating activities of $26.4 million during the year ended December 31, 2013. The increase in cash provided by operating activities was primarily due to receipt in the year ended December 31, 2013 of a non-refundable upfront payment of $35.0 million related to our collaboration with Celgene and a non-refundable upfront payment of $4.0 million related to our collaboration with Jazz Pharmaceuticals. Net cash used in operating activities was $26.4 million for the year ended December 31, 2012 compared to $18.1 million for the year ended December 31, 2011. The increase in cash used in operating activities in 2012 was driven by a $4.0 million decrease in milestone revenue from collaborations, an increase of $1.3 million in interest payments relating to indebtedness incurred in December 2011 and March 2012 under our debt facility with Hercules and a $1.2 million decrease in accounts payable.

Investing activities. Net cash provided by (used in) investing activities consisted of purchases of fixed assets, purchases of short-term and long-term investments, and proceeds from the maturity of short-term and long-term investments. Net cash used in investing activities for the year ended December 31, 2013 was $3.6 million compared to

net cash used in investing activities of $1.2 million for the year ended December 31, 2012. The increase in net cash used in investing activities was primarily due to a decrease in maturities of investments of $11.0 million, partially offset by a decrease in purchases of investments of $8.5 million. Net cash used in investing activities for the year ended December 31, 2012 was $1.2 million compared to net cash provided by investing activities of $22.9 million for the year ended December 31, 2011. The decrease in net cash provided by investing activities was primarily due to decreased maturities of investments of $26.4 million, partially offset by a decrease in purchase of investments of $2.5 million.

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Financing activities. Net cash used in financing activities for the year ended December 31, 2013 was $7.2 million compared to net cash provided by financing activities of $12.2 million for the year ended December 31, 2013. The decrease in net cash provided by financing activities was primarily due to our receipt during the year ended December 31, 2012 of proceeds of $12.5 million under our debt facility with Hercules, combined with an increase in principal payments under our debt facility with Hercules of $4.9 million and a $2.0 million increase in deferred issuance costs related to our IPO for the year ended December 31, 2013 as compared to the prior year period. Net cash provided by financing activities for the year ended December 31, 2012 was $12.2 million compared to $7.0 million for the year ended December 31, 2011. The increase in net cash provided by financing activities was primarily due to an increase of $5.2 million in proceeds under our debt facility with Hercules.

Credit Facilities

In December 2011, we executed a Loan and Security Agreement with Hercules, which provided for up to $20.0 million in funding, to be made available in two tranches. We borrowed the first tranche of $7.5 million in December 2011 and the second tranche of $12.5 million in March 2012. As of December 31, 2013, an aggregate of $15.1 million of principal and accrued interest remained outstanding under the Loan and Security Agreement.

Each advance under the Loan and Security Agreement bears interest at a variable rate equal to the greater of 8.5% and an amount equal to 8.5% plus the prime rate of interest minus 5.25%, provided however that the per annum rate of interest rate shall not exceed 11%. We were required to pay interest only on the indebtedness through April 30, 2013. We are now repaying our remaining indebtedness under the Loan and Security Agreement in 22 equal monthly payments of principal and interest of $0.7 million through October 1, 2015.

The loan is collateralized by a blanket lien on all of our corporate assets, excluding intellectual property, and by a negative pledge on our intellectual property. The loan and security agreement contains default provisions that include the occurrence of a material adverse effect, as defined therein, that would entitle the lender to declare all principal, interest and other amounts owed by us under the loan and security agreement immediately due and payable.

In connection with the December 2011 borrowing under the Loan and Security Agreement, we issued to Hercules a warrant to purchase an aggregate of 200,000 shares of Series C preferred stock with an exercise price of $2.50 per share. In connection with the March 2012 borrowing under the Loan and Security Agreement, the warrant we issued to Hercules automatically became exercisable for an additional 200,000 shares of Series C preferred stock. Upon completion of our IPO in February 2014 the warrant became exercisable for an aggregate of 70,796 shares of our common stock at an exercise price of $14.13 per share and the related warrant liability was reclassified to additional paid-in capital.

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 regulatory 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.

We believe our existing cash and cash equivalents and investments as of December 31, 2013 combined with the proceeds from our IPO completed in February 2014, will enable us to fund our operating expenses, debt service and

capital expenditure requirements into the first half of 2016, without giving effect to potential milestone payments that we may receive under existing collaboration agreements. This estimate assumes we either enter into a collaboration agreement pursuant to which a partner funds further development of CTP-499 or

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we do not otherwise expend significant funds for further development of this product candidate. However, we may require additional capital for the further development of our existing product candidates and may also need to raise additional funds sooner to pursue other development activities related to additional product candidates.

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. 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.

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 and additional collaborations, strategic alliances and licensing arrangements. 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 debt or equity securities, it could result in dilution to our existing stockholders, increased fixed payment obligations and these securities may have rights senior to those of our common stock. We are subject to covenants under our existing loan and security agreement with Hercules, and 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. In addition, the pledge of substantially all of our assets with the exception of our intellectual property as collateral, and the negative pledge with respect to our intellectual property, under our debt facility with Hercules limit our ability to obtain additional debt financing.

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 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.

Contractual obligations

The following table summarizes our contractual obligations at December 31, 2013:

(in thousands)	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
Long-term debt obligations[1]	$ 16,370	$ 8,908	$ 7,462	$	$
Operating lease obligations[2]	3,216	1,824	1,392		

Total contractual obligations	$ 19,586	$ 10,732	$ 8,854	$	$

(1) Consists of payment obligations for principal and interest under our debt facility with Hercules. As of December 31, 2013, we had $15.1 million in outstanding borrowings under the debt facility, bearing interest at a variable rate of the greater of 8.5% and an amount equal to 8.5% plus the prime rate of interest

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minus 5.25%, subject to a cap of 11%. Under the terms of the loan and security agreement governing the debt facility, we were required to pay interest only through April 30, 2013, which from January 1, 2013 to April 30, 2013 consisted of monthly payments of $0.1 million. Following April 30, 2013, we are required to repay this indebtedness in equal monthly payments of $0.7 million through October 15, 2015. The loans under the debt facility are collateralized by a lien on substantially all of our corporate assets, excluding intellectual property, which is subject to a negative pledge under the loan and security agreement. The loan and security agreement contains default provisions that include the occurrence of a material adverse effect, as defined therein, that would entitle the lender to declare all principal, interest and other amounts owed by us under the loan and security agreement immediately due and payable.

(2) *Consists of future lease payments and repayment obligations with respect to leasehold improvements under the operating lease for our office and laboratory space at 99 Hayden Avenue, Lexington, Massachusetts. The operating lease expires on September 30, 2015.*

We also have obligations to make future payments to third parties that become due and payable on the achievement of certain development, regulatory and commercial milestones, such as the start of a clinical trial, filing of an NDA, approval by the FDA or product launch. We have not included these commitments on our balance sheet or in the table above because the achievement and timing of these milestones is not fixed and determinable. These commitments include:

An obligation to make a payment to GSK of up to $2.8 million if we commercialize CTP-499 or if, prior to a specified date in 2018, we re-license or transfer rights to our CTP-499 program prior to a specified date in 2018.

Obligations to make milestone payments to Fast Forward not in excess of a low-single digit multiple of the $0.8 million Fast Forward funding amount if we commercialize CTP-354 or license the development and commercialization of CTP-354 to a third party.

We enter into contracts in the normal course of business with contract research organizations for preclinical research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

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 exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term available-for-sale securities and interest on our debt facility accrues at a variable rate that references the prime rate.

We had cash and cash equivalents and investments of $32.7 million as of December 31, 2013 and $27.6 million as of December 31, 2012, in each case primarily money market mutual funds consisting of U.S. government-backed

securities. Our available-for-sale securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio.

We had outstanding borrowings under our debt facility with Hercules of $15.1 million as of December 31, 2013 and $20.0 million as of December 31, 2012. Interest is payable at a variable rate of the greater of 8.5% and an amount equal to 8.5% plus the prime rate of interest minus 5.25%, provided however, that the per annum interest

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rate shall not exceed 11%. As a result of the 11% maximum annual interest rate and interest rate protection until prime exceeds 5.25%, we have limited exposure to changes in interest rates on borrowings under this facility. An immediate 10% change in the prime rate as of December 31, 2013 would have no effect on the amount of our required interest payments under the debt facility over the next twelve-month period.

We contract with suppliers of raw materials and contract manufacturers internationally. Transactions with these providers are predominantly settled in U.S. dollars and, therefore, we believe that we have only minimal exposure to foreign currency exchange risks. We do not hedge against foreign currency risks.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2011, 2012 and 2013.

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ITEM 8. Financial Statements and Supplementary Data
INDEX TO FINANCIAL STATEMENTS

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders

Concert Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Concert Pharmaceuticals, Inc. (the Company) as of December 31, 2012 and 2013, and the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders deficit, and cash flows for each of the three years in the period ended December 31, 2013. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company s internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Concert Pharmaceuticals, Inc. at December 31, 2012 and 2013 and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2013, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 31, 2014

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Concert Pharmaceuticals, Inc.

CONSOLIDATED BALANCE SHEETS

	December 31, 2012	2013
	(In thousands, except share and per share data)	
Assets		
Current assets:		
Cash and cash equivalents	$ 7,490	$ 9,638
Short-term investments, available for sale	20,067	23,039
Interest receivable	102	92
Accounts receivable	13	170
Prepaid expenses and other current assets	1,178	1,106
Total current assets	28,850	34,045
Property and equipment, net	3,454	2,473
Restricted cash	706	706
Other assets	119	2,549
Total assets	$ 33,129	$ 39,773
Liabilities, redeemable convertible preferred stock and stockholders deficit		
Current liabilities:		
Accounts payable	$ 813	$ 971
Accrued expenses and other liabilities	1,953	2,475
Deferred revenue, current portion		4,321
Leasehold improvement loan, current portion	332	332
Loans payable, net of discount	4,812	7,818
Total current liabilities	7,910	15,917
Deferred revenue, net of current portion	2,750	15,310
Leasehold improvement loan, net of current portion	581	249
Deferred lease incentive, net of current portion	898	385
Deferred rent, net of current portion	451	208
Warrant to purchase redeemable securities	459	463
Loan payable, net of current portion and discount	14,919	7,101
Total liabilities	27,968	39,633
Commitments *(Note 9)*		
Redeemable convertible preferred stock (Series A, B, C and D), $0.001 par value per share; 62,916,667 shares authorized; 56,047,067 shares issued and outstanding	111,848	112,244

at December 31, 2012 and 2013; aggregate liquidation preference of $112,993 at December 31, 2012 and 2013		
Stockholders deficit:		
Common stock, $0.001 par value per share; 83,716,667 shares authorized; 1,290,238 and 1,298,300 shares issued and outstanding at December 31, 2012 and 2013	1	1
Additional paid-in capital	889	1,528
Accumulated other comprehensive income	4	4
Accumulated deficit	(107,581)	(113,637)
Total stockholders deficit	(106,687)	(112,104)
Total liabilities, redeemable convertible preferred stock and stockholders deficit	$ 33,129	$ 39,773

See accompanying notes.

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Concert Pharmaceuticals, Inc.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Year ended December 31,		
	2011	2012	2013
	(In thousands, except per share data)		
Revenue:			
License and research and development revenue	$ 13,967	$ 11,349	$ 23,408
Milestone revenue	5,500	1,500	2,000
Total revenue	19,467	12,849	25,408
Operating expenses:			
Research and development	23,436	24,193	21,790
General and administrative	7,377	7,266	8,028
Total operating expenses	30,813	31,459	29,818
Loss from operations	(11,346)	(18,610)	(4,410)
Investment income	44	22	21
Interest and other expense	(18)	(1,856)	(1,667)
Net loss	$ (11,320)	$ (20,444)	$ (6,056)
Other comprehensive loss:			
Unrealized gain (loss) on investments	16	(5)	
Comprehensive loss	$ (11,304)	$ (20,449)	$ (6,056)
Reconciliation of net loss to net loss applicable to common stockholders:			
Net loss	$ (11,320)	$ (20,444)	$ (6,056)
Accretion on redeemable convertible preferred stock	(1,069)	(388)	(396)
Net loss applicable to common stockholders basic and diluted	$ (12,389)	$ (20,832)	$ (6,452)
Net loss per share applicable to common stockholders basic and diluted	$ (9.66)	$ (16.15)	$ (4.99)
Weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted	1,283	1,290	1,292

See accompanying notes.

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Concert Pharmaceuticals, Inc.

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS DEFICIT

	Redeemable convertible preferred stock		Common stock		Additional paid-in capital	Accumulated other comprehensive income	Accumulated deficit	Total stockholders deficit
	Shares	Carrying value	Shares	Amount				
	(In thousands, except share data)							
Balance at December 31, 2010	56,047,067	$ 110,391	1,277,275	$ 1	$ 560	$ (7)	$ (75,817)	$ (75,263)
Accretion of redeemable convertible preferred stock to redemption value		1,069			(1,069)			(1,069)
Exercise of stock options			12,963		15			15
Unrealized gain on short-term investments						16		16
Stock-based compensation expense					903			903
Net loss							(11,320)	(11,320)
Balance at December 31, 2011	56,047,067	111,460	1,290,238	1	409	9	(87,137)	(86,718)
Accretion of redeemable convertible preferred stock to redemption value		388			(388)			(388)
Unrealized gain on short-term investments						(5)		(5)
Stock-based compensation expense					868			868
Net loss							(20,444)	(20,444)

Balance at December 31, 2012	56,047,067	111,848	1,290,238	1	889	4	(107,581)	(106,687)
Accretion of redeemable convertible preferred stock to redemption value		396			(396)			(396)
Exercise of stock options			8,062		32			32
Unrealized gain on short-term investments								
Stock-based compensation expense					1,003			1,003
Net loss							(6,056)	(6,056)
Balance at December 31, 2013	56,047,067	$ 112,244	1,298,300	$ 1	$ 1,528	$ 4	$ (113,637)	$ (112,104)

See accompanying notes.

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Concert Pharmaceuticals, Inc.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31,		
	2011	2012	2013
	(In thousands)		
Operating activities			
Net loss	$ (11,320)	$ (20,444)	$ (6,056)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:			
Depreciation and amortization	1,619	1,452	1,346
Stock-based compensation expense	903	868	1,003
Accretion of premiums and discounts on short-term investments	774	365	302
Amortization of discount on loan payable		96	97
Amortization of deferred financing costs		39	38
Re-measurement of warrant to purchase redeemable securities		291	4
Amortization of deferred lease incentive	(513)	(513)	(513)
Changes in operating assets and liabilities:			
Accounts receivable	1,000	487	(157)
Interest receivable	114	26	10
Prepaid expenses and other current assets	(29)	(364)	32
Other assets	(70)	5	69
Accounts payable	403	(764)	158
Accrued expenses and other liabilities	274	432	(15)
Deferred rent	(62)	(131)	(181)
Deferred revenue	(11,178)	(8,272)	16,881
Net cash (used in) provided by operating activities	(18,085)	(26,427)	13,018
Investing activities			
Purchases of property and equipment	(290)	(468)	(363)
Purchases of short-term investments	(40,879)	(38,398)	(29,929)
Maturities of short-term investments	64,070	37,666	26,655
Net cash provided by (used in) investing activities	22,901	(1,200)	(3,637)
Financing activities			
Proceeds from issuance of loan payable, net of issuance costs	7,302	12,500	
Principal payments on loan payable			(4,909)
Repayment of leasehold improvement loan	(332)	(332)	(332)
Proceeds from issuance of common stock	15		32
Payment of initial public offering costs			(2,024)

Net cash provided by (used in) financing activities	6,985	12,168	(7,233)
Net increase (decrease) in cash and cash equivalents	11,801	(15,459)	2,148
Cash and cash equivalents at beginning of period	11,148	22,949	7,490
Cash and cash equivalents at end of period	$ 22,949	$ 7,490	$ 9,638
Supplemental cash flow information:			
Cash paid for interest	$	$ 1,339	$ 1,601
Initial public offering costs incurred but unpaid at period end	$	$	$ 475

See accompanying notes.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of business

Concert Pharmaceuticals, Inc. (Concert or the Company) was incorporated on April 12, 2006 (inception) as a Delaware corporation, with operations based in Lexington, Massachusetts. The Company is a clinical stage biopharmaceutical company that applies its extensive knowledge of deuterium chemistry to discover and develop novel small molecule drugs. The Company s approach starts with approved drugs, advanced clinical candidates or previously studied compounds that the Company believes can be improved with deuterium substitution to provide better pharmacokinetic or metabolic properties and thereby enhance clinical safety, tolerability or efficacy. The Company believes this approach may enable drug discovery and clinical development that is more efficient and less expensive than conventional small molecule drug development.

The Company has generated an accumulated deficit of $113.6 million since inception through December 31, 2013 and will require substantial additional capital to fund its research and development. It is subject to risks common to companies in the biotechnology industry, including, but not limited to, risks of failure of preclinical studies and clinical trials, 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.

The Company had cash and cash equivalents and investments of $32.7 million at December 31, 2013. The Company believes that its existing cash and cash equivalents and investments together with the net proceeds from its initial public offering completed in February 2014, further described in Note 16, Subsequent events, will be sufficient to allow the Company to fund its current operating plan for at least the next 12 months. Management expects the Company to continue to incur losses for the foreseeable future. The Company s ability to achieve profitability in the future is dependent upon the successful development, approval, and commercialization of its product candidates and achieving a level of revenues adequate to support the Company s cost structure. The Company may never achieve profitability, and unless and until it does, the Company will continue to need to raise additional capital. Management intends to fund future operations through additional private or public debt or equity offerings, and may seek additional capital through arrangements with collaborators or from other sources. There can be no assurances, however, that additional funding will be available on terms acceptable to the Company, or at all.

Unless otherwise indicated, all amounts are in thousands except per share amounts.

2. Summary of significant accounting policies

The accompanying financial statements reflect the application of certain significant accounting policies as described in this note and elsewhere in the accompanying financial statements and notes.

Principles of consolidation

The accompanying consolidated financial statements include the accounts of Concert Pharmaceuticals, Inc. and its wholly owned subsidiary, Concert Pharmaceuticals Securities Corporation, which is a Massachusetts subsidiary

created to buy, sell and hold securities. All intercompany transactions and balances have been eliminated.

Use of estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles (GAAP) requires management to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. Actual results could materially differ from those estimates.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. Management s estimation process often may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: revenue recognition for multiple-element revenue arrangements; stock-based compensation expense, including estimating the fair value of the Company s common stock; the valuation of liability-classified warrants; accrued expenses; and income taxes.

Reverse stock split

In January 2014, the Company s board of directors and stockholders approved a one-for-5.65 reverse stock split of the Company s common stock. The reverse stock split became effective on January 29, 2014. All share and per share amounts in the financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the reduction in par value to additional paid-in capital.

Segment information

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 views its operations and manages its business in one operating segment. All material long-lived assets of the Company reside in the United States.

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. Premiums or discounts from par value are amortized to investment income over the life of the underlying investment.

Cash, cash equivalents and investments included the following at December 31, 2012 and 2013 (in thousands):

	Average maturity	Amortized cost	Unrealized gains	Unrealized losses	Fair value
December 31, 2012					
Cash		$ 593	$	$	$ 593
Money market funds		6,897			6,897

Cash and cash equivalents		$ 7,490	$	$	$ 7,490
U.S. Treasury obligations	230 days	$ 1,504	$	$	$ 1,504
Government agency securities	279 days	18,559	4		18,563
Short-term investments		$ 20,063	$ 4	$	$ 20,067

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

	Average maturity	Amortized cost	Unrealized gains	Unrealized losses	Fair value
December 31, 2013					
Cash		$ 2,188	$	$	$ 2,188
Money market funds		7,450			7,450
Cash and cash equivalents		$ 9,638	$	$	$ 9,638
U.S. Treasury obligation	301 days	$ 500	$	$	$ 500
Government agency securities	324 days	22,535	4		22,539
Short-term investments		$ 23,035	$ 4	$	$ 23,039

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses. During 2012 and 2013, there were no realized gains or losses on sales of investments, and no investments were adjusted for other than temporary declines in fair value.

Concentrations of credit risk

Financial instruments that potentially subject the Company to concentration of credit risk consist principally of money market funds and investments. 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. At December 31, 2012 and 2013, substantially all of the Company s cash was deposited in accounts at two highly rated financial institutions, thus limiting the amount of credit exposure to any one financial institution. These amounts at times may exceed federally insured limits.

Deferred issuance costs

Deferred issuance costs, which primarily consist of direct and incremental legal and accounting fees relating to the Company s initial public offering of common stock, are capitalized as incurred. Deferred issuance costs related to the Company s initial public offering will be offset against initial public offering proceeds upon the consummation of the offering and are included as a component of other assets in the accompanying consolidated balance sheets. No amounts were deferred related to the Company s proposed initial public offering as of December 31, 2012 and $2.5 million was deferred as of December 31, 2013.

Fair value of financial measurements

The Company measures certain financial assets and liabilities at fair value on a recurring basis (principally cash equivalents, short-term and long-term investments and the preferred stock warrant liability) that have been classified

as Level 1, 2 or 3 within the fair value hierarchy as described below. Fair values determined by Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities that the Company has the ability to access. Fair values determined by Level 2 inputs utilize data points that are observable, such as quoted prices, interest rates, and yield curves. Fair values determined by Level 3 inputs utilize unobservable data points for the asset or liability. The Company s investments in money market funds, U.S. treasury obligations, and government agency securities have been classified as Level 1 because their fair values are based on quoted market prices. The disclosed fair value of the Company s loan payable is determined using current applicable rates for similar instruments as of the balance sheet date. The carrying value of the Company s loan payable approximates fair value because of the length of the remaining term of the loan and an interest rate yield that is

Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

near current market rate yields. The disclosed fair value of the Company s loan payable is a Level 3 liability within the fair value hierarchy. The preferred stock warrant liability is classified as Level 3 because certain inputs to the valuation of the warrant are based on unobservable inputs. The assumptions used to value the warrant are more fully described in Note 12.

The carrying amount of financial instruments not carried at fair value, including loan payable and leasehold improvement loan approximate fair value due to either their short-term maturities or interest rates which approximate market rates.

Property and equipment

Property and equipment are recognized at cost and depreciated over their estimated useful lives using the straight-line method. 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 through December 31, 2013.

Revenue recognition

The Company has primarily generated revenue through arrangements with collaborators and nonprofit organizations for the development and commercialization of product candidates.

The Company recognizes revenue in accordance with Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) Topic 605, *Revenue Recognition* (ASC 605). Accordingly, revenue is recognized when all of the following criteria are met:

Persuasive evidence of an arrangement exists;

Delivery has occurred or services have been rendered;

The seller s price to the buyer is fixed or determinable; and

Collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in the Company s consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months

following the balance sheet date are classified as deferred revenue, current portion. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

The Company s revenue is currently generated through collaborative research and development and licensing agreements. The terms of these agreements typically contain multiple elements, or deliverables, which may include licenses, or options to obtain licenses, to product candidates, referred to as exclusive licenses, as well as research and development activities to be performed by us on behalf of the collaboration partner related to the licensed product candidates. The terms of these agreements may include payments to the Company of one or more of the following: a nonrefundable, 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.

When evaluating multiple element arrangements, the Company considers whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and

Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the consideration of the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company determines the estimated selling price for deliverables within each agreement using vendor-specific objective evidence (VSOE) of selling price, if available, third-party evidence (TPE) of selling price if VSOE is not available, or best estimate of selling price (BESP) if neither VSOE nor TPE is available. Determining the BESP for a deliverable requires significant judgment. The Company has used its BESP to estimate the selling price for licenses to the Company s proprietary technology, since the Company does not have VSOE or TPE of selling price for these deliverables. In those circumstances where the Company utilizes BESP to determine the estimated selling price of a license to the Company s proprietary technology, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreement, estimated development costs, and the probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating the Company s BESP, the Company evaluates whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple deliverables.

The Company s multiple-element revenue arrangements may include the following:

Exclusive Licenses. The deliverables under the Company s collaboration agreements generally include exclusive licenses to develop, manufacture and commercialize one or more deuterated compounds. To account for this element of the arrangement, management evaluates whether the exclusive license has standalone value from the undelivered elements based on the consideration of the relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner. The Company may recognize the arrangement consideration allocated to licenses upon delivery of the license if facts and circumstances indicate that the license has standalone value from the undelivered elements, which generally include research and development services. The Company defers arrangement consideration allocated to licenses if facts and circumstances indicate that the delivered license does not have standalone value from the undelivered elements.

When management believes the license does not have stand-alone value from the other deliverables to be provided in the arrangement, the Company generally recognizes revenue attributed to the license on a straight-line basis over the Company s contractual or estimated performance period, which is typically the term of the Company s research and development obligations. If management cannot reasonably estimate when the Company s performance obligation ends, then revenue is deferred until management can reasonably estimate when the performance obligation ends. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the research and development and licensing agreement. Such a change could have a material impact on the amount of revenue the Company records in future periods.

Research and Development Services. The deliverables under the Company s collaboration and license agreements may include deliverables related to research and development services to be performed by the Company on behalf of the collaboration partner. As the Company is principally responsible for the performance of these services under the agreements, the Company recognizes revenue on a gross basis for research and development services as those services are performed.

Payments or reimbursements resulting from the Company s research and development efforts are recognized as the services are performed and presented on a gross basis because the Company is the principal for such efforts,

Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

so long as there is persuasive evidence of an arrangement, the fee is fixed or determinable, and collection of the related amount is reasonably assured.

Option Agreements. The Company s arrangements may provide a collaborator with the right to select a deuterated compound for licensing within an initial pre-defined selection period. Under these agreements, a fee would be due to the Company upon the exercise of an option to acquire a license. The accounting for option arrangements is dependent on the nature of the option granted to the collaboration partner. An option is considered substantive if, at the inception of the arrangement, the Company is at risk as to whether the collaboration partner will choose to exercise the option to secure exclusive licenses. Factors that the Company considers in evaluating whether an option is substantive include the overall objective of the arrangement, the benefit the collaborator might obtain from the arrangement without exercising the option, the cost to exercise the option relative to the total upfront consideration and the additional financial commitments or economic penalties imposed on the collaborator as a result of exercising the option. For arrangements under which an option to secure a license is considered substantive, the Company does not consider the license underlying the option to be a deliverable at the inception of the arrangement. For arrangements under which the option to secure a license is not considered substantive, the Company considers the license underlying the option to be a deliverable at the inception of the arrangement and, upon delivery of the license, would apply the multiple-element revenue arrangement criteria to the license and any other deliverables to determine the appropriate revenue recognition. A significant and incremental discount included in an otherwise substantive option is considered to be a separate deliverable at the inception of the arrangement.

Milestone Revenue. The Company s collaboration agreements generally include contingent milestone payments related to specified development milestones, regulatory milestones and sales-based milestones. Development milestones are typically payable when a product candidate initiates or advances in clinical trial phases or achieves defined clinical events such as proof-of-concept. Regulatory milestones are typically payable upon submission for marketing approval with regulatory authorities or upon receipt of actual marketing approvals for a compound, approvals for additional indications, upon commercial launch or upon the first commercial sale. Sales-based milestones are typically payable when annual sales reach specified levels.

At the inception of each arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (i) the entity s performance to achieve the milestone or (ii) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity s performance to achieve the milestone; (b) the consideration relates solely to past performance; and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. Milestones that are not considered substantive are accounted for as license payments and recognized on a straight-line basis over the remaining period of performance.

Research and development costs

Costs incurred in the research and development of the Company s products 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. Nonrefundable advance payments for goods and services that will be used in future research

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

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.

Accounting for stock-based compensation

The Company accounts for its stock-based compensation awards in accordance with FASB ASC Topic 718, *Compensation Stock Compensation* (ASC 718). ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock and modifications to existing stock options, to be recognized in the consolidated statements of operations and comprehensive loss based on their fair values. The Company uses the Black-Scholes option pricing model to determine the fair value of options granted.

Compensation expense related to awards to employees is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Awards to non-employees are adjusted through share-based compensation expense as the award vests to reflect the current fair value of such awards and expensed using an accelerated attribution model.

The Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its common stock. Each valuation methodology includes estimates and assumptions that require management s judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions affecting the biotechnology industry, the prices at which the Company sold shares of redeemable convertible preferred stock, the superior rights and preferences of securities senior to the common stock, and the likelihood of achieving a liquidity event, such as an initial public offering or sale. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

Income taxes

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 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.

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 9, Commitments. The Company has a standard indemnification arrangement under the lease that requires it to

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

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.

As of December 31, 2012 and 2013, 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 comprised of net loss and other comprehensive income or loss. Other comprehensive income or loss consists of unrealized gains and losses on short-term investments.

Net income (loss) per share

Net income (loss) per share information is determined using the two-class method, which includes the weighted-average number of common shares outstanding during the period and other securities that participate in dividends (a participating security). The Company s redeemable convertible preferred stock are participating securities as defined by ASC 260-10, *Earnings Per Share*.

Under the two-class method, basic net income (loss) per share applicable to common stockholders is computed by dividing the net income (loss) applicable to common stockholders by the weighted-average number of common shares outstanding for the reporting period. Diluted net income (loss) per share is computed using the more dilutive of (1) the two-class method or (2) the if converted method. The Company allocates net income first to preferred stockholders based on dividend rights under the Company s articles of incorporation and then to preferred and common stockholders based on ownership interests. Net losses are not allocated to preferred stockholders as they do not have an obligation to share in the Company s net losses.

Diluted net income (loss) per share gives effect to all potentially dilutive securities, including redeemable convertible preferred stock, and shares issuable upon the exercise of outstanding warrants and stock options, using the treasury stock method. For the years ended December 31, 2011, 2012 and 2013, the Company has excluded the effects of all potentially dilutive shares, which include redeemable convertible preferred stock, a warrant to purchase redeemable convertible preferred stock and outstanding common stock options, from the weighted-average number of common shares outstanding as their inclusion in the computation for all periods would be anti-dilutive due to net losses.

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect (in thousands):

	Year ended December 31,		
	2011	2012	2013
Preferred stock	9,920	9,920	9,920
Warrant	71	71	71
Outstanding stock options	1,952	1,960	1,953
	11,943	11,951	11,944

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

Subsequent events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. Refer to Note 16, Subsequent events.

Application of new or revised accounting standards

On April 5, 2012, the Jump-Start Our Business Startups Act (the JOBS Act) was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an emerging growth company. As an emerging growth company the Company has elected to not take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards, and as a result, will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

Recently adopted accounting pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material effect on its financial position or results of operations upon adoption.

3. Restricted cash

At December 31, 2012 and 2013, $0.7 million of the Company s cash is restricted by a bank as collateral for a stand-by letter of credit issued by the Company to its landlord in connection with the lease of the Company s corporate headquarters.

4. Property and equipment

Property and equipment consists of the following at December 31, 2012 and 2013 (in thousands):

	Estimated useful life (in years)	December 31, 2012	December 31, 2013
Laboratory equipment	5	$ 2,383	$ 2,062
Computer and telephone equipment	3	278	142
Software	3	141	66
Furniture	3	167	1

Leasehold improvements	Lesser of useful life or lease term (7 years)	5,863	5,848
		8,832	8,119
Less accumulated depreciation and amortization		(5,378)	(5,646)
		$ 3,454	$ 2,473

Depreciation and amortization expense was charged to operations in the amounts of $1.6 million for the year ended December 31, 2011, $1.5 million for the year ended December 31, 2012 and $1.3 million for the year ended December 31, 2013.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

5. Accrued expenses and other liabilities

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

	December 31,	
	2012	2013
Accrued professional fees and other	$ 393	$ 569
Employee compensation and benefits		290
Research and development expenses	866	860
Deferred lease incentive, current portion	513	513
Deferred rent, current portion	181	243
	$ 1,953	$ 2,475

6. Redeemable convertible preferred stock

The Company has issued Series A, Series B, Series C and Series D redeemable convertible preferred stock (collectively, the Preferred Stock). The Company classifies the Preferred Stock outside of stockholders deficit because the shares contain contingent redemption features that are not solely within the Company s control.

Preferred Stock consisted of the following as of December 31, 2012 (in thousands):

	Preferred shares authorized	Preferred shares issued and outstanding	Redemption value / liquidation preference	Carrying value	Common stock issuable upon conversion
Series A	10,000	10,000	$ 10,000	$ 9,990	1,770
Series B	24,250	24,250	48,500	48,482	4,292
Series C	22,000	15,130	37,826	37,799	2,678
Series D	6,667	6,667	16,667	15,577	1,180
	62,917	56,047	$ 112,993	$ 111,848	9,920

Preferred Stock consisted of the following as of December 31, 2013 (in thousands):

	Preferred shares authorized	Preferred shares issued and outstanding	Redemption value / liquidation preference	Carrying value	Common stock issuable upon conversion
Series A	10,000	10,000	$ 10,000	$ 9,993	1,770
Series B	24,250	24,250	48,500	48,488	4,292
Series C	22,000	15,130	37,826	37,809	2,678
Series D	6,667	6,667	16,667	15,954	1,180
	62,917	56,047	$ 112,993	$ 112,244	9,920

The Preferred Stock have the following rights and preferences:

Voting. The holders of the Preferred Stock are entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote, except with respect to matters on which Delaware General Corporation Law requires that a vote will be by a separate class. Each preferred stockholder is entitled to the number of votes equal to the number of shares of common stock into which each preferred share is convertible at

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

the time of such vote. The holders of at least 60% of the outstanding Series A Preferred Stock voting together as a single class are entitled to elect two directors to the Company s Board of Directors. The holders of at least 60% of the outstanding Series B Preferred Stock voting together as a single class are entitled to elect two directors to the Company s board of directors. The holders of Preferred Stock and the holders of common stock, voting together as a single class on an as-converted to common stock basis, are entitled to elect the remaining directors.

Dividends. The holders of Preferred Stock are entitled to receive dividends when and if declared by the board of directors. No dividends may be paid on shares of common stock until the Company has first paid to the holders of Preferred Stock a dividend equal to 6% per annum of the aggregate conversion prices for the Preferred Stock accruing from the original issue dates of the Preferred Stock. No dividends have been declared through December 31, 2013.

Liquidation preference. In the event of any liquidation, dissolution or winding up of the affairs of the Company, the holders of the then-outstanding Preferred Stock shall receive the greater of (1) $1.00 per share for Series A Preferred Stock, $2.00 per share for Series B Preferred Stock, $2.50 per share for Series C Preferred Stock, and $2.50 per share for Series D Preferred Stock, plus all declared but unpaid dividends, or (2) such amount per share of Preferred Stock payable as converted into common stock. Any remaining assets of the Company shall be distributed ratably among the holders of common stock. If the assets or surplus funds to be distributed to the holders of the Preferred Stock are insufficient to permit the payment to such holders of their full preferential amount, the assets and surplus funds legally available for distribution shall be distributed ratably among the holders of the Preferred Stock in proportion to the full preferential amount that each holder is otherwise entitled to receive.

Conversion. Each share of Preferred Stock, at the option of the holder, is convertible into a number of fully paid shares of common stock as determined by dividing $1.00 for Series A Preferred Stock, $2.00 for Series B Preferred Stock, $2.50 for Series C Preferred Stock, and $2.50 for Series D Preferred Stock by the conversion price in effect at the time. The conversion price of Series A Preferred Stock is $5.65 per share, the conversion price of Series B Preferred Stock is $11.30 per share, the conversion price of Series C Preferred Stock is $14.13 per share and the conversion price of Series D Preferred Stock is $14.13 per share. These conversion prices are subject to adjustment in accordance with anti-dilution provisions contained in the Company s Certificate of Incorporation. Conversion is automatic immediately upon the closing of a firm commitment underwritten public offering in which the gross proceeds are not less than $30 million, or upon the written election of the holders of at least 60% of the then-outstanding shares of Series B Preferred Stock and at least 50% of the then-outstanding shares of Series C Preferred Stock.

Redemption. Commencing 90 days prior to October 31, 2015, the holders of at least 60% of the-then outstanding shares of Series B Preferred Stock and at least 50% of the-then outstanding shares of Series C Preferred Stock may require the Company to redeem the Preferred Stock in three equal annual installments, the first occurring as of a date that is at least 90 days after the redemption election, at $1.00 per share for Series A Preferred Stock, $2.00 per share for Series B Preferred Stock, $2.50 per share for Series C Preferred Stock and $2.50 per share for Series D Preferred Stock plus any declared but unpaid dividends. The Company is accreting the shares to the redemption values over the period from issuance to October 31, 2015, such that the carrying amount of the securities will equal the redemption

amounts of $1.00 for Series A Preferred Stock, $2.00 for Series B Preferred Stock, $2.50 for Series C Preferred Stock and $2.50 for Series D Preferred Stock. The difference between the redemption values and the carrying amount at December 31, 2012 and December 31, 2013 are the issuance costs associated with each offering and the unamortized premium on Series D Preferred Stock (see Note 10, Collaboration agreements). The accretion amounts are recognized as an increase to the carrying value of the Preferred Stock with a corresponding charge to additional paid-in capital, and amounted to $1.1 million for the

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

year ended December 31, 2011, $0.4 million for the year ended December 31, 2012 and $0.4 million for the year ended December 31, 2013. The annual accretion is expected to be $0.1 million for the year ended December 31, 2014 and none thereafter due to the automatic conversion of all outstanding preferred stock on February 19, 2014.

The Company has evaluated the Preferred Stock and determined it should be considered an equity host and not a debt host as defined by ASC 815, *Derivatives and Hedging*. This evaluation is necessary in order to determine if any embedded features require bifurcation and, therefore, separate accounting as a derivative liability. The Company s analysis followed the whole instrument approach, which compares an individual feature against the entire preferred stock instrument which includes that feature. The Company s analysis was based on a consideration of the Preferred Stock s economic characteristics and risks and more specifically evaluated all the stated and implied substantive terms and features including (i) whether the Preferred Stock included redemption features, (ii) whether the preferred stockholders were entitled to dividends, (iii) the voting rights of the Preferred Stock and (iv) the existence and nature of any conversion rights. As a result of the Company s determination that the Preferred Stock is an equity host, the embedded conversion feature is not considered a derivative liability.

In connection with the closing of the Company s initial public offering on February 19, 2014, all of the Company s outstanding preferred stock converted into 9,919,821 shares of common stock.

7. Stockholders deficit

Stock incentive plan

The Company s Amended and Restated 2006 Stock Option and Grant Plan (the 2006 Plan) provides for the issuance of a total of 2,212,389 shares of common stock in the form of incentive stock options, non-qualified stock options, awards of stock and direct stock purchase opportunities to directors, officers, employees and consultants of the Company.

Generally, the Company s stock options are granted with an exercise price equal to the estimated fair value of the underlying common stock on the date of grant as determined by the board of directors, expire no later than ten years from the date of grant, and vest over various periods not exceeding four years. At December 31, 2013, 168,584 shares were available for future grant under the 2006 Plan.

In January 2014, the Company adopted the 2014 Stock Incentive Plan (the 2014 Plan). The 2014 Plan became effective on February 11, 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. Upon the closing of the Company s initial public offering on February 19, 2014, 2,249,911 shares of common stock were reserved for issuance under the 2014 Plan. The number of shares reserved under the 2014 Plan is subject to further increase by the number of shares of common stock subject to outstanding awards under the 2006 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased. 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. The annual increase will be added on the first day of each year beginning in 2015 and each subsequent anniversary until 2024, equal to the lowest of 2,000,000 shares of common stock, 4.0% of the number of shares of common stock outstanding on January 1 of each such fiscal year and an amount determined by the board of directors.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

The following is a summary of option activity under the 2006 Plan:

	Number of shares (in thousands)	Weighted-average exercise price per share	Weighted-average remaining contractual term (in years)	Aggregate intrinsic values (in thousands)
Outstanding at December 31, 2012	1,960	$ 3.15	6.6	$ 11,000
Granted	81	3.73		
Forfeited and expired	(80)	3.80		
Exercised	(8)	3.99		
Outstanding at December 31, 2013	1,953	$ 3.14	5.2	$ 14,603
Exercisable at December 31, 2013	1,674	$ 3.06	4.9	$ 12,644
Unvested at December 31, 2013	279	$ 3.60	7.4	
Vested and expected to vest at December 31, 2013[(1)]	1,944	$ 3.14	5.2	$ 14,540

(1) This represents the number of vested options as of December 31, 2013, plus the number of unvested options expected to vest as of December 31, 2013, based on the unvested options at December 31, 2013, adjusted for the estimated forfeiture rate of 5%.

The intrinsic value of options exercised during the year ended December 31, 2011 was $32 thousand, during the year ended December 31, 2012 was $0 and during the year ended December 31, 2013 was $0.1 million.

The weighted-average fair values of options granted during the year ended December 31, 2011 was $2.26, during the year ended December 31, 2012 was $6.53, and during the year ended December 31, 2013 was $13.77.

The aggregate intrinsic values in the preceding table represent the total pre-tax intrinsic value (the difference between the Company s common stock price on the last day of the reporting period and the exercise price, multiplied by the number of in-the-money stock options) that would have been received by the stock option holders had all stock option holders exercised their stock options at the end of the reporting period. The amount of aggregate intrinsic value will change based on the fair value of the Company s common stock.

Stock-based compensation expense

The Company estimates the fair value of its stock-based awards using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of the expected term of the award, (c) the risk-free interest rate, (d) expected dividends and (e) the fair value of the Company s common stock on the date of grant.

Due to the lack of a public market for the trading of the Company s common stock prior to its initial public offering and a lack of company specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. When selecting these public companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected term of the stock-based awards. The Company computes historical volatility data using the daily closing prices for the selected companies shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

The expected term was determined using the simplified method, which is the mid-point between the vesting date and the end of the contractual term.

The Company is required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from those estimates. The Company has applied an annual forfeiture rate of 5% to employee options granted during the years ended December 31, 2011, 2012 and 2013. The annual forfeiture rate was estimated based upon actual historical forfeitures.

The risk-free rate is determined by reference to U.S. Treasury zero-coupon issues with remaining maturities similar to the expected term of the options.

The Company has not paid, and does not anticipate paying, cash dividends on shares of common stock; therefore, the expected dividend yield is assumed to be zero.

The fair values of options granted during the years ended December 31, 2011, 2012 and 2013 were calculated using the following estimated weighted-average assumptions:

	December 31,		
	2011	2012	2013
Expected volatility	78.1%	72.8%	70.1%
Expected term (in years)	6.0	6.0	6.0
Risk-free interest rate	1.09%	0.95%	1.69%
Expected dividend yield	%	%	%

The Company recognized stock-based compensation from grants of stock options to employees and non-employees of $0.9 million for the year ended December 31, 2011, $0.9 million for the year ended December 31, 2012 and $1.0 million for the year ended December 31, 2013. Total compensation cost recognized for all stock-based compensation awards in the consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Year ended December 31,		
	2011	2012	2013
Research and development	$ 572	$ 564	$ 583
General and administrative	331	304	420
Total stock-based compensation expense	$ 903	$ 868	$ 1,003

As of December 31, 2013 there was $1.5 million of total unrecognized compensation cost related to unvested options. Total unrecognized compensation cost will be adjusted for future changes in forfeitures. The Company expects to recognize that cost over a weighted-average period of 2.0 years.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

Reserved shares

The Company had reserved the following shares of common stock as of December 31, 2013 for the potential conversion of outstanding Preferred Stock and warrants and the exercise of stock options (in thousands):

	December 31, 2013
Series A Preferred Stock	1,770
Series B Preferred Stock	4,292
Series C Preferred Stock (including warrant)	2,749
Series D Preferred Stock	1,180
Common stock options	2,121
	12,112

8. Income taxes

During 2011, 2012 and 2013, the Company did not record a benefit for income taxes related to its operating losses. The Company has provided a full valuation allowance against its net deferred tax assets, as the Company believes that it is more likely than not that the deferred tax assets will not be realized.

A reconciliation of the federal statutory income tax rate and the Company s effective income tax rate is as follows:

	Year ended December 31,		
	2011	2012	2013
Federal statutory income tax rate	34.0%	34.0%	34.0%
State income taxes	5.3	5.3	5.3
Change in valuation allowance	(44.5)	(34.9)	(43.3)
Credits	9.2	1.2	31.7
Permanent items	(2.8)	(1.8)	(5.9)
Expiring state net operating loss carryforward	(1.2)	(3.8)	(21.8)
Effective income tax rate	0.0%	0.0%	0.0%

The significant components of the Company s net deferred tax assets consist of the following (in thousands):

	December 31,	
	2012	2013
Net operating loss carryforwards	$ 38,059	$ 38,585
Deferred revenue	1,081	1,081
Research and development credit carryforwards	4,335	6,277
Depreciation	1,032	47
Start-up costs	22	18
Other	(166)	978
	44,363	46,986
Valuation allowance	(44,363)	(46,986)
Net deferred tax assets	$	$

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

At December 31, 2013, the Company had federal net operating loss carryforwards of $103.5 million and state net operating loss carryforwards of $64.1 million available to reduce future taxable income, which expire at various dates beginning in 2014 through 2034. The Company also had federal and state research and development tax credit carryforwards of $4.9 million and $2.1 million, respectively, available to reduce future tax liabilities, and which expire at various dates through 2034.

Realization of the future tax benefits is dependent on many factors, including the Company s ability to generate taxable income within the net operating loss carryforward period. Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50 percent, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed several financings since its inception which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

At December 31, 2013, 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 accompanying statement of operations. As of December 31, 2013, the Company had no accrued interest related to uncertain tax positions. In many cases, the Company s uncertain tax positions are related to years that remain subject to examination by relevant tax authorities. 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.

9. Commitments

In February 2008, the Company entered into a seven-year, non-cancelable operating lease for approximately 45,000 square feet of office and laboratory space (the 2008 Lease Agreement) in Lexington, Massachusetts, which serves as the Company s headquarters.

The 2008 Lease Agreement provides for escalating rent payments over the seven-year lease term. The Company is accounting for the corresponding rent differential as deferred rent, and is recognizing rental expense on a straight-line

basis, beginning in February 2008.

The 2008 Lease Agreement included certain lease incentives in the form of two tenant improvement allowances. The first tenant improvement allowance of $3.7 million was for general improvements to the facility s office space and HVAC systems. The Company was required to manage the improvements including making payment for them up front, and then submitting requests to the landlord for reimbursement. Once approved, the landlord reimbursed the Company. The Company was not required to repay the landlord for any of this allowance. The Company has capitalized the improvements made with the first tenant improvement allowance into fixed assets,

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

and has established a liability in the accompanying balance sheet under the caption deferred lease incentive. The Company is amortizing the deferred lease incentive and amortizing the related fixed assets over the lease term.

The second tenant improvement allowance of $2.3 million was for improvements to be made to build laboratory space to the Company s specifications. The second tenant improvement allowance is similar to the first, except that the Company must repay the reimbursements to the landlord monthly over the lease term, plus interest at a 10% annual rate. The amount to be repaid to the landlord, exclusive of interest, is reflected in the accompanying balance sheet and table below as leasehold improvement loan. The Company has capitalized the improvements made with the second tenant improvement allowance into fixed assets, and is amortizing them over the lease term.

The future minimum lease payments (including base rent obligations and repayment of the leasehold improvement loan, including interest accrued at 10% per annum) under the 2008 Lease Agreement is as follows (in thousands):

	Base rent obligations	Repayment of leasehold improvement loan[(1)]	Total obligations
At December 31, 2013			
2014	$ 1,361	$ 463	$ 1,824
2015	1,045	347	1,392
	$ 2,406	810	$ 3,216
Less amounts representing interest		(229)	
Less leasehold improvement loan, current portion		(332)	
Leasehold improvement loan, net of current portion		$ 249	

(1) Includes interest accrued at 10% per annum.

Rent expense was $0.7 million for the year ended December 31, 2011, $0.7 million for the year ended December 31, 2012 and $0.7 million for the year ended December 31, 2013.

Employment agreements

Five of the Company s employees are covered by employment agreements, covering salary, certain benefits and incentive compensation. Under these agreements, the executives could be entitled to severance pay up to 12 months of base salary, paid COBRA insurance coverage for 12 months and acceleration of stock option vesting (assuming for such acceleration a termination without cause or on death or disability or resignation for good reason within one year after a change in control). During 2013, the Company accrued $0.3 million in severance and benefit obligations in connection with the departure of its Chief Medical Officer, with the associated costs allocated to research and development expenses on the statement of operations and comprehensive loss. Approximately $69 thousand of cash payments related to these obligations were made during 2013, resulting in a total recorded liability of $0.3 million related to this obligation as of December 31, 2013.

10. Collaboration agreements

Celgene

In April 2013, the Company entered into a master development and license agreement (the Celgene Agreement) with Celgene Corporation and Celgene International Sàrl (Celgene), which is primarily focused on the research,

Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

development and commercialization of deuterated compounds that are deuterated analogs of certain non-deuterated compounds targeting cancer or inflammation. The collaboration will initially focus on one program, but has the potential to encompass up to four programs.

For the initial program, the Company granted Celgene an exclusive worldwide license to develop, manufacture and commercialize products that contain deuterated analogs of a selected non-deuterated compound and several close chemical derivatives thereof. The Company further granted Celgene licenses with respect to two additional programs and an option with respect to a third additional program. The Company and Celgene have agreed on the non-deuterated compounds for each of the two additional license programs. For the option program, Celgene may select the non-deuterated compound at a later time, which, unless otherwise agreed by the Company, will be limited to a compound for which Celgene possesses exclusive rights. With respect to the two additional license programs, on the effective date of the Celgene Agreement the Company granted Celgene an exclusive worldwide license to develop, manufacture and commercialize products that contain deuterated analogs of the agreed upon non-deuterated compounds. Celgene is restricted from utilizing their research, development and commercialization rights under each of the upfront licenses unless, within seven years of the effective date of the Celgene Agreement, Celgene pays the Company a license exercise fee. If Celgene does not elect to pay the license exercise fee during the seven year period, the license will expire. With respect to the option program, once a compound is selected, Celgene may exercise its option by paying the Company an option exercise fee within seven years of the effective date of the Celgene Agreement, and upon Celgene s exercise of the option the Company will grant to Celgene an exclusive worldwide license to develop, manufacture and commercialize deuterated products that contain deuterated analogs of the selected non-deuterated compound.

The Company is responsible, at its own expense, for conducting research and early development activities for the initial program pursuant to agreed upon development plans. This includes the completion of single and multiple ascending dose Phase 1 clinical trials and any mutually agreed upon additional Phase 1 clinical trials, as set forth in the development plan and approved by the joint steering committee (JSC) for the collaboration.

The Company does not have any obligation to conduct any research or development activities for any of the additional programs unless and until Celgene exercises its rights with respect to such program and pays us the applicable exercise fee. If Celgene exercises its rights with respect to any additional program and pays the Company the applicable exercise fee, the Company is responsible, at its own expense, for conducting research and development activities for such program pursuant to agreed upon development plans until the completion of Phase 1 clinical trial, which will be defined in each development plan on a program-by-program basis. In addition, if Celgene exercises its rights with respect to the option program and pays the Company the applicable option exercise fee, the Company is responsible for seeking to generate a deuterated compound for clinical development in the selected option program. Oversight of the development program for each program under the Celgene Agreement is guided by separate JSCs.

Celgene is solely responsible for all research, development and commercialization costs with respect to the initial program beyond the Phase 1 clinical trials that the Company conducts. If Celgene exercises its rights with respect to any additional program, Celgene will be solely responsible for all research, development and commercialization costs

for such program following the completion of the first Phase 1 clinical trial for such program.

Following its assumption of responsibility for development costs of a product candidate, Celgene is required to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize the product candidate until such time, if any, as Celgene determines in its reasonable discretion based on comparative metrics that the product candidate does not represent a substantial improvement over the corresponding non-deuterated compound.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

Under the terms of the Celgene Agreement, the Company received a $35.0 million non-refundable upfront payment from Celgene. In addition, the Company is eligible to earn up to $23.0 million in development milestone payments, up to $247.5 million in regulatory milestone payments and up to $50.0 million in sales-based milestone payments related to products within the initial program. The next milestone payment the Company might be entitled to receive under the initial program is $8.0 million related to the completion of a Phase 1 clinical trial. If Celgene exercises its rights with respect to either of the two additional license programs, the Company will receive a license exercise fee of $30.0 million and will also be eligible to receive up to $23.0 million in development milestone payments and up to $247.5 million in regulatory milestone payments for such program. With respect to one of the additional license programs, the Company is eligible to receive up to $100.0 million in sales-based milestone payments based on net sales of products, and with respect to the other additional license program, the Company is eligible to receive up to $50.0 million in sales-based milestone payments based on net sales of products. If Celgene exercises its option with respect to the option program, the Company will receive an option exercise fee of $10.0 million and will be eligible to earn up to $23.0 million in development milestone payments and up to $247.5 million in regulatory milestone payments.

In addition, with respect to each program, Celgene is required to pay the Company royalties on net sales of each licensed product at defined percentages ranging from the mid-single digits to low double digits below 20%, on worldwide net product sales of licensed products. The royalty term for each licensed product in each country is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the latest of expiration of specified patent coverage, expiration of regulatory exclusivity or 10 years following commercial launch. The royalty rate is reduced on a country-by-country basis during any period within the royalty term when there is no patent claim or regulatory exclusivity covering the licensed product in the particular country.

During the term of the Celgene Agreement, the Company may not research, develop or commercialize, or grant or offer to grant a third party a license to research, develop or commercialize, any licensed product, and with respect to the option program, certain products that Celgene has the right to select as an option product, other than pursuant to the Celgene Agreement.

The Celgene Agreement will expire upon the later of the seventh anniversary of the effective date of the Celgene Agreement and the expiration of all royalty terms with respect to each licensed product in each country. Celgene has the right to terminate the Celgene Agreement, in whole or only with respect to a particular licensed product, upon 60 days prior written notice to the Company. The Celgene Agreement may also be terminated by the Company in the event of an uncured material breach by Celgene. If the Celgene Agreement is terminated for any reason, the licenses granted by the Company to Celgene will terminate and specified rights to licensed products will revert to the Company. There are no cancellation, termination or refund provisions in this arrangement that contain material financial consequences to the Company.

The Company s arrangement with Celgene contains the following deliverables: (i) an exclusive worldwide license to develop, manufacture and commercialize deuterated analogs of a selected compound related to the initial program (the License Deliverable), (ii) obligations to perform research and development services associated with the initial program

(the R&D Services Deliverable), (iii) obligation to supply preclinical and clinical trial material related to the initial program (the Supply Deliverable), (iv) participation on the JSC during the term of the initial program (the JSC Deliverable), (v) significant and incremental discount related to the first additional license program for which the non-deuterated compound has been selected (the First Discount Deliverable) and (vi) significant and incremental discount related to the second additional license program for which the non-deuterated compound has been selected (the Second Discount Deliverable).

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

As a result of the restrictions placed on the two additional license programs that preclude Celgene from exercising its rights under the respective licenses without the payment of a significant license exercise fee, for accounting purposes the Company concluded that it had effectively provided Celgene an option to obtain licenses to those programs. The Company has determined that the rights with respect to the three additional programs are substantive options. Celgene is not contractually obligated to exercise its rights and there is a significant fee that is due upon exercise of the rights. Therefore, it is uncertain as to whether Celgene will decide to exercise its rights for any of the three additional programs. Consequently, the Company is at risk with regard to whether Celgene will exercise its rights. Accordingly, none of the licenses with respect to the three additional programs are considered deliverables at the inception of the arrangement and the associated license right or option fees are not included in the allocable arrangement consideration. Similarly, the Company has determined that for each additional program the potential obligations to perform research and development services, supply preclinical and clinical trial material and participate on the respective JSC are contingent upon Celgene exercising its rights with respect to such programs. Therefore, consistent with the treatment of the associated license right or option, the Company s related potential obligations are also not considered deliverables at the outset of the arrangement.

As it relates solely to the option program for which the non-deuterated compound has not yet been selected, the Company has determined that such option is not priced at a significant and incremental discount as the option fee approximates the best estimate of selling price of the underlying license. As it relates to the two additional programs for which the non-deuterated compound has been selected, the Company concluded the respective license exercise fee was less than the aggregate BESP for the respective license and related obligations to perform research and development services, supply preclinical and clinical trial materials and participate on the JSC. Accordingly, pursuant to the provisions of ASC 605-25, the Company concluded that the license exercise fees were priced at a significant and incremental discount. As a result, the Company has concluded for accounting purposes that the discounts for these two additional programs represent separate elements in the arrangement at inception.

The Company has concluded that the License Deliverable has standalone value because Celgene can fully utilize the underlying license for its intended purpose without receipt of the remaining deliverables in the arrangement. This conclusion considered Celgene s internal product development expertise and commercialization capabilities that enable it to use the License Deliverable for its intended purpose without the involvement of the Company. Moreover, the rights conveyed by the Company to Celgene in connection with the License Deliverable include the contractual right to sublicense. Similarly, all of the remaining deliverables were deemed to have standalone value upon delivery. Factors considered in this determination included, among other things, whether any other vendors sell the items separately and if the customer could use the item for its intended purpose without the receipt of the remaining deliverables. Additionally, there are no refund provisions in the Celgene Agreement. Accordingly, each deliverable included in the Celgene arrangement qualifies as a separate unit of accounting.

The Company determined that neither VSOE of selling price nor TPE of selling price was available for any of the units of accounting identified at the inception of the arrangement with Celgene. Accordingly, the selling price of each unit of accounting was determined based on management s BESP. The Company developed BESP for the License Deliverable in reference to its other licensing transactions, applicable market conditions, relevant entity-specific

factors, and those factors contemplated in negotiating the agreement, including territories covered by the license, the stage of development and market potential of the product candidate, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license and the Company s pricing practices and pricing objectives. The Company developed BESP for the R&D Services Deliverable, the Supply Deliverable and the JSC Deliverable based on the nature of the services to be performed and estimates of the associated effort and cost of the services adjusted for a reasonable profit margin such that they represented estimated market rates for similar services sold on a standalone basis. The Company developed

Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

BESP for the First Discount Deliverable and the Second Discount Deliverable based on the estimated value of the associated in-the-money license right. In developing such estimate, the Company considered the period to exercise the license right, an appropriate discount rate and the likelihood that a market participant who was entitled to the discount would exercise the license right.

Allocable arrangement consideration at inception is limited to the $35.0 million non-refundable upfront payment. Total allocable arrangement consideration was allocated among the separate units of accounting using the relative selling price method as follows: (i) $17.0 million to the License Deliverable; (ii) $8.7 million to the R&D Services Deliverable; (iii) $3.2 million to the Supply Deliverable; (iv) $0.1 million to the JSC Deliverable; (v) $3.0 million to the First Discount Deliverable; and (vi) $3.0 million to the Second Discount Deliverable.

The arrangement consideration allocated to the License Deliverable was recognized upon delivery. Amounts allocated to the R&D Services Deliverable and Supply Deliverable are recognized under the proportional performance method over the expected period of performance, or 39 months. The amount allocated to the JSC Deliverable is recognized ratably over the expected period of performance, or 39 months. Amounts allocated to the First Discount Deliverable and the Second Discount Deliverable are deferred and will be recognized at the earlier of when the associated license rights are exercised and licenses are delivered or upon lapsing of the underlying right, if the respective right expires unexercised. The Company reassesses the estimated periods of performance for each unit of accounting at the end of each reporting period. The Company will recognize royalty revenue in the period of sale of the related licensed product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable assuming all other revenue recognition criteria are met.

In the event Celgene exercises its rights with respect to either of the two additional license programs, the license exercise fee would be considered a license fee and would be allocated among the license and the related R&D Services Deliverable, Supply Deliverable, and JSC Deliverable using the relative selling price method. The revenue recognition for the amounts allocated to the various deliverables would be consistent with the revenue recognition described in the previous paragraphs.

The Company has evaluated all of the milestones that may be received in connection with the Celgene arrangement. All development and regulatory milestones are considered substantive on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. All sales-based milestones will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any milestone or royalty payments from Celgene.

During the year ended December 31, 2013, the Company recognized revenue of $17.0 million upon delivery of the license deliverable, $0.7 million for the R&D Services Deliverable and $0.6 million for the Supply Deliverable. The

revenue is classified as license and research and development revenue in the accompanying consolidated statement of operations and comprehensive loss. As of December 31, 2013, there is $16.7 million of deferred revenue related to the Company s collaboration with Celgene, $4.2 million of which is classified as current and $12.5 million of which is classified as long-term, in the accompanying consolidated balance sheet.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

Jazz Pharmaceuticals

In February 2013, the Company signed a development and license agreement with Jazz Pharmaceuticals, Inc. (Jazz Pharmaceuticals) that provides Jazz Pharmaceuticals worldwide rights to develop and commercialize the Company s deuterated sodium oxybate (D-SXB) compounds (the Jazz Pharmaceuticals Agreement). Jazz Pharmaceuticals has principal responsibility for ongoing development activities. Pursuant to the terms of the license agreement, Jazz Pharmaceuticals has the option to require the Company to provide development support services through a single Phase 1 clinical trial. If Jazz Pharmaceuticals exercises its option, the Company will receive payment for any development support services provided and will be reimbursed for all external costs related to the development support services including preclinical, manufacturing, regulatory and clinical costs.

Under the terms of the Jazz Pharmaceuticals Agreement, the Company received a $4.0 million non-refundable upfront payment. In addition, the Company is eligible to earn up to $8.0 million in development milestone payments, up to $35.0 million in regulatory milestone payments and up to $70.0 million in sales-based milestone payments. The next milestone payment that the Company might be entitled to receive under this agreement is $4.0 million related to the completion of a Phase 1 clinical trial.

In addition, Jazz Pharmaceuticals is required to pay the Company royalties at defined percentages ranging from the mid-single digits to low double digits below 20%, on a country-by-country and licensed product-by-licensed product basis, on worldwide net product sales of licensed products. The royalty term for each licensed product in each country is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the later of the expiration of specified patent coverage or 10 years following commercial launch. The royalty rate is lowered on a country-by-country basis, under certain circumstances as specified in the agreement.

The Jazz Pharmaceuticals Agreement will expire on a licensed product-by-licensed product and country-by-country basis on the date of the expiration of the applicable royalty term with respect to each licensed product in each country. Jazz Pharmaceuticals may terminate the agreement, on a country-by-country basis or in its entirety, upon 90 days prior written notice. The Company may terminate the agreement upon written notice to Jazz Pharmaceuticals if Jazz Pharmaceuticals decides to permanently cease development and commercialization of all licensed products. The Company may also terminate the agreement if Jazz Pharmaceuticals has abandoned development or commercialization activities for licensed products and following notice from the Company does not resume development or commercialization activities. The agreement may also be terminated by either party in the event of an uncured material breach by the other party. If the agreement is terminated for any reason, the licenses granted by the Company to Jazz Pharmaceuticals with respect to D-SXB products will terminate and specified rights to licensed products will revert to the Company. There are no cancellation, termination or refund provisions in this arrangement that contain material financial consequences to the Company.

The Company determined that there were three deliverables under the Jazz Pharmaceuticals Agreement: (i) an exclusive, royalty-bearing sub-licensable worldwide license to develop and commercialize D-SXB compounds (the License Deliverable), (ii) participation on a joint steering committee (the JSC Deliverable) and (iii) a deliverable

to direct external patent activities and bear a portion of the external patent fees (the Patent Support Deliverable).

The development support services were evaluated at the inception of the arrangement and determined to be a substantive option as the Company is not obligated to deliver services unless and until such time as Jazz Pharmaceuticals elects to exercise the option and the consideration for the development support services is not priced at a significant and incremental discount. The nature of the development support services is such that they are not essential to Jazz Pharmaceuticals use of the License Deliverable as Jazz Pharmaceuticals could

Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

perform the services themselves or obtain them from another service provider, if so desired. Therefore, the Company concluded that the License Deliverable had value to Jazz Pharmaceuticals on a standalone basis and was therefore separable from the option to procure development support services.

The Company has concluded that the License Deliverable has standalone value upon delivery because Jazz Pharmaceuticals can fully utilize the underlying license for its intended purpose without the receipt of other deliverables in the arrangement. This conclusion considered Jazz Pharmaceuticals internal product development expertise that enables it to use the License Deliverable for its intended purposes without the involvement of the Company or the receipt of the other deliverables. Moreover, the rights conveyed by the Company to Jazz Pharmaceuticals in connection with the License Deliverable include the contractual right to sublicense. Similarly, all of the remaining deliverables were deemed to have standalone value based on their nature. Factors considered in this determination included, among other things, whether any other vendors sell the items separately and if the customer could use the item for its intended purpose without the receipt of the remaining deliverables. Additionally, there are no refund provisions in the Jazz Pharmaceuticals Agreement. Accordingly, each deliverable included in the Jazz Pharmaceuticals Agreement qualifies as a separate unit of accounting.

The Company allocated the non-refundable upfront consideration of $4.0 million among the deliverables based on management s best estimate of selling price of each deliverable using the relative selling price method. The Company did not have VSOE or TPE of selling price for such deliverables. The Company s BESP for the License Deliverable considered the market opportunity for the development and commercialization of D-SXB compounds, the probability of successfully developing and commercializing such compounds, the remaining development costs to develop such compounds, and the estimated time to commercialization. The Company s analysis included the following market conditions and entity-specific factors: (a) the specific rights provided under the license deliverable, (b) the potential indications pursuant to the license, (c) the relevant territories for the license, (d) the development risk, (e) the market size, (f) the expected product life assuming commercialization and (g) the competitive environment. The Company developed BESP for the JSC Deliverable and Patent Support Deliverable based on the nature of the services to be performed and estimates of the associated effort and cost of the services adjusted for a reasonable profit margin such that they represented estimated market rates for similar services sold on a standalone basis.

The Company allocated arrangement consideration of $3.7 million to the License Deliverable, $0.1 million to the JSC Deliverable and $0.2 million to the Patent Support Deliverable. The Company recognized the arrangement consideration allocated to the License Deliverable upon delivery and will recognize revenue related to the JSC Deliverable and the Patent Support Deliverable over the respective periods of performance which is estimated to be 46 months.

The Company has evaluated all of the milestones that may be received in connection with the Jazz Pharmaceuticals Agreement. All development and regulatory milestones are considered substantive on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is

achieved, assuming all other revenue recognition criteria are met. All sales-based milestones will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

For the year ended December 31, 2013, the Company recognized revenue of $3.7 million upon delivery of the License Deliverable, approximately $17 thousand related to the JSC Deliverable and approximately $44 thousand related to the Patent Support Deliverable.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

For the year ended December 31, 2013, the Company recognized revenue of $0.8 million related to the performance of development support services and revenue of approximately $0.3 million for reimbursements of travel and intellectual property expenses, the cost of which is recorded within general and administrative expenses.

Avanir

In February 2012, the Company signed a license agreement (the Avanir Agreement) with Avanir Pharmaceuticals, Inc. (Avanir) that provides Avanir worldwide rights to develop and commercialize Concert s deuterated dextromethorphan (D-DM). The agreement includes the rights to multiple D-DM compounds. Avanir will have overall responsibility for research, development and commercialization of D-DM. Avanir has the option to require the Company to provide manufacturing services through a first IND filing. If Avanir exercises its option, the Company will receive payment for any manufacturing services provided and will be reimbursed for all external costs related to the manufacturing services.

Under the terms of the Avanir Agreement, the Company received a $2.0 million non-refundable upfront payment in March 2012. During the year ended December 31, 2013, the Company recognized as revenue a $2.0 million milestone payment received from Avanir based on positive data from Avanir s Phase 1 clinical trial of AVP-786. AVP-786 includes one of the D-DM analogs licensed to Avanir. In addition, the Company is eligible to earn up to $4.0 million in development milestone payments, up to $37.0 million in regulatory milestone payments and up to $125.0 million in sales-based milestone payments. The next potential milestone the Company might be entitled to receive under the Avanir Agreement is $2.0 million for initiation of dosing in a Phase 2 or Phase 3 clinical trial study for AVP-786.

Avanir also is required to pay the Company royalties at defined percentages ranging from the mid-single digits to low double digits below 20% on worldwide net product sales of licensed products. The royalty term for each licensed product in each country is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the later of expiration of specified patent coverage or 10 years following commercial launch. The royalty rate is reduced, on a country-by-country basis, during any period within the royalty term when there is no patent claim, covering the licensed product in the particular country.

The Agreement will expire on a licensed product-by-licensed product and country-by-country basis on the date of the expiration of the applicable royalty term with respect to each licensed product in each country. Following the earlier of the completion of a specified Phase 2 clinical trial milestone or the second anniversary of the effective date of the agreement, Avanir has the right to terminate the agreement upon 90 days prior written notice to us. We may terminate the agreement if Avanir ceases to develop or commercialize licensed products and does not recommence development or commercialization efforts following our notice to Avanir. The agreement may also be terminated by either Avanir or us in the event of an uncured material breach by the other party. If the agreement is terminated for any reason, the licenses granted by us to Avanir will terminate subject to certain specified conditions.

The Company determined that the deliverables under the Avanir Agreement were the exclusive, royalty-bearing sub-licensable license to D-DM delivered at the inception of the arrangement as well as participation on a joint

steering committee through a first IND filing.

Pursuant to the terms of the agreement, the Company is only required to participate in the joint steering committee through a specified event. Accordingly, the Company estimated that its participation on the joint steering committee would not extend more than two years from the date the agreement was executed and therefore concluded the estimated selling price of this deliverable was insignificant.

Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

The manufacturing services were evaluated and determined to be a substantive option as the Company is not obligated to deliver manufacturing services unless and until such time as Avanir elects to exercise the option and the consideration for the manufacturing services is not priced at a significant and incremental discount. The nature of the manufacturing services is such that they are not essential to the D-DM license and Avanir could perform the manufacturing services themselves or obtain them from another service provider, if so desired. Therefore, the Company concluded that the D-DM license had standalone value to Avanir and was separable from the option to procure manufacturing services as the D-DM license is sub licensable, there are no restrictions as to Avanir s use of the license and Avanir has the requisite scientific expertise in the central nervous system disorder field to utilize the D-DM license for its intended purpose without the involvement of the Company.

The Company has concluded that the license deliverable has standalone value upon delivery because Avanir can fully utilize the underlying license for its intended purpose without the receipt of the other deliverables in the arrangement. This conclusion considered Avanir s internal product development expertise that enables it to use the license deliverable for its intended purposes without the involvement of the Company or the receipt of the other deliverables. Moreover, the rights conveyed by the Company to Avanir in connection with the license deliverable include the contractual right to sublicense.

The Company allocated arrangement consideration of $2.0 million to the license and an insignificant amount to the Company s participation on the joint steering committee. Accordingly, the Company recognized the $2.0 million non-refundable upfront fee as revenue upon delivery of the D-DM license during the year ended December 31, 2012.

The Company has evaluated all of the milestones that may be received in connection with the Avanir license agreement. All development and regulatory milestones are considered substantive on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. All sales-based milestones will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Since June 2012, Avanir has elected to conduct all research and development activities, including manufacturing activities; however, the Company has continued to receive intellectual property cost reimbursements. The Company recognized $0.2 million for the year ended December 31, 2012 and $0.2 million for the year ended December 31, 2013 within license and research and development revenue for intellectual property cost reimbursements, the cost of which is recorded within general and administrative expense.

GSK

In May 2009, the Company entered into a Research and Development Collaboration and License Agreement (the GSK Agreement) with Glaxo Group Limited (GSK) for the development and commercialization of deuterium-containing

medicines. The Company was responsible for the development of three programs through completion of proof of concept studies, two of which were identified, and for providing deuterated versions of three GSK pipeline compounds (to be selected by GSK) for GSK to develop.

Under the terms of the GSK Agreement, GSK paid the Company a non-refundable upfront cash payment of $18.3 million in June 2009. In addition, GSK purchased 6,666,667 shares of Series D Preferred Stock at a per share price of $2.50, resulting in gross proceeds to the Company of $16.7 million. The Company determined that the price of $2.50 per share included a premium of $0.58 per share over the fair value of the Series D Preferred

Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

Stock of $1.92 per share based on the results of a contemporaneous valuation. The Company concluded all of the deliverables at the inception of the arrangement should be accounted for as a single unit of accounting because neither VSOE or TPE of fair value existed for the undelivered elements. Accordingly, the entire premium paid of $3.9 million and the $18.3 million non-refundable upfront cash payment were included in deferred revenue until the third program was identified and the period of the Company s performance obligations could be determined.

In March 2011, the Company and GSK signed an amendment to the GSK Agreement. Under this amendment GSK paid the Company a $2.75 million payment and returned all rights in the second identified program to the Company. This $2.75 million amount is subject to repayment to GSK in the event that the Company commercializes CTP-499 or if, at any time during the seven year period from the date of the amendment, the Company re-licenses or otherwise transfers the rights to the Company s CTP-499 program to a third party at any time during the seven year period from the date of the amendment. The payment was classified as deferred revenue and will not be recognized as revenue until all repayment obligations lapse. This amendment also extended the deadlines for selection of (i) the third program for which the Company was responsible for development and (ii) deuterated versions of two GSK pipeline compounds for GSK to develop.

The Company determined that the amendment resulted in a material modification of the GSK Agreement pursuant to the provisions of ASU 2009-13, because the amendment changed the overall arrangement consideration, deliverables, and expected timing of performance by a material amount. As such, on the date of modification, the remaining activities under the GSK Agreement were evaluated under ASC 605-25 (as amended by ASU 2009-13) to determine if they represented a multiple element revenue arrangement. The Company determined that the GSK Agreement, as amended, included the following units of accounting that remained undelivered on the date of modification:

- A combined unit of accounting comprised of research and development services for CTP 298 (the CTP-298 Program) and an option to license CTP-298;

- A combined unit of accounting comprised of an option to license a third program and related research and development services for that program (the Unselected Program); and

- A deliverable to provide deuterated versions of two GSK pipeline compounds (to be selected by GSK) for GSK to develop (the Research Programs).

The Company combined the delivered options and related research and development services into combined units of accounting because the delivered options were determined to not have standalone value apart from the related research and development services because only the Company was capable of performing such services. The Company further determined that each unit of accounting had stand-alone value from the other units of accounting. Therefore, the Company allocated the non-refundable upfront consideration of $22.2 million among the units of accounting on the

date of modification based on management s BESP of the deliverables included in each unit of accounting using the relative selling price method. The Company did not have VSOE or TPE of selling price for such deliverables. The Company s BESP considered the market opportunity for the development and commercialization of each program, the probability of GSK selecting a third program (the Unselected Program) and successfully developing and commercializing such program, the remaining development costs for each program, and the estimated time to clinical proof of concept for each program.

The Company s analysis included an assessment of comparable market transactions in which exclusive options were sold without related research and development services, an estimate of the internal and external costs and effort that would be required to complete proof of concept for the each program assuming market rates for full time employee services and external costs, and in the case of the Unselected Program and the Research Programs, an assessment of the probability that GSK would exercise its rights to select a compound for such deliverables and require the Company to perform the related research and development services.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

The Company allocated arrangement consideration of $20.7 million to the CTP-298 Program, $1.5 million to the Unselected Program, and $37 thousand to the Research Programs. Revenue for the CTP-298 Program was to be recognized over the period of performance from the GSK Agreement effective date through the estimated delivery date of the CTP-298 option package in early 2013. Revenue for the Unselected Program and Research Program would be recognized upon selection by GSK or the lapsing of the deadline.

For the year ended December 31, 2011, the Company recognized $13.9 million of revenue related to the CTP-298 Program, including a cumulative catch up adjustment on the date of the amendment for services previously performed of $8.5 million. In addition during 2011, the Company recognized $37 thousand of revenue upon the lapsing of the Research Programs selection deadline. Also during the year ended December 31, 2011, the Company recognized milestone revenue of $4.0 million for achieving certain clinical criteria in the first-in-human clinical trial and $1.5 million for toxicology and regulatory achievements.

In first quarter of 2012, the Company received and recognized a $1.5 million milestone for opening an IND for CTP-298.

For the year ended December 31, 2012, the Company recognized the remaining deferred revenue of $6.8 million associated with the CTP-298 Program upon GSK s exercise of its opt out right in May 2012 with respect to this program and the remaining deferred revenue of $1.5 million upon the lapsing of the Unselected Program deadline.

Other than with respect to the Company s repayment obligation, the GSK Agreement is no longer in effect and, as a result, the Company does not expect to receive additional payments under the GSK Agreement.

11. Sponsored research agreement

In February 2012, the Company entered into a sponsored research agreement with Fast Forward LLC (Fast Forward), the National Multiple Sclerosis Society s subsidiary devoted to research and drug development. Under the research agreement, Fast Forward provided $0.8 million of funding for the preclinical advancement of CTP-354 (the Compound), a deuterated subtype-selective $GABA_A$ modulator developed by Concert with the therapeutic potential of treating spasticity. Concert received the funding as it met certain preclinical milestones.

In certain circumstances, the Company is obligated to make milestone payments to Fast Forward not in excess of a low-single digit multiple of the funding amount. The Company will account for any milestone payments paid to Fast Forward as royalty expenses when it becomes probable that any royalties will be owed to Fast Forward. As of December 31, 2012 and 2013, it was not probable any royalties would be owed to Fast Forward.

During the year ended December 31, 2012, Concert received payments totaling $0.7 million from Fast Forward, which were recognized as revenue within license and research and development revenue in the accompanying statement of operations and comprehensive loss. The revenue recognized is commensurate with the services performed in 2012, and such payments are non-refundable as the Company has incurred costs in excess of the

amounts funded.

During the year ended December 31, 2013, Concert received payments totaling $45 thousand from Fast Forward, which were recognized as revenue within license and research and development revenue in the accompanying statement of operations and comprehensive loss. The revenue recognized is commensurate with the services performed in 2013, and such payments are non-refundable as the Company has incurred costs in excess of the amounts funded.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

12. Loan payable and warrant to purchase redeemable securities

On December 22, 2011, the Company entered into a Loan and Security Agreement (the Loan and Security Agreement) with Hercules Technology Growth Capital, Inc. (Hercules). The Loan and Security Agreement provides for aggregate advances of up to $20 million. The advances under the Loan and Security Agreement were to be made in two tranches: (i) $7.5 million funded at closing, and (ii) up to an additional $12.5 million through March 31, 2012. The maximum amount of principal outstanding allowable under the Loan and Security Agreement is $20 million. Under the first tranche of the Loan and Security Agreement, the Company obtained an advance on December 22, 2011 totaling $7.5 million (the December 2011 Advance). Under the second tranche of the Loan and Security Agreement, the Company obtained an advance on March 29, 2012 totaling $12.5 million (the March 2012 Advance). The Company incurred $0.2 million in loan issuance costs paid directly to the lenders, which have been offset against the loan proceeds as a loan discount.

Each advance made under the Loan and Security Agreement bears interest at a variable rate of the greater of 8.5% and an amount equal to 8.5% plus the prime rate of interest minus 5.25%, provided however, that the per annum interest rate shall not exceed 11%. Through December 31, 2013, the December 2011 Advance and the March 2012 Advance had an interest rate of 8.5%. Interest-only payments are due monthly on the first day of each month beginning the month after the date of the respective advance until April 30, 2013. Then, the aggregate principal balance outstanding is payable in 30 equal monthly installments of principal and interest beginning May 1, 2013 and continuing through the maturity date on October 1, 2015.

Additionally, the advances are to be repaid in full immediately upon an event of default, as defined. The Loan and Security Agreement defines events of default, including the occurrence of an event that results in a material adverse effect upon the Company s business operations, properties, assets or condition (financial or otherwise), its ability to perform its obligations under and in accordance with the terms of the new loan agreement, or upon the ability of the lenders to enforce any of their rights or remedies with respect to such obligations, or upon the collateral under the Loan and Security Agreement or upon the liens of the lenders on such collateral or upon the priority of such liens. The Company does not believe that any events have occurred that could reasonably be deemed to have a material adverse effect. Substantially all assets of the Company are pledged as collateral, with the exception of intellectual property, which is the subject of a negative pledge under the Loan and Security Agreement. The lenders security interest in the collateral is a first priority security interest. There are no financial covenants associated with the Loan and Security Agreement.

As of December 31, 2013, the future minimum payments due under the Loan and Security Agreement are as follows (in thousands):

Year	Minimum Payments

	2014	$ 8,908
	2015	7,462
		16,370
Less amounts representing interest		(1,279)
Present value of minimum payments		15,091
Less discount		(172)
Less current portion		(7,818)
Loan payable net of current portion and unamortized discount		$ 7,101

In connection with the Loan and Security Agreement, the Company granted Hercules a warrant (the Warrant) to purchase up to 200,000 shares of Series C Preferred Stock at an exercise price of $2.50 per share which vested

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

immediately upon the December 2011 Advance. Upon the draw of the March 2012 Advance, the warrant became exercisable for an additional 200,000 shares of Series C Preferred Stock at an exercise price of $2.50 per share.

Pursuant to ASC Topic 480, *Distinguishing Liabilities from Equity*, the Warrant is classified as a liability and is re-measured to the-then current value at each balance sheet date. The following table sets forth a summary of changes in the fair value of the Warrant which represents a recurring measurement that is classified within Level 3 of the fair value hierarchy wherein fair value is estimated using significant unobservable inputs (in thousands):

	Year ended December 31,		
	2011	2012	2013
Beginning balance	$	$ 168	$ 459
Change in fair value	168	291	4
Ending balance	$ 168	$ 459	$ 463

The Warrant expires on the earlier of: (i) ten years from the effective date of the Loan and Security Agreement or (ii) five years after the closing of an initial public offering of the Company s common stock.

The Company measured the fair value of the Warrant as of December 31, 2011 using the Black-Scholes option pricing method. The Company measured the fair value of the Warrant as of December 31, 2012 and December 31, 2013 using a hybrid method that is consistent with the manner in which the Company estimated the fair value of its common stock on those dates. Using the hybrid method, the Company used the Black-Scholes option pricing method to value the Warrant based on the results of the initial public offering scenarios and the option pricing method to value the Warrant based on the results of the other assumed scenarios (sale or liquidation). The results of those valuations were then weighted consistent with the weightings used in the Company s common stock valuation to determine the warrant fair value. The significant assumptions used in estimating the fair value of the Warrant include the exercise price, volatility of the stock underlying the warrant, risk-free interest rate, estimated fair value of the preferred stock underlying the warrant, and the estimated life of the warrant.

Where the fair value of the Warrant was estimated using the Black-Scholes option pricing model, the Company used the following weighted-average assumptions:

	Year ended December 31,		
	2011	2012	2013

Expected volatility	70%	70%	70%
Expected term (in years)	10.0	7.9	5.3
Risk-free interest rate	2.0%	0.95%	1.75%
Expected dividend yield	%	%	%

Fair value

The Company estimated the fair value of its shares of Series C Preferred Stock as of December 31, 2012 and December 31, 2013, using a hybrid approach based on a probability-weighted average expected return method and the option pricing method. The Company estimated the fair value of its shares of Series C Preferred Stock as of December 31, 2011 using the probability-weighted expected return method.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

Expected volatility

The Company estimated the expected volatility based on actual historical volatility of the stock price of similar companies with publicly-traded equity securities. The Company calculated the historical volatility of the selected companies by using daily closing prices over a period of the expected term of the associated award. The companies were selected based on their enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected term of the associated award.

Expected term

The Company based the expected term on the actual remaining contractual term as of each respective measurement date.

Risk-free interest rate

The Company estimated the risk-free interest rate in reference to the yield on U.S. Treasury securities with a maturity date commensurate with the expected term of the Warrant.

Expected dividend yield

The Company estimated the expected dividend yield based on consideration of its historical dividend experience and future dividend expectations. The Company has not historically declared or paid dividends to stockholders. Moreover, it does not intend to pay dividends in the future, but instead expects to retain any earnings to invest in the continued growth of the business. Accordingly, the Company assumed an expected dividend yield of 0.0%.

13. Related-party transactions

For the year ended December 31, 2013, the Company paid a consultant related to a founding stockholder $25 thousand in fees for services as a clinical consultant. These fees were recognized as research and development expense.

14. 401(k) retirement plan

In January 2008, the Company established the Concert Pharmaceuticals 401(k) Retirement Plan (the 401(k) Plan) in which substantially all of its permanent employees are eligible to participate 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 $0.2 million for the year ended December 31, 2011, $0.2 million for the year ended December 31, 2012 and $0.2 million for the year ended December 31, 2013.

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Concert Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (continued)

15. Quarterly Financial Information (unaudited)

	Three Months Ended			
	March 31, 2012	June 30, 2012	September 30, 2012	December 31, 2012
	(in thousands, except per share data) (unaudited)			
Revenue	$ 6,589	$ 5,773	$ 264	$ 223
Operating expenses	8,050	7,357	8,597	7,455
Loss from operations	(1,461)	(1,584)	(8,333)	(7,232)
Other expense, net	(245)	(537)	(525)	(527)
Net loss	$ (1,706)	$ (2,121)	$ (8,858)	$ (7,759)
Net loss per share basic and diluted	$ (1.40)	$ (1.72)	$ (6.94)	$ (6.09)

	Three Months Ended			
	March 31, 2013	June 30, 2013	September 30, 2013	December 31, 2013
	(in thousands, except per share data) (unaudited)			
Revenue	$ 5,873	$ 17,441	$ 681	$ 1,413
Operating expenses	7,003	8,026	7,797	6,992
(Loss) income from operations	(1,130)	9,415	(7,116)	(5,579)
Other expense, net	(649)	(650)	(11)	(336)
Net (loss) income	$ (1,779)	$ 8,765	$ (7,127)	$ (5,915)
Net loss per share basic and diluted	$ (1.46)	$ 0.00	$ (5.59)	$ (4.64)

16. Subsequent events

The Company reviews all activity subsequent to year end hut prior to the issuance of the financial statements for events that could require disclosure or that could impact the carrying value of assets or liabilities as of the balance sheet date. All significant subsequent events have been properly disclosed in the financial statements.

In January 2014, the Company s board of directors and stockholders approved an amendment of the Company s certificate of incorporation to, among other things, change the definition of a qualified public offering to remove the per share price requirement and provide that mandatory conversion of the Company s preferred stock would occur upon the closing of a firm commitment underwritten public offering of common stock with gross proceeds to the Company of not less than $30 million.

In February 2014, the Company closed the initial public offering (IPO) of its common stock pursuant to a registration statement on Form S- 1, as amended. An aggregate of 6,649,690 shares of common stock registered under the registration statement were sold at a price to the public of $14.00 per share, including the over-allotment option. Net proceeds of the IPO were $83.1 million. In conjunction with this transaction, all outstanding shares of the Company s preferred stock were converted into 9,919,821 shares of common stock and the outstanding warrant to purchase 400,000 shares of Series C redeemable convertible preferred stock converted into a warrant to purchase 70,796 shares of common stock at an exercise price of $14.13 per share.

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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 Securities Exchange Act of 1934, as amended, or 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 Securities and Exchange Commission 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, 2013, 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

This Annual Report on Form 10-K does not include a report of management s assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

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, 2013 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. Other Information
None.

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PART III

Item 10. Directors, Executive Officers and Corporate Governance

EXECUTIVE OFFICERS AND DIRECTORS

The following table sets forth the name, age and positions of each of our executive officers and directors as of February 28, 2014.

Name	Age	Position(s)
Executive Officers		
Roger D. Tung, Ph.D.	54	President and Chief Executive Officer, Director
Nancy Stuart	55	Chief Operating Officer
Ryan Daws	40	Chief Financial Officer
Ian Robert Silverman, J.D., Ph.D.	61	Senior Vice President and General Counsel
Non-Employee Directors		
Richard H. Aldrich[2][3]	59	Director, Chairman of the Board of Directors
Ronald W. Barrett, Ph.D.[2]	58	Director
John G. Freund, M.D.[1]	60	Director
Peter Barton Hutt[3]	79	Director
Wilfred E. Jaeger, M.D.[1][2]	58	Director
Helmut M. Schühsler, Ph.D.[1]	54	Director
Wendell Wierenga, Ph.D.[3]	66	Director

(1) Member of audit committee.
(2) Member of compensation committee.
(3) Member of the nominating and corporate governance committee.

Executive Officers

Roger D. Tung, Ph.D. is our co-founder and has served as our President and Chief Executive Officer and as a member of our board of directors since April 2006. Before Concert, Dr. Tung was a founding scientist at Vertex, a pharmaceutical company, where he was employed from 1989 to 2005, most recently as its Vice President of Drug Discovery. Prior to Vertex, he held various positions at Merck, Sharp & Dohme Research Laboratories, a global healthcare provider, and The Squibb Institute for Medicinal Chemistry. Dr. Tung received a B.A. in Chemistry from Reed College and a Ph.D. in Medicinal Chemistry at the University of Wisconsin-Madison. We believe that Dr. Tung s detailed knowledge of our company and his 28 year career in the global pharmaceutical and biotechnology industries, including his roles at Vertex, provide a critical contribution to our board of directors.

Nancy Stuart has served as our Chief Operating Officer since October 2007 and was our Senior Vice President, Corporate Strategy and Operations from July 2006 to October 2007. Prior to joining Concert, Ms. Stuart held various business operations and business development positions at Amgen Inc., a biopharmaceutical company, Kinetix Pharmaceuticals, Inc., a pharmaceutical company subsequently acquired by Amgen, Scion Pharmaceuticals, Inc., a pharmaceutical company, Vertex and Genzyme Corporation, a biotechnology company subsequently acquired by Sanofi S.A. Ms. Stuart holds a B.S. from the University of Michigan, and an M.B.A. from the Simmons College

Graduate School of Management.

Ryan Daws has served as our Chief Financial Officer since January 2014. Prior to joining Concert, Mr. Daws served as an independent consultant from June 2013 to January 2014, including an engagement with Concert from September 2013 to January 2014. Mr. Daws served as a Director in the Healthcare Investment Banking Group at Stifel, Nicolaus & Company, Inc., a financial services company, from September 2010 to June 2013. From March 1999 to June 2010, he served in positions of increasing responsibility within the Healthcare

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Investment Banking Group of Cowen and Company, LLC, a financial services firm. Mr. Daws holds a B.S. in Finance and Organizational Management from the University of South Carolina and an International M.B.A. from the University of South Carolina s Moore School of Business.

Ian Robert Silverman, J.D., Ph.D. has served as our Senior Vice President and General Counsel since December 2010 and prior to that was our Vice President and General Counsel from January 2007 to December 2010. Prior to joining Concert, he served in various legal related roles at Millennium Pharmaceuticals, Inc., a pharmaceutical company, Vertex and FMC Corporation, a chemical manufacturing company. Dr. Silverman received his J.D. from Rutgers-Camden Law School, a Ph.D. in organic chemistry from the University of New Mexico and a B.A. from Lehigh University.

Non-Employee Directors

Richard H. Aldrich is our co-founder and has served as a member of our board of directors and as Chairman of our board of directors since May 2006. Mr. Aldrich is a Founder and has been Partner of Longwood Fund, a venture capital firm, since February 2010. Mr. Aldrich founded RA Capital Management LLC, a hedge fund, in 2004 and served as a Managing Member from 2004 to 2008 and as a Co-Founding Member from 2008 until 2011. Mr. Aldrich has co-founded several biotechnology companies including Sirtris Pharmaceuticals, Inc., which was acquired by GlaxoSmithKline in 2008, and Alnara Pharmaceuticals, Inc., which was acquired by Eli Lilly in 2011. He has also held management positions at Vertex, where he was a co-founding employee, and Biogen Corporation (now Biogen Idec Inc., a biotechnology company). Mr. Aldrich co-founded and serves on the board of directors of Verastem, Inc., a public biopharmaceutical company and also serves on the boards of directors of OvaScience, Inc., a public life sciences company of which he serves as chairman of the board, and PTC Therapeutics, Inc., a public biopharmaceutical company. Mr. Aldrich received his undergraduate degree from Boston College, and an M.B.A. from the Amos Tuck School at Dartmouth College. We believe Mr. Aldrich s broad-based experience in business, including his leadership and board experience at life science companies, and his familiarity with our business as a co-founder of our company allows him to be a key contributor to our board of directors.

Ronald W. Barrett, Ph.D. has served as a member of our board of directors since December 2007. Dr. Barrett is a founder of XenoPort, Inc., a public biopharmaceutical company, and has served as its Chief Executive Officer since 2001, its Chief Scientific Officer from 1999 to 2001 and as a member of its board of directors since 1999. Prior to XenoPort he held various positions at Affymax Research Institute, a drug discovery company now owned by GlaxoSmithKline plc, and Abbott Laboratories, a healthcare company. Dr. Barrett received a B.S. from Bucknell University and a Ph.D. in pharmacology from Rutgers University. We believe that Dr. Barrett s industry and board experience, including his experience as the chief executive officer of a publically traded biopharmaceutical company, makes him a key contributor to our board of directors.

John G. Freund, M.D. has served as a member of our board of directors since December 2013. Dr. Freund co-founded Skyline Ventures in 1997 and has served as a partner at Skyline since its founding. Prior to joining Skyline, Dr. Freund served as managing director in the private equity group of Chancellor Capital Management, a private capital investment firm. In 1995, he co-founded Intuitive Surgical, a medical device company, and served on its board of directors until 2000. From 1988 to 1994, Dr. Freund served in various positions at Acuson Corporation, a maker of ultrasound equipment that is now part of Siemens, most recently as Executive Vice President. Prior to joining Acuson, Dr. Freund worked at Morgan Stanley Venture Partners from 1987 to 1988. From 1982 to 1988, Dr. Freund was a general partner at Morgan Stanley & Co., an investment banking company, where he co-founded the Healthcare Group in the Corporate Finance Department in 1983. He has served on the board of directors of XenoPort, Inc., a publicly traded biopharmaceutical company, since 1999, and Tetraphase Pharmaceuticals, Inc., a publicly traded biopharmaceutical company, since 2012. Dr. Freund also serves on the board of directors of the following private

companies; Advion Inc., Collegium Pharmaceuticals, Inc., DiscoveRx Corporation, Protein Therapeutics, Inc., Si Bono, Inc. and Sutro Biopharma, Inc., and three U.S. registered investment funds managed by Capital Research and Management. He also previously served on the board of directors of five publicly traded companies; Map Pharmaceuticals, a biopharmaceutical company, Hansen

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Medical, a medical device company, Sirtris Pharmaceuticals, a biopharmaceutical company, LJL Biosystems a life sciences instrumentation company, and Mako Surgical Corp., a medical device company. Dr. Freund is a member of the Advisory Board for the Harvard Business School Healthcare Initiative, and is a member of the Therapeutics Advisory Council of Harvard Medical School. Dr. Freund received a B.A. in history from Harvard College, an M.D. from Harvard Medical School and an M.B.A. from Harvard Business School. We believe that Dr. Freund s extensive finance and investment experience, his experience as an executive and his service on the board of directors of numerous public and privately held companies allows him to be a key contributor to our board of directors.

Peter Barton Hutt has served as a member of our board of directors since December 2006. Mr. Hutt has practiced law at Covington & Burling LLP, specializing in food and drug law, since 1960 (except for the period from 1971 to 1975) and currently serves as senior counsel. From 1971 to 1975 he was Chief Counsel for the Food and Drug Administration. Mr. Hutt is a member of the board of directors of Momenta Pharmaceuticals, Inc., a public pharmaceutical company, DBV Technologies SA, Q Therapeutics, Inc. and Xoma Ltd., each of which is a public biotechnology company, as well as numerous private companies. During the last five years, Mr. Hutt also served as a member of the board of directors of Celera Genomics, a public biotechnology company that was acquired by Quest Diagnostics, Inc. in 2011, CV Therapeutics, Inc., a public biotechnology company that was acquired by Gilead Sciences, Inc. in 2009, and Ista Pharmaceuticals, Inc., a public pharmaceuticals company that was acquired by Bausch & Lomb Inc. in 2012. Mr. Hutt received a B.A. from Yale University, an LL.B. from Harvard Law School and an LL.M. from New York University School of Law. We believe Mr. Hutt s extensive knowledge of regulatory and legal issues related to drug development and his service on numerous boards of directors allows him to be a key contributor to our board of directors.

Wilfred E. Jaeger, M.D. has served as a member of our board of directors since May 2006. Dr. Jaeger co-founded Three Arch Partners, a venture capital firm, in 1993 and has served as a Partner since that time. Prior to co-founding Three Arch Partners, Dr. Jaeger was a general partner at Schroder Ventures. He is also a member of the board of directors of Threshold Pharmaceuticals, Inc., a public pharmaceutical company, as well as numerous private companies. Dr. Jaeger received a B.S. in Biology from the University of British Columbia, his M.D. from the University of British Columbia School of Medicine and an M.B.A. from Stanford University. In addition to representing one of our principal stockholders, we believe that that Dr. Jaeger s financial and medical knowledge and experience allows him to be a key contributor to our board of directors.

Helmut M. Schühsler, Ph.D. has served as a member of our board of directors since September 2011. Dr. Schühsler has worked for TVM Capital, a group of life science venture capital and healthcare private equity firms, since 1990 and currently serves as its Chairman and Managing Partner. During 2007 and 2008, Dr. Schühsler also served as Chairman of the European Private Equity and Venture Capital Association. Dr. Schühsler currently serves as a member of the board of Enanta Pharmaceuticals, Inc., a public pharmaceutical company, several other healthcare growth companies and Max Planck Innovation, the technology transfer organization of the German Max Planck Society. For several years he was a member of the Selection Committee for the Technology Pioneers program. Prior to joining TVM Capital, Dr. Schühsler worked for Horizonte Venture Management, a venture capital firm, and was an assistant professor for corporate finance at the Institute for Advanced Studies in Vienna. Dr. Schühsler received a Ph.D. in the Social and Economic Sciences from the University of Economics in Vienna. In addition to representing one of our principal stockholders, we believe that Dr. Schühsler s business and financial experience as a director and investor in several companies in our industry allows him to be a key contributor to our board of directors.

Wendell Wierenga, Ph.D. has served as a member of our board of directors since March 2014. From June 2011 to February 2014, Dr. Wierenga worked as Executive Vice President, Research and Development of Santarus, Inc., a public biopharmaceutical company that was acquired by Salix Pharmaceuticals, Ltd. in January 2014. From 2007 to May 2011, Dr. Wierenga served as Executive Vice President, Research and Development of Ambit Biosciences

Corporation, a biopharmaceutical company engaged in the discovery and development of small-molecule kinase inhibitors. From 2003 to 2007, he served as Executive Vice President, Research and

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Development of Neurocrine Biosciences, Inc., a biopharmaceutical company developing therapeutics for neuropsychiatric, neuroinflammatory and neurodegenerative diseases. From 2000 to 2003, Dr. Wierenga served as the Chief Executive Officer of Syrrx, Inc., biotechnology company focused on small-molecule drug compounds. Prior to joining Syrrx, from 1990 to 2000, he was senior vice president of worldwide pharmaceutical sciences, technologies and development at Parke-Davis, a division of Warner Lambert Co., a pharmaceutical company that was acquired by Pfizer Inc. in 2000. Prior to Parke-Davis, Dr. Wierenga worked at Upjohn Co., later Pharmacia & Upjohn, Inc., a pharmaceutical and biotechnology company, for 16 years in various positions, most recently as executive director of discovery research. Pfizer acquired Pharmacia & Upjohn, then named Pharmacia Corp., in 2002. Dr. Wierenga received a B.S. from Hope College and a Ph.D. in chemistry from Stanford University. Dr. Wierenga is a member of the boards of directors of Cytokinetics, Incorporated, Ocera Therapeutics, Inc. and XenoPort, Inc., which are publicly traded biopharmaceutical companies. During the last five years, Dr. Wierenga also served as a member of the boards of directors of Onyx Pharmaceuticals, Inc., a public biopharmaceutical company that was acquired by Amgen in 2013. We believe that Dr. Wierenga s extensive experience in biopharmaceutical research and development and his service on the boards of directors of several public biopharmaceutical companies allows him to be a key contributor to our board of directors.

AUDIT COMMITTEE

Our board of directors has established an audit committee, which operates under a charter that has been approved by our board of directors. The members of our audit committee are John G. Freund, Wilfred E. Jaeger and Helmut M. Schühsler. Dr. Schühsler is the chair of the audit committee. Our board of directors has determined that each of these directors is independent within the meaning of Rule 10A-3 under the Securities Exchange Act of 1934, or the Exchange Act. In addition, our board of directors has determined that each of Dr. Schühsler and Dr. Jaeger qualifies as an audit committee financial expert within the meaning of Securities and Exchange Commission, or SEC, regulations and the NASDAQ Listing Rules. In making this determination with respect to each of these directors, our board has considered the formal education and nature and scope of his previous experience, coupled with past and present service on various audit committees. Our audit committee assists our board of directors in its oversight of our accounting and financial reporting process and the audits of our financial statements. Our audit committee s responsibilities include:

- appointing, approving the compensation of, and assessing the independence of the our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;

overseeing our internal audit function, if any;

discussing our risk management policies;

establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;

meeting independently with our internal auditing staff, our independent registered public accounting firm and management;

reviewing and approving or ratifying any related person transactions; and

preparing the audit committee report required by SEC rules.

All audit services to be provided to us and all non-audit services, other than de minimis non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

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CODE OF BUSINESS CONDUCT AND ETHICS

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A copy of the code is posted on the Corporate Governance section of our website, which is located at www.concertpharma.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

SECTION 16(A) BENEFICIAL OWNERSHIP REPORTING COMPLIANCE

Section 16(a) of the Exchange Act requires our directors and certain officers and holders of more than 10% of our common stock to file with the SEC initial reports of ownership of our common stock and other equity securities on a Form 3 and reports of changes in such ownership on a Form 4 or Form 5. These Section 16 reporting persons are required by SEC regulations to furnish us with copies of all Section 16(a) forms they file. However, during the fiscal year ended December 31, 2013, we did not have any class of equity security registered under Section 12 of the Exchange Act, accordingly no reports were required to be filed pursuant to Section 16(a) by these Section 16 reporting persons with respect to our common stock during that fiscal year.

Item 11. Executive Compensation

This section discusses the material elements of our executive compensation policies for our named executive officers and the most important factors relevant to an analysis of these policies. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers named in the Summary compensation table below, or our named executive officers, and is intended to place in perspective the data presented in the following tables and the corresponding narrative.

In connection with becoming a public company, we have begun a thorough review of all elements of our executive compensation program, including the function and design of our equity incentive programs. We have begun, and we expect to continue in the coming months, to evaluate the need for revisions to our executive compensation program to ensure our program is competitive with the companies with which we compete for executive talent and is appropriate for a public company.

SUMMARY COMPENSATION TABLE

The following table sets forth information regarding compensation earned by our President and Chief Executive Officer, our next two highest paid executive officers during the year ended December 31, 2013 and one individual who would have been one of our next two highest paid executive officers during the year ended December 31, 2013 but for the fact that this individual was not serving as one of our executive officers as of December 31, 2013. We refer to these individuals as our named executive officers.

Name	Year	Salary ($)	Non-equity incentive plan compensation ($)	All other compensation ($)	Total ($)
Roger D. Tung, Ph.D.	2013	373,171	212,211[(1)]	8,178[(2)]	593,560

President and Chief Executive Officer	2012	365,863	31,025[3]	8,028[4]	404,916
Nancy Stuart	2013	300,054	127,901[1]	8,178[2]	436,133
Chief Operating Officer	2012	294,180	18,699[3]	8,028[4]	320,907
Ian Robert Silverman, J.D., Ph.D.	2013	295,399	125,911[1]	8,178[2]	429,488
Senior Vice President and General Counsel					
James Shipley, M.D.[5]	2013	261,627	60,013[6]	365,188[7]	686,828
Former Chief Medical Officer	2012	324,038	20,005[3]	8,028[4]	352,071

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(1) *Consists of a cash bonus paid under our 2013 executive bonus program that was earned as of the end of 2013 and a cash bonus under our 2012 executive bonus program that became payable during 2013 as the result of the satisfaction of a contingency during 2013. See the Narrative disclosure to summary compensation table described below for a description of these programs.*

(2) *Consists of $7,650 that we matched pursuant to our 401(k) plan and $528 in life insurance premiums.*

(3) *Consists of a cash bonus paid under our 2012 executive bonus program that was earned and no longer remained subject to contingencies at the end of 2012. See the Narrative disclosure to summary compensation table described below for a description of this program.*

(4) *Consists of $7,500 that we matched pursuant to our 401(k) plan and $528 in life insurance premiums.*

(5) *Dr. Shipley served as our Chief Medical Officer until his departure from our company effective October 15, 2013.*

(6) *Consists of a cash bonus under our 2012 executive bonus program that became payable during 2013 as the result of the satisfaction of a contingency during 2013. See the Narrative disclosure to summary compensation table described below for a description of this program.*

(7) *Consists of $7,650 that we matched pursuant to our 401(k) plan, $440 in life insurance premiums and $357,098 in severance, accrued vacation and continuation of medical and dental benefits payable in connection with termination of Dr. Shipley s employment with us.*

Narrative disclosure to summary compensation table

Base salary. In 2013, we paid annual base salaries of $373,171 to Dr. Tung, $300,054 to Ms. Stuart, $295,399 to Dr. Silverman and, prior to his departure from our company effective October 15, 2013, $261,627 to Dr. Shipley. We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

Annual bonus. Our board of directors may, in its discretion, award bonuses to our named executive officers from time to time. We typically establish annual bonus targets based around a set of specified corporate goals for our named executive officers and conduct an annual performance review to determine the attainment of such goals. Our management may propose bonus awards to the compensation committee of the board or the board primarily based on such review process. Our board of directors makes the final determination of the eligibility requirements for and the amount of such bonus awards. With respect to 2013, we awarded and paid bonuses of $119,136 to Dr. Tung, $71,804 to Ms. Stuart and $70,687 to Dr. Silverman, in each case as determined by our board of directors based on our achievement of company goals, with such amounts representing 80% of their respective bonus targets. With respect to 2012, we awarded and paid bonuses of $124,100 to Dr. Tung, $74,796 to Ms. Stuart, $73,632 to Dr. Silverman and $80,018 to Dr. Shipley, in each case as determined by our board of directors based on our achievement of company goals, with such amounts representing 85% of their respective bonus targets. Of these amounts, 25% was awarded and paid on December 31, 2012 as reflected in the summary compensation table above, while the remaining amounts remained contingent on the closing of a licensing transaction with Celgene, which occurred on April 4, 2013. These remaining amounts were subsequently paid on April 30, 2013.

Equity incentives. Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentivizes our executive officers to remain in our employment during the vesting period. Accordingly, our compensation committee and board of directors periodically review the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options.

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We typically grant stock option awards at the start of employment to each executive and our other employees. Through 2013, we have not maintained a practice of granting additional equity on an annual basis, but we have retained discretion to provide additional targeted grants in certain circumstances.

We award our stock options on the date our board of directors or compensation committee approves the grant. We set the option exercise price and grant date fair value based on our per-share estimated valuation on the date of grant. For grants in connection with initial employment, vesting begins on the initial date of employment. Time vested stock option grants to our executives and other employees typically vest 25% on the first anniversary of grant or, if earlier, the initial employment date and 6.25% per quarter thereafter, through the fourth anniversary of the vesting commencement date, and have a term of 10 years from the grant date. In 2013, we did not grant equity awards to any of our named executive officers.

OUTSTANDING EQUITY AWARDS AT YEAR END

The following table sets forth information regarding outstanding stock options held by our named executive officers as of December 31, 2013.

	Option awards			
Name	**Number of securities underlying unexercised options (#) exercisable**	**Number of securities underlying unexercised options (#) unexercisable**	**Option exercise price ($)**	**Option expiration date**
Roger D. Tung, Ph.D.	88,495		1.13	12/11/2017
	53,097		4.58	12/19/2018
	38,052		4.41	12/10/2019
	21,902[1]	7,300	3.79	12/14/2020
	19,911[2]	19,911	3.51	12/15/2021
Nancy Stuart	79,646		0.57	8/30/2016
	35,398		1.13	12/11/2017
	53,097		4.58	12/19/2018
	34,512		4.41	12/10/2019
	15,929[1]	5,309	3.79	12/14/2020
	11,061[2]	11,061	3.51	12/15/2021
Ian Robert Silverman, J.D., Ph.D.	53,097		1.13	6/4/2017
	19,469		1.13	12/11/2017
	14,159		4.58	12/19/2018
	30,973		4.41	12/10/2019
	15,929[1]	5,309	3.79	12/14/2020
	11,062[2]	11,061	3.51	12/15/2021
James Shipley, M.D.	79,093[3]		3.79	3/24/2021
	9,679[4]		3.51	12/15/2021

(1) This option vested as to 6.25% of the shares on March 14, 2011 and vests as to an additional 6.25% of the shares at the end of each successive three-month period through and including December 14, 2014.

(2) This option vested as to 6.25% of the shares on March 15, 2012 and vests as to an additional 6.25% of the shares at the end of each successive three-month period through and including December 15, 2015.

(3) This option provided for vesting as to 25% of the shares on January 1, 2012 and as to an additional 6.25% of the shares at the end of each successive three-month period through and including January 1, 2015. All vesting under this option ceased upon Dr. Shipley s departure from our company on October 15, 2013, after which this option remained exercisable for a period of one year.

(4) This option provided for vesting as to 6.25% of the shares on March 15, 2012 and as to an additional 6.25% of the shares at the end of each successive three-month period through and including December 15, 2015. All vesting under this option ceased upon Dr. Shipley s departure from our company on October 15, 2013, after which this option remains exercisable for a period of one year.

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EMPLOYMENT AGREEMENTS, SEVERANCE AND CHANGE IN CONTROL ARRANGEMENTS

Employment agreements

We have entered into employment agreements with each of Dr. Tung, Ms. Stuart, Mr. Daws and Dr. Silverman. The employment agreements confirm the executive officers titles, compensation arrangements, eligibility for benefits made available to employees generally and also provide for certain benefits upon termination of employment under specified conditions. Each named executive officer s employment is at will.

Because we entered into Mr. Daws agreement in connection with his joining us as chief financial officer, his agreement also provides that he receive:

- a one-time signing bonus of $97,000, repayable by him if his employment with us ends within the first 12 months because of a voluntary resignation other than for good reason or a termination for cause, each as defined in the agreement, and

- an option to purchase 123,893 shares of our common stock, which option was granted to him on February 19, 2014 in connection with the closing of our initial public offering, with an exercise price of $14.09 per share, the closing price of our common stock on the NASDAQ Global Market on the date of grant, and which is scheduled to vest, assuming he remains employed with us, as to 25% on January 20, 2015 and thereafter ratably over the next 12 quarters as of the last day of each quarter.

Benefits provided upon termination without cause

Under the terms of the employment agreements we have entered into with each of Dr. Tung, Ms. Stuart, Mr. Daws and Dr. Silverman, if an executive s employment is terminated by us without cause and other than as a result of death or disability or by such executive officer for good reason, each as defined in such employment agreement, prior to a change of control, as defined in such employment agreement, and subject to the executive s execution of a general release of potential claims against us, we will be obligated to (1) pay an amount equal to his or her then-current monthly base salary for a period of 12 months (six months for Mr. Daws), any bonus that has been awarded to and earned by him or her but that has not been paid before termination, any base salary earned but not paid through the date of termination and any vacation time accrued but unused on the date of termination and (2) continue to provide medical and dental benefits to the extent that he or she was receiving them at the time of termination for up to 12 months, subject to certain legal restrictions.

In connection with Dr. Shipley s departure from our company effective October 15, 2013, we entered into a separation agreement with Dr. Shipley under which we agreed to (1) make severance payments to Dr. Shipley in the amount of his then-current base salary for 12 months following his termination and (2) continue to provide medical and dental benefits to the extent that he was receiving them at the time of termination for 12 months.

Benefits provided upon a change of control

Under the terms of the employment agreements we have entered into with each of Dr. Tung, Ms. Stuart, Mr. Daws and Dr. Silverman, if the executive s employment is terminated by us or our successor without cause or by such executive officer for good reason, as defined in such employment agreement, within one year following a change of control, as defined in such employment agreement, and subject to the executive s execution of a general release of

potential claims against us, in lieu of the severance benefits described above:

If the change of control constituted a change in our ownership or effective control, or a change in the ownership of a substantial portion of our assets, each within the meaning of Treasury Regulation Section 409A, or a 409A change of control event, we will be obligated to pay the executive, in a lump sum payment, an amount equal to his or her then-current monthly base salary for a period of 12 months (six months for Mr. Daws).

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If the change of control is not a 409A change of control event, we will be obligated to pay the executive an amount equal to his or her then-current monthly base salary for a period of 12 months (six months for Mr. Daws) over the course of one year in installments in accordance with our normal payroll practices.

We will be obligated to pay the executive any bonus that has been awarded to and earned by him or her but that has not been paid before termination, any base salary earned but not paid through the date of termination and any vacation time accrued but unused on the date of termination.

The executive will be entitled to medical and dental benefits, to the extent that he or she was receiving them at the time of such termination, for up to 12 months, subject to certain legal restrictions.

In addition, if a change of control, as defined in such employment agreement, occurs and within one year following such change of control we or our successor terminate the executive s employment other than for cause, as defined in such employment agreement, or the executive s employment ends on death or disability, or the executive terminates his or her employment for good reason, as defined in such employment agreement, all stock options held by the executive will immediately vest in full.

Other agreements

We have also entered into employee confidentiality, non-competition and proprietary information agreements with each of our named executive officers. Under the employee confidentiality, non-competition and proprietary information agreements, each named executive officer has agreed (1) not to compete with us during his or her employment and for a period of one year after the termination of his or her employment, (2) not to solicit our employees during his employment and for a period of one year after the termination of his or her employment, (3) to protect our confidential and proprietary information and (4) to assign to us related intellectual property developed during the course of his or her employment.

401(k) retirement plan

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our employees are eligible to participate, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to $17,500 in 2014, and have the amount of the reduction contributed to the 401(k) plan. Currently, we match 50% of employee contributions up to 6% of the employee s salary, subject to the statutorily prescribed limit, equal to $7,800 in 2014. The match immediately vests in full.

DIRECTOR COMPENSATION

In December 2013, our board of directors approved a director compensation program that became effective at the time of our initial public offering in February 2014. Under this director compensation program, we pay our non-employee directors retainers in cash. Each non-employee director receives a cash retainer for service on the board of directors and for service on each committee of which the director is a member. The chairmen of the board and of each committee 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 of directors and for service on each committee of the board of directors of which the director is a member are as follows:

	Member Annual Fee	Chairman Annual Fee
Board of Directors	$ 30,000	$ 60,000
Audit Committee	$ 7,500	$ 15,000
Compensation Committee	$ 5,000	$ 10,000
Nominating and Corporate Governance Committee	$ 3,000	$ 7,000

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We also reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of director and committee meetings.

In addition, under our director compensation program, each new director elected to our board of directors receives an option to purchase 25,000 shares of our 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 our company. Further, on the date of the first board meeting held after each annual meeting of stockholders, each director that has served on our board of directors for at least six months will receive an option to purchase 10,000 shares of our 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 upon a change in control of our company. The exercise price of these options will equal the fair market value of our common stock on the date of grant.

This policy is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors interests with those of our stockholders.

Prior to our initial public offering in February 2014, we did not have a formal non-employee director compensation policy, however, we provided compensation for board service to Richard H. Aldrich, Ronald W. Barrett and Peter Barton Hutt in the form of an annual cash retainer and an equity stock option grant. Mr. Hutt received additional cash compensation for his service on board committees. None of our other non-employee directors received any compensation prior to our initial public offering, though we reimbursed our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of director and committee meetings.

We did not grant stock options or other equity-based awards to any of our non-employee directors during 2013.

The compensation of our non-employee directors prior to our initial public offering was established through arm s length negotiation, taking into account the responsibilities of each director and the director s qualifications and prior experience and industry data for such positions. This compensation was approved by our compensation committee. We did not pay any compensation to our President and Chief Executive Officer in connection with his service on our board of directors prior to our initial public offering, however, as described above, our President and Chief Executive Officer is now eligible to receive annual stock option grants as compensation for his service on our board of directors. The compensation that we paid to our President and Chief Executive Officer in 2013 is discussed above in this Executive compensation section.

The following table sets forth information regarding compensation earned by our non-employee directors during 2013.

Name	Fees earned or paid in cash ($)	Option awards ($)[1]	Total ($)
Richard H. Aldrich	60,000		60,000
Ronald W. Barrett, Ph.D.	30,000		30,000
Douglas G. Cole, M.D.[2]			
John G. Freund, M.D.			
Peter Barton Hutt	30,000		30,000
Wilfred E. Jaeger, M.D.			
Helmut M. Schühsler, Ph.D.			

(1) We did not grant stock options or other equity-based awards to any of our non-employee directors during 2013. As of December 31, 2013:

Mr. Aldrich held stock options to purchase 21,236 shares of common stock in the aggregate, which were vested in full;

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Dr. Barrett held stock options to purchase 31,855 shares of common stock in the aggregate, which were vested in full; and

Mr. Hutt held stock options to purchase 36,279 shares of common stock in the aggregate, which were vested in full.

(2) Dr. Cole resigned from our board of directors effective January 9, 2014.

COMPENSATION COMMITTEE INTERLOCKS AND INSIDER PARTICIPATION

None of our executive officers serves, or in the past has served, as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any entity that has one or more executive officers who serve as members of our board of directors or our compensation committee. None of the members of our compensation committee is an officer or employee of our company, nor have they ever been an officer or employee of our company.

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

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information regarding the beneficial ownership of our common stock as of February 28, 2014 by:

each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock;

each of our named executive officers;

each of our directors; and

all of our directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include shares of common stock issuable upon the exercise of stock options that are immediately exercisable or exercisable within 60 days after February 28, 2014. Except as otherwise indicated, all of the shares reflected in the table are shares of common stock and all persons listed below have sole voting and investment power with respect to the shares beneficially owned by them, subject to community property laws, where applicable. The information is not necessarily indicative of beneficial ownership for any other purpose.

The percentage ownership calculations for beneficial ownership are based on 17,249,895 shares of common stock outstanding as of February 28, 2014. Except as otherwise indicated in the table below, addresses of named beneficial owners are in care of Concert Pharmaceuticals, Inc., 99 Hayden Avenue, Suite 500, Lexington, Massachusetts 02421.

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In computing the number of shares of common stock beneficially owned by a person and the percentage ownership of that person, we deemed outstanding shares of common stock subject to options held by that person that are currently exercisable or exercisable within 60 days after February 28, 2014. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

Name of beneficial owner	Number of shares beneficially owned	Percentage of shares beneficially owned
5% Stockholders		
Entities affiliated with Three Arch Partners(1)	1,638,854	9.5%
Brookside Capital Partners Fund, L.P.(2)	1,497,833	8.7%
Entities affiliated with TVM Capital(3)	1,483,672	8.6%
Entities affiliated with GlaxoSmithKline(4)	1,356,533	7.9%
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.(5)	1,208,920	7.0%
Executive Officers and Directors		
Roger D. Tung, Ph.D.(6)	787,717	4.5%
Nancy Stuart(7)	232,353	1.3%
James Shipley, M.D.(8)	88,771	*
Ian Robert Silverman, J.D., Ph.D.(9)	147,398	*
Richard H. Aldrich(10)	472,562	2.7%
Ronald W. Barrett, Ph.D.(11)	31,855	*
John G. Freund, M.D.(12)	1,208,920	7.0%
Peter Barton Hutt(13)	40,703	*
Wilfred E. Jaeger, M.D.(14)	1,638,854	9.5%
Helmut M. Schühsler, Ph.D.(15)	1,483,672	8.6%
Wendell Wierenga, Ph.D.(16)	15,927	*
All current executive officers and directors as a group (12 persons)(17)	6,148,732	34.1%

* *Represents beneficial ownership of less than 1% of our outstanding stock.*

(1) *Consists of 801,726 shares of common stock held by Three Arch Partners IV, L.P., 777,620 shares of common stock held by Three Arch Partners III, L.P., 41,807 shares of common stock held by Three Arch Associates III, L.P. and 17,701 shares of common stock held by Three Arch Associates IV, L.P. The voting and dispositive decisions with respect to the shares held by Three Arch Associates III, L.P. and Three Arch Partners III, L.P., are made by the following managing members of their general partner, Three Arch Management III, L.L.C.: Mark Wan and Wilfred Jaeger, each of whom disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The voting and dispositive decisions with respect to the shares held by Three Arch Partners IV, L.P. and Three Arch Associates IV, L.P. are made by the following managing members of their general partner, Three Arch Management IV, L.L.C.: Mark Wan and Wilfred Jaeger, each of whom disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address for the funds affiliated with Three Arch Partners is 3200 Alpine Road, Portola Valley, CA 94028.*

(2) *Brookside Capital, LLC is the investment adviser to Brookside Capital Management, LLC (BCM). BCM is the sole general partner of Brookside Capital Investors, L.P. (BCI) and BCI is the sole general partner of*

Brookside Capital Partners Fund, L.P. (BCPF). BCM and BCI each may be deemed to share voting and dispositive powers with respect to the shares held by BCPF. Each of BCM and BCI disclaims beneficial ownership of such securities, except to the extent of its pecuniary interest therein.

(3) *Consists of 1,104,969 shares of common stock held by TVM Life Science Ventures VI GMBH & Co. KG and 378,703 shares of common stock held by TVM Life Science Ventures VI LP. Alexandra Goll, Helmut Schühsler, Hubert Birner, Stefan Fischer and Axel Polack are members of the investment committee of TVM Life Science Ventures VI Management Limited Partnership, a special limited partner of TVM Life Science Ventures VI GMBH & Co. KG and TVM Life Science Ventures VI LP with voting and dispositive power over the shares held by those entities. TVM Life Science Venture VI Management Limited Partnership and these*

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individuals each disclaim beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address for each of the individuals and entities listed above is c/o TVM Capital GmbH, Maximilianstrasse 35, Entrance C, 80539 Munich, Germany.

(4) *Consists of 1,179,941 shares of common stock held by Glaxo Group Limited and 176,592 shares of common stock held by S.R. One, Limited, each of whom are wholly owned subsidiaries of GlaxoSmithKline plc. The address of these entities is 980 Great West Road, Brentford, Middlesex, United Kingdom TW8 9GS.*

(5) *John G. Freund and Yasunori Kaneko are the Managing Members of Skyline Venture Management IV, LLC, which is the sole general partner of Skyline Venture Partners Qualified Purchaser Fund IV, L.P., and as such Drs. Freund and Kaneko may be deemed to share voting and dispositive power with respect to all shares held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. Each of Drs. Freund and Kaneko disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address for each of the individuals and entities listed above is 525 University Ave, Suite 610, Palo Alto, California 94301.*

(6) *In addition to shares of common stock held directly, includes 134,761 shares of common stock held by the Roger D. Tung 2011 GRAT, for which Dr. Tung is the sole trustee, 12,389 shares of common stock held by the RD Tung Irrevocable Trust, for which Dr. Tung s wife is a co-trustee, and 13,274 shares of common stock held by the Tung Family Investment Trust, for which Dr. Tung is a co-trustee. Includes 225,771 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.*

(7) *Consists of 232,353 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.*

(8) *Consists of 88,771 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014. Dr. Shipley departed our company effective October 15, 2013 upon which date all vesting of Dr. Shipley options ceased. Accordingly this number of shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014 includes vesting of such options only through October 15, 2013.*

(9) *Consists of 147,398 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.*

(10) *In addition to shares of common stock held directly, includes 61,946 shares of common stock held by RA Capital Associates, Inc. and 102,417 shares of common stock held by the Richard H. Aldrich 2011 GRAT. Mr. Aldrich is the sole stockholder of RA Capital Associates, Inc. and is the sole trustee of the Richard H Aldrich 2011 GRAT. Includes 21,236 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.*

(11) *Consists of 31,855 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.*

(12) *Consists of the shares described in note (5) above. Dr. Freund is a Managing Member of Skyline Venture Management IV, LLC, which is the sole general partner of Skyline Venture Partners Qualified Purchaser Fund IV, L.P., and as such may be deemed to share voting and dispositive power with respect to all shares held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. Dr. Freund disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Freund s address is 525 University Ave, Suite 610, Palo Alto, California 94301.*

(13) *Includes 36,279 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.*

(14) *Consists of the shares described in note (1) above. Dr. Jaeger is a managing member of Three Arch Management III, L.L.C, the general partner of Three Arch Associates III, L.P. and Three Arch Partners III, L.P., and Three Arch Management IV, L.L.C, the general partner of Three Arch Partners IV, L.P. and Three Arch Associates IV, L.P. Dr. Jaeger disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Jaeger s address is 3200 Alpine Road, Portola Valley, CA 94028.*

(15) *Consists of the shares described in note (3) above. Dr. Schühsler is a member of the investment committee of TVM Life Science Ventures VI Management Limited Partnership, the general partner of TVM Life Science*

Ventures VI GMBH & Co. KG and TVM Life Science Ventures VI LP, and as such Dr. Schühsler

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may be deemed to share voting and dispositive power with respect to all shares held by these entities Dr. Schühsler disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Schühsler s address is c/o TVM Capital GmbH, Maximilianstrasse 35, Entrance C, 80539 Munich, Germany.

(16) Includes 3,538 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.

(17) Includes 787,201 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.

SECURITIES AUTHORIZED FOR ISSUANCE UNDER OUR EQUITY COMPENSATION PLANS

The following table provides information about the securities authorized for issuance under our equity compensation plans as of December 31, 2013.

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders	1,952,578[1]	$ 3.14	168,584[2]
Equity compensation plans not approved by security holders			
Total	1,952,578	$ 3.14	168,584

(1) Consists of stock options outstanding as of December 31, 2013 under our Amended and Restated 2006 Stock Option and Grant Plan, which we refer to as the 2006 Plan.

(2) Consists of shares of common stock authorized under the 2006 Plan that remained available for grant under future awards as of December 31, 2013. In January 2014, in connection with our initial public offering, our board of directors determined that we would not grant any further stock options or other awards under the 2006 Plan following the closing of our initial public offering, which occurred in February 2014. In addition, in January 2014, our board of directors and our stockholders approved our 2014 Stock Incentive Plan, which became effective on February 11, 2014 and which we refer to as the 2014 Plan. Upon the closing of our initial public offering, 2,249,911 shares of common stock were reserved for issuance under the 2014 Plan. The number of shares reserved under the 2014 Plan is subject to further increase by (i) the number of shares of our common stock subject to outstanding awards under the 2006 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased and (ii) an annual increase, to be added on January 1 of each year, from and after 2015 through 2024, equal to the lowest of (a) 2,000,000 shares of our common stock, (b) 4% of the number

of our outstanding shares on January 1 of each such fiscal year and (c) an amount determined by our board of directors.

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

The following is a description of transactions since January 1, 2013 to which we have been a party, and in which any of our directors, executive officers or beneficial owners of more than 5% of our voting securities, or affiliates or immediate family members of any of our directors, executive officers or beneficial owners of more than 5% of our voting securities, had or will have a direct or indirect material interest. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, from unrelated third parties.

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SEVERANCE AND CHANGE IN CONTROL AGREEMENTS

See the Item 11. Executive Compensation EMPLOYMENT AGREEMENTS, SEVERANCE AND CHANGE IN CONTROL ARRANGEMENTS above for a discussion of these arrangements.

INDEMNIFICATION OF OFFICERS AND DIRECTORS

Our certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with each of our directors and executive officers that may be broader in scope than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements require us, among other things, to indemnify each such director and executive officer for some expenses, including attorneys fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or executive officers. In addition, we maintain standard policies of insurance under which coverage is provided to our directors and officers against losses arising from claims made by reason of breach of duty or other wrongful act, and to us with respect to payments which may be made by us to such directors and officers pursuant to the above indemnification provisions or otherwise as a matter of law.

PURCHASES IN INITIAL PUBLIC OFFERING

In our initial public offering, beneficial owners of more than 5% of our voting securities and their affiliates purchased an aggregate of 831,000 shares of our common stock at the initial public offering price of $14.00 per share. The following table sets forth the number of shares of our common stock purchased and the aggregate cash purchase price paid by each of these entities in our initial public offering.

Purchaser	Shares of Common Stock	Purchase Price
Brookside Capital Partners Fund, L.P.	350,000	$ 4,900,000
S.R. One, Limited	35,000	$ 490,000
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.(1)	150,000	$ 2,100,000
Entities affiliated with Three Arch Partners(2)	207,000	$ 2,898,000
Entities affiliated with TVM Capital(3)	89,000	$ 1,246,000

(1) John G. Freund, a member of our board of directors, is a Managing Member of Skyline Venture Management IV, LLC, which is the sole general partner of Skyline Venture Partners Qualified Purchaser Fund IV, L.P.

(2) The purchase amounts disclosed on this line consist of the aggregate purchase amounts of Three Arch Associates III, L.P., Three Arch Partners III, L.P., Three Arch Associates IV, L.P. and Three Arch Partners IV, L.P. Wilfred E. Jaeger, a member of our board of directors, is a managing member of Three Arch Management III, L.L.C, the general partner of Three Arch Associates III, L.P. and Three Arch Partners III, L.P., and Three Arch Management IV, L.L.C, the general partner of Three Arch Partners IV, L.P. and Three Arch Associates IV, L.P.

(3) The purchase amounts disclosed on this line consist of the aggregate purchase amounts of TVM Life Science Ventures VI GMBH & Co. KG and TVM Life Science Ventures VI LP. Helmut M. Schühsler, a member of our board of directors, is a member of the investment committee of TVM Life Science Ventures VI Management Limited Partnership, the general partner of TVM Life Science Ventures VI GMBH & Co. KG and TVM Life

Science Ventures VI LP.

POLICIES AND PROCEDURES FOR RELATED PERSON TRANSACTIONS

Our board of directors has adopted a written related person transaction policy to set forth policies and procedures for the review and approval or ratification of related person transactions. This policy covers any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, the amount involved exceeds $120,000, and a related person had or will have a

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direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person.

Our related person transaction policy contains exceptions for any transaction or interest that is not considered a related person transaction under SEC rules as in effect from time to time. In addition, the policy provides that an interest arising solely from a related person s position as an executive officer of another entity that is a participant in a transaction with us will not be subject to the policy if each of the following conditions is met:

- the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity;
- the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction with us and do not receive any special benefits as a result of the transaction; and
- the amount involved in the transaction equals less than the greater of $200,000 or 5% of the annual gross revenue of the company receiving payment under the transaction.

The policy provides that any related person transaction proposed to be entered into by us must be reported to our General Counsel and will be reviewed and approved by our audit committee in accordance with the terms of the policy, prior to effectiveness or consummation of the transaction whenever practicable. The policy provides that if our chief financial officer determines that advance approval of a related person transaction is not practicable under the circumstances, our audit committee will review and, in its discretion, may ratify the related person transaction at the next meeting of the audit committee. The policy also provides that alternatively, our chief financial officer may present a related person transaction arising in the time period between meetings of the audit committee to the chair of and audit committee, who will review and may approve the related person transaction, subject to ratification by the audit committee at the next meeting of the audit committee.

In addition, the policy provides that any related person transaction previously approved by the audit committee or otherwise already existing that is ongoing in nature will be reviewed by the audit committee annually to ensure that such related person transaction has been conducted in accordance with the previous approval granted by the audit committee, if any, and that all required disclosures regarding the related person transaction are made.

The policy provides that transactions involving compensation of executive officers will be reviewed and approved by our compensation committee in the manner to be specified in the charter of the compensation committee.

A related person transaction reviewed under this policy will be considered approved or ratified if it is authorized by the audit committee in accordance with the standards set forth in the policy after full disclosure of the related person s interests in the transaction. As appropriate for the circumstances, the policy provides that the audit committee will review and consider:

- the related person s interest in the related person transaction;

the approximate dollar value of the amount involved in the related person transaction;

the approximate dollar value of the amount of the related person s interest in the transaction without regard to the amount of any profit or loss;

whether the transaction was undertaken in the ordinary course of business of our company;

whether the transaction with the related person is proposed to be, or was, entered into on terms no less favorable to us than the terms that could have been reached with an unrelated third party;

the purpose of, and the potential benefits to us of, the transaction; and

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any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The policy provides that the audit committee will review all relevant information available to it about the related person transaction. The policy provides that the audit committee may approve or ratify the related person transaction only if the audit committee determines that, under all of the circumstances, the transaction is in, or is not inconsistent with, our best interests. The policy provides that the audit committee may, in its sole discretion, impose such conditions as it deems appropriate on us or the related person in connection with approval of the related person transaction.

DIRECTOR INDEPENDENCE

Rule 5605 of the NASDAQ Listing Rules requires a majority of a listed company s board of directors to be comprised of independent directors within one year of listing. In addition, the NASDAQ Listing Rules require that, subject to specified exceptions, each member of a listed company s audit, compensation and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Exchange Act. Under Rule 5605(a)(2), a director will only qualify as an independent director if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

In December 2013, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. In January 2014 and March 2014, our board of directors further considered the independence of John G. Freund and Wendell Wierenga, respectively, in connection with their respective appointments to our board of directors. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Dr. Tung, is an independent director as defined under Rule 5605(a)(2) of the NASDAQ Listing Rules. Our board of directors also determined that John G. Freund, Wilfred E. Jaeger and Helmut M. Schühsler, who comprise our audit committee, and Richard H. Aldrich, Ronald W. Barrett and Wilfred E. Jaeger, who comprise our compensation committee, satisfy the independence standards for such committees established by the SEC and the NASDAQ Listing Rules, as applicable. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

Item 14. Principal Accountant Fees and Services

AUDITORS FEES

The following table summarizes the fees of Ernst & Young LLP, our registered public accounting firm, billed to us for each of the last two fiscal years.

Fee Category	2012	2013
Audit Fees[1]	$ 65,000	$ 785,000
Audit-Related Fees		
Tax Fees[2]	11,660	12,000
All Other Fees		
Total Fees	$ 76,660	$ 797,000

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(1) Audit fees consist of fees for the audit of our financial statements, the review of our interim financial statements and services associated with our registration statement on Form S-1.

(2) Tax fees consists of fees incurred for tax compliance, tax advice and tax planning and includes fees for tax return preparation and tax consulting.

All such accountant services and fees were pre-approved by our audit committee in accordance with the Pre-Approval Policies and Procedures described below.

PRE-APPROVAL POLICIES AND PROCEDURES

The audit committee of our board of directors has adopted policies and procedures for the pre-approval of audit and non-audit services for the purpose of maintaining the independence of our independent auditor. We may not engage our independent auditor to render any audit or non-audit service unless either the service is approved in advance by the audit committee, or the engagement to render the service is entered into pursuant to the audit committee s pre-approval policies and procedures. Notwithstanding the foregoing, pre-approval is not required with respect to the provision of services, other than audit, review or attest services, by the independent auditor if the aggregate amount of all such services is no more than 5% of the total amount paid by us to the independent auditor during the fiscal year in which the services are provided, such services were not recognized by us at the time of the engagement to be non-audit services and such services are promptly brought to the attention of the audit committee and approved prior to completion of the audit by the audit committee.

From time to time, our audit committee may pre-approve services that are expected to be provided to us by the independent auditor during the following 12 months. At the time such pre-approval is granted, the audit committee must identify the particular pre-approved services in a sufficient level of detail so that our management will not be called upon to make a judgment as to whether a proposed service fits within the pre-approved services and, at each regularly scheduled meeting of the audit committee following such approval, management or the independent auditor shall report to the audit committee regarding each service actually provided to us pursuant to such pre-approval.

The audit committee has delegated to its chairman the authority to grant pre-approvals of audit or non-audit services to be provided by the independent auditor. Any approval of services by the chairman of the audit committee is reported to the committee at its next regularly scheduled meeting.

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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

The exhibits filed as part of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding such Exhibits, which Exhibit Index is incorporated herein by reference.

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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 March 31, 2014.

CONCERT PHARMACEUTICALS, INC.

By: /s/ Roger D. Tung
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 Roger D. Tung, Ph.D.	Director, President and Chief Executive Officer (Principal Executive Officer)	March 31, 2014
/s/ Ryan Daws Ryan Daws	Chief Financial Officer (Principal Financial Officer)	March 31, 2014
/s/ Pauline McGowan Pauline McGowan	Vice President, Finance and Corporate Controller (Principal Accounting Officer)	March 31, 2014
/s/ Richard H. Aldrich Richard H. Aldrich	Chairman	March 31, 2014
/s/ Ronald W. Barrett Ronald W. Barrett, Ph.D.	Director	March 31, 2014
/s/ John G. Freund John G. Freund, M.D.	Director	March 31, 2014
/s/ Peter Barton Hutt Peter Barton Hutt	Director	March 31, 2014

/s/ Wilfred E. Jaeger Wilfred E. Jaeger, M.D.	Director	March 31, 2014
/s/ Helmut M. Schühsler Helmut M. Schühsler, Ph.D.	Director	March 31, 2014
/s/ Wendell Wierenga Wendell Wierenga, Ph.D.	Director	March 31, 2014

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EXHIBIT INDEX

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 (File No. 001-36310) filed with the SEC on February 20, 2014)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant s current report on Form 8-K (File No. 001-36310) filed with the SEC on February 20, 2014)
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 (File No. 333-193335), filed with the SEC on February 3, 2014)
10.1	Third Amended and Restated Registration Rights Agreement, dated as of June 1, 2009, as amended (incorporated by reference to Exhibit 10.1 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.2	Warrant to purchase shares of Series C Convertible Preferred Stock issued by the Registrant to Hercules Technology Growth Capital, Inc. (incorporated by reference to Exhibit 10.2 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.3 #	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 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.4 #	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 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.5 #	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 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.6 #	2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on February 3, 2014)
10.7 #	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 (File No. 333-193335), filed with the SEC on February 3, 2014)
10.8 #	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 (File No. 333-193335), filed with the SEC on February 3, 2014)
10.9 #	Amended and Restated Employment Agreement, dated as of January 10, 2014, by and between the Registrant and Roger Tung, as amended (incorporated by reference to Exhibit 10.9 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.10 #	Amended and Restated Employment Agreement, dated as of January 10, 2014, by and between the Registrant and Nancy Stuart, as amended (incorporated by reference to Exhibit 10.10 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)

10.11 #	Separation Agreement, dated as of October 2, 2103, by and between the Registrant and James E. Shipley, as amended (incorporated by reference to Exhibit 10.11 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.12 #	Amended and Restated Employment Agreement, dated as of January 10, 2014, by and between the Registrant and I. Robert Silverman, as amended (incorporated by reference to Exhibit 10.12 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)

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Exhibit number	Description
10.13 #	Form of Director and Officer Indemnification Agreement by and between the Registrant and each of Roger D. Tung, Nancy Stuart, D. Ryan Daws, James E. Shipley, Ian Robert Silverman, Pauline McGowan, Richard H. Aldrich, Ronald W. Barrett, John G. Freund, Peter Barton Hutt, Wilfred E. Jaeger, Helmut M. Schühsler and Wendell Wierenga (incorporated by reference to Exhibit 10.13 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.14	Loan and Security Agreement, dated as of December 22, 2011, between the Registrant and Hercules Technology Growth Capital, Inc. (incorporated by reference to Exhibit 10.14 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.15	Lease Agreement, dated as of February 12, 2008, by and between the Registrant and One Ledgemont LLC (incorporated by reference to Exhibit 10.15 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.16	Development and License Agreement, dated as of February 24, 2012, between the Registrant and Avanir Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.16 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on February 3, 2014)
10.17	Development and License Agreement, dated as of February 26, 2013, between the Registrant and Jazz Pharmaceuticals Ireland Limited (incorporated by reference to Exhibit 10.17 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on February 3, 2014)
10.18	Master Development and License Agreement, dated as of April 4, 2013, among the Registrant, Celgene International Sàrl and Celgene Corporation (incorporated by reference to Exhibit 10.18 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on February 3, 2014)
10.19 #	Summary of Executive Bonus Program (incorporated by reference to Exhibit 10.19 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.20 #	Summary of Director Compensation Program (incorporated by reference to Exhibit 10.20 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
10.21 #	Employment Agreement, dated as of January 16, 2014, by and between the Registrant and D. Ryan Daws (incorporated by reference to Exhibit 10.21 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on February 3, 2014)
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to the Registrant s registration statement on Form S-1 (File No. 333-193335), filed with the SEC on January 13, 2014)
31.1*	Chief 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*	Chief 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*	Chief 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*	

Chief Financial Officer Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

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

Management contracts or compensatory plans or arrangements required to be filed as an exhibit hereto pursuant to Item 15(a) of Form 10-K.