CONCERT PHARMACEUTICALS, INC.
Form 10-K
March 06, 2017
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

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FORM 10-K

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(Mark One)
ýANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2016
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

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CONCERT PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

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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 ý
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 ý
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 ý No ¨
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 ý 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. ¨

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 x
Non-accelerated filer ¨ (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 ý

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2016 was approximately $135,211,000, based on the closing price of the registrant's common stock on the NASDAQ Global Market on that date.

The number of shares outstanding of the registrant's Common Stock as of February 27, 2017: 22,328,982

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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 context 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," "pro "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.

Part I
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. Selective incorporation of deuterium into known molecules has the potential, on a case-by-case basis, to provide better pharmacokinetic or metabolic properties, thereby enhancing their clinical safety, tolerability or efficacy. Our approach typically starts with approved drugs that may be improved with deuterium substitution. Our technology provides the opportunity to develop products that may compete with the non-deuterated drug in existing markets or to leverage the known activity of approved drugs to expand into new indications. Our deuterated chemical entity platform, or DCE Platform®, has broad potential across numerous therapeutic areas. The following table summarizes our clinical pipeline of product candidates. All of these candidates are small molecules being developed for oral administration.

OUR STRATEGY

Our strategy is to apply our deuterium technology to well characterized molecules in order to leverage their known safety and efficacy profiles. We select pipeline candidates based on the medical needs of patients, commercial opportunity, regulatory considerations, and competitive landscape.

Our approach aims to enable drug discovery and clinical development that is more efficient and less expensive than conventional small molecule drug research and development. Key elements of our strategy include:

- using deuterium technology to develop deuterated product candidates with substantially improved safety, tolerability or efficacy profiles to compete directly with the non-deuterated compound in its approved indication and develop deuterated product candidates that are based on approved drugs but for new indications that we believe are promising in view of the known biology of the approved drug;

- developing our deuterated product candidates quickly through proof-of-concept clinical trials, which could be as early as Phase 1, and then determining whether to advance it independently or with a partner; and

- commercializing product candidates on our own, or with a strategic partner.

DEUTERIUM

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

Potential advantages of product candidates based on our DCE Platform

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

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

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

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

OUR PRODUCT CANDIDATES

Our pipeline is focused on leveraging our deuterium expertise and proprietary product platform to develop novel medications designed to enhance patient outcomes in diverse therapeutic areas including pulmonary diseases, including cystic fibrosis, autoimmune and inflammatory diseases, and central nervous systems (CNS) disorders. The discussion below highlights our current clinical programs including those being developed by our collaborators.

CTP-656

Background on Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 70,000 people worldwide. There is no known cure for cystic fibrosis. The median predicted survival age is close to 40 years and nearly half of the cystic fibrosis population is 18 or older. Cystic fibrosis is caused by mutations in the gene that encodes the cystic fibrosis transmembrane conductance regulator protein, or CFTR, a chloride channel that regulates the movement of salt and

water into and out of cells. Children who develop cystic fibrosis inherit two defective CFTR genes, one from each parent, which are referred to as alleles. There are more than 1,900 known mutations in the CFTR gene, some of which result in cystic fibrosis, including the most prevalent F508del mutation and the less prevalent G551D gating mutation. In the United States, it is estimated that approximately 85% of individuals with cystic fibrosis have at least one F508del mutation and approximately 4.4% of people with cystic fibrosis have

a G551D gating mutation. Each mutation causes a different defect in the CFTR protein. When there is a defect caused by the G551D gating mutation, the defective CFTR protein reaches the surface of a cell but does not efficiently transport chloride ions across the cell membrane. The F508del mutation results in a different defect that largely prevents the CFTR protein from reaching the cell surface and also impairs its ability to transport chloride ions.

Defective CFTR results in decreased chloride secretion and reduced hydration of the mucus layer leading to the buildup of thick mucus in the lungs and other vital organs. Lung disease, the most critical manifestation of cystic fibrosis, is characterized by airway obstruction, infection and inflammation, such that more than 90% of all cystic fibrosis patients die of lung disease. Cystic fibrosis patients typically require lifelong treatment, with multiple daily medications, in many cases hospitalization due to lung infections, and potentially lung transplantation.

Ivacaftor (Kalydeco®) is a drug marketed by Vertex Pharmaceuticals, Inc., or Vertex, and initially approved for patients with the G551D gating mutation. The label has been expanded to include patients with certain other mutations. Ivacaftor is a CFTR potentiator, which keeps the CFTR protein channels on the cell surface open more often, to increase the flow of salt and water into and out of the cell. Vertex has also incorporated ivacaftor into the fixed dose combination drug, Orkambi®, which is marketed for patients homozygous for the F508del mutation.

CTP-656 Opportunity

CTP-656 is a novel, next generation potentiator that we are initially developing for the treatment of cystic fibrosis in patients who have gating mutations, including the G551D mutation. CTP-656 was discovered by applying our deuterium chemistry technology to modify ivacaftor, which is the current standard of care for this population. Due to its differentiated pharmacokinetic profile, CTP-656 has the potential to offer a greater therapeutic benefit relative to ivacaftor for this patient population. The potential benefits of CTP-656 include improved efficacy due to better treatment adherence, as a result of once-daily dosing and increased exposure to the parent drug, which is more active than the metabolites; and fewer drug-drug interactions.

CTP-656 also has the potential to be a key component of combination therapies that enable the treatment of patients having many other CFTR mutations. To advance combination therapies of CTP-656, we intend to collaborate with companies who are focused on developing drugs that target other mechanisms of action and that we believe may be suitable to combine with CTP-656.

On March 3, 2017, we entered into an Asset Purchase Agreement with Vertex, through Vertex Pharmaceuticals (Europe) Limited, pursuant to which we agreed to sell and assign, subject to the satisfaction or waiver of certain conditions, the cystic fibrosis assets of the Company, including CTP-656, for up to $250 million. Additional information concerning the sale of CTP-656 is discussed further in Note 18 in the consolidated financial statements, Item 1A. and Item 9B., each appearing elsewhere in this Annual Report on Form 10-K.

Clinical Development of CTP-656

In December 2016, we announced the initiation of a U.S.-based Phase 2 clinical trial evaluating CTP-656 in patients who have gating mutations, including the G551D mutation. The Phase 2 clinical trial is a randomized, parallel-group, double-blind, placebo-controlled, clinical trial to evaluate the safety and efficacy of CTP-656 in cystic fibrosis patients with gating mutations who are receiving stable treatment with Kalydeco. Patients enrolled in the 28-day study will receive either 20 mg, 100 mg, or 150 mg of CTP-656 once-daily or placebo. There will also be an open-label Kalydeco comparator arm in the trial. Approximately 30-40 patients will be enrolled in the Phase 2 trial. The primary endpoint of the Phase 2 trial is a change from baseline in sweat chloride at Day 28. Secondary endpoints include change in percent predicted forced expiratory volume (FEV1) and change from baseline in CFQ-R Respiratory Domain. The U.S. Phase 2 trial is being conducted at multiple study sites within the Cystic Fibrosis Foundation’s Therapeutic Development Network. Top-line data are expected by year-end 2017.

In January 2017, subsequent to the initiation of the study, the U.S. Food and Drug Administration, or FDA, informed Concert that, in order to support dose selection for Phase 3, an adequate washout period, in which Kalydeco treatment is withheld, would be required in addition to a placebo-control.

Following the Asset Purchase Agreement with Vertex, we do not intend to initiate any new clinical trials with CTP-656 at this time.

In January 2017, we also announced that the FDA granted orphan drug designation for CTP-656, which provides various incentives for companies to develop products for rare diseases affecting fewer than 200,000 people in the United States.

During 2015 and 2016, we completed multiple Phase 1 clinical trials evaluating CTP-656. In Phase 1, CTP-656 demonstrated an increase in half-life, decreased clearance, and an overall increase in exposure compared to Kalydeco. We also showed that CTP-656 plasma exposure was less dependent on dietary conditions than has been reported for Kalydeco, allowing CTP-656 to be dosed without regard to fat content of food. CTP-656 was well-tolerated and its safety profile was comparable to that of Kalydeco. No serious adverse events were reported in Phase 1 studies.

CTP-543

Background on Alopecia Areata

Alopecia areata is an autoimmune disease affecting up to 650,000 Americans at any given time and that results in partial or complete loss of hair on the scalp or body. The scalp is the most commonly affected area. Onset of the disease can occur throughout life, however, disease onset typically occurs in patients 30 years of age or younger and affects both men and women. Alopecia areata can be associated with serious psychological consequences, including anxiety and depression. There are currently no drugs approved by the U.S. Food and Drug Administration (FDA) for the treatment of alopecia areata. Alopecia areata is one of the disease areas that the FDA will focus on under its Patient-Focused Drug Development Initiative (PFDDI) in 2017. The goal of the PFDDI is to bring patient perspectives into an earlier stage of product development.

CTP-543 Opportunity

CTP-543 was discovered by applying Concert's deuterium chemistry technology to modify ruxolitinib, which is commercially available under the name Jakafi® in the United States for the treatment of certain blood disorders. Ruxolitinib has been used to treat alopecia areata in academic settings, including an investigator-sponsored clinical trial, and has been shown to promote hair growth in individuals with moderate-to-severe disease. Published findings from an open-label clinical trial of 12 patients with moderate to severe alopecia areata conducted by investigators at Columbia University demonstrated that 20 mg of ruxolitinib administered orally twice daily resulted in substantial efficacy, including nearly complete reversal of the disease in most cases, in 75% of patients.

Clinical Development of CTP-543

In 2016, we completed single and multiple ascending dose Phase 1 trials. The single and multiple ascending dose trials enrolled a total of 77 healthy volunteers. The pharmacokinetic measurements showed increased exposure with increasing doses. CTP-543 was well-tolerated across all dose groups and there were no serious adverse events reported in subjects who received CTP-543. The safety and exposure observed with 16 mg of CTP-543 twice daily appeared comparable to the reported exposure of 20 mg ruxolitinib twice daily. In the multiple ascending dose Phase 1 trial of CTP-543, pharmacodynamic analyses were performed to assess the inhibition of IL-6- and IFN-gamma-mediated JAK/STAT signaling. Consistent with the established pharmacological activity of CTP-543, a dose-related reduction in IL-6-stimulated phosphorylated STAT3 was observed. Also, IFN-gamma-mediated STAT1 signaling, which is believed to play a key role in the pathogenesis of alopecia areata, was significantly inhibited in disease-relevant immune cell types at all doses evaluated.

We also conducted a Phase 1 crossover study evaluating the metabolite profiles of CTP-543 and ruxolitinib. In this study, except for the presence of deuterium, no new metabolites were observed with CTP-543.

The Company's planned Phase 2a trial will enroll approximately 100 patients with moderate-to-severe alopecia areata. The dose-ranging trial will evaluate four active arms of CTP-543 (4, 8, 12 and 16 mg BID) and a placebo control. The primary outcome measure of the Phase 2a trial will be the effect on treating hair loss as measured by the severity of alopecia tool (SALT) after 24 weeks of dosing. The trial will include an additional 28 weeks of dosing where all patients enrolled in the study will receive CTP-543. The trial is expected to commence in the first quarter of 2017 and top-line primary outcome data are expected by the end of 2017.

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Collaboration Product Candidates

We have entered into several collaborative arrangements with companies to develop deuterium-modified versions of their marketed products. The deuterium product candidates may be developed for an existing indication or in new indications.

AVP-786

In February 2012, we granted Avanir Pharmaceuticals, Inc., or Avanir, an exclusive worldwide license to develop and commercialize deuterated dextromethorphan analogs, including the d_6-dextromethorphan compound, deudextromethorphan . Subsequent to our agreement, Avanir was acquired by Otsuka Pharmaceutical Co., Ltd. and is now a wholly owned subsidiary of Otsuka America, Inc.

Avanir is developing AVP-786, which is a combination of deudextromethorphan and an ultra-low dose of quinidine. In November 2015, Avanir announced the initiation of the Phase 3 clinical program to evaluate the safety and efficacy of AVP-786 for the treatment of agitation associated with Alzheimer's disease. It expects to enroll approximately 700 patients in two Phase 3 trials. The Phase 3 trials are expected to be completed in the third quarter of 2018.

In addition, Avanir is conducting multiple Phase 2 trials exploring additional neurological indications.

CTP-730

In April 2013, we entered into a strategic worldwide collaboration with Celgene Pharmaceuticals, Inc., Celgene International Sarl and Celgene Corporation, together referred to as Celgene, related to certain deuterium-substituted compounds for the treatment of inflammation or cancer. While the collaboration has the potential to encompass multiple programs, it is initially focused on one program, CTP-730.

CTP-730 is a deuterated analog of apremilast. Apremilast is a selective phosphodiesterase 4 (PDE4) inhibitor approved for the treatment of psoriasis and psoriatic arthritis. We have completed the Phase 1 clinical evaluation of CTP-730. Once daily dosing of 50 mg of CTP-730 administered for seven days in the Phase 1 clinical trial demonstrated similar steady state exposure to historical data for 30 mg of apremilast twice daily. Treatment with CTP-730 was generally well-tolerated and no serious adverse events were observed. Celgene is responsible for any development of CTP-730 beyond the completed Phase 1 clinical trials. Celgene is assessing the path forward for CTP-730. However, CTP-730 has not advanced into new trials at this time.

JZP-386

In February 2013, we licensed the commercial rights to deuterated analogs of sodium oxybate, including JZP-386, to Jazz Pharmaceuticals under an exclusive worldwide license agreement. Sodium oxybate is the active ingredient in Xyrem®, marketed in the United States by Jazz Pharmaceuticals to treat two of the key symptoms of narcolepsy, excessive daytime sleepiness and cataplexy. JZP-386 is being developed for the potential treatment of patients with narcolepsy.

In May 2015, we and Jazz Pharmaceuticals announced the completion of a Phase 1 clinical study. Clinical data from this Phase 1 study demonstrated that JZP-386 provided favorable deuterium-related effects, including higher serum concentrations and correspondingly increased PD effects at clinically relevant time points compared to Xyrem® (sodium oxybate) oral solution. The safety profile of JZP-386 was similar to that observed with Xyrem. Jazz Pharmaceuticals is responsible for any further development of JZP-386 and is continuing to evaluate once-nightly dosing.

INTELLECTUAL PROPERTY

We protect our product candidates through the use of patents, trade secrets and careful monitoring of our proprietary know-how. Our patents and patent applications, if they issue as patents, for our lead programs expire between 2028 and 2034. The expected expiration dates are before any patent term extension to which we may be entitled under the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly referred to as the Hatch-Waxman Amendments) or equivalent laws in other jurisdictions where we have issued patents.

AVP-786

We hold U.S. patents and pending applications covering the composition of matter and methods of use of deudextromethorphan and other deuterated dextromethorphan analogs, as well as a U.S. patent application covering methods of use of certain other dextromethorphan compounds. These patents and patent applications are expected to expire between 2028 and 2030. We have

corresponding patents and patent applications in Europe and Japan that are expected to expire in 2028. We have granted exclusive licenses under these patent rights to Avanir.

CTP-656

We hold U.S. patents covering the composition of matter of deuterated analogs of ivacaftor and methods of treating cystic fibrosis, and a corresponding U.S. patent application. The patents and the patent application are expected to expire in 2032. We have corresponding patent applications in Europe and Japan that are expected to expire in 2032. We have retained all of the CTP-656 patent rights.

CTP-543

We hold a U.S. patent covering the composition of matter of deuterated analogs of ruxolitinib and a corresponding U.S. patent application. The patent and the patent application are expected to expire in 2033. We have corresponding patent applications in Europe and Japan that are expected to expire in 2033. We have retained all of the CTP-543 patent rights.

JZP-386

We hold a U.S. patent, as well as a corresponding U.S. patent application, covering the composition of matter of deuterated analogs of sodium oxybate, including JZP-386, and methods of using them for treating certain diseases and disorders, including narcolepsy. This patent and patent application are expected to expire in 2030. We hold a corresponding European patent that is expected to expire in 2030. We also have U.S. patents covering pharmaceutical compositions of JZP-386 and methods of use of JZP-386 for treating certain diseases and disorders, including narcolepsy, as well as patent applications in the United States, Europe and Japan, covering the composition of matter and methods of use of JZP-386, that are expected to expire in 2032. We have granted exclusive licenses under these patent rights to Jazz Pharmaceuticals.

CTP-730

We hold U.S. patents and a U.S. patent application covering the composition of matter of CTP-730. The patents and the patent application are expected to expire in 2030. We also hold corresponding patents in Europe and Japan that are expected to expire in 2030. We have granted exclusive licenses under these patent rights to Celgene.

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

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

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- 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 vitro and in vivo systems; and
- our methods to determine the degree of deuterium substitution in compounds we manufacture.

MANUFACTURING AND SUPPLY

We currently rely, and expect to continue to rely, on third parties for the manufacture of product candidates for our clinical trials. We obt