CATALYST PHARMACEUTICALS, INC.
Form 10-K
March 14, 2018
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

[Mark One]

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

For the Fiscal Year Ended December 31, 2017

OR

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

Commission File No. 001-33057

CATALYST PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**76-0837053**
(State of jurisdiction of	**(IRS Employer**
incorporation or organization)	**Identification No.)**
355 Alhambra Circle, Suite 1250	
Coral Gables, Florida	**33134**
(Address of principal executive offices)	**(Zip Code)**

Registrant s telephone number, including area code: (305) 420-3200

Securities Registered Pursuant to Section 12(b) of the Act.

Common Stock, par	
value $0.001 per share	**Nasdaq Capital Market**
(Title of each class)	**(Name of exchange on which registered)**

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically 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 of this chapter) 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, a smaller reporting company or an emerging growth company. See the 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	(Do not check if a smaller reporting company)	Smaller reporting company
		Emerging Growth Company

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

As of June 30, 2017, the last business day of the Registrant s most recently completed second quarter, the aggregate market value of all voting, and non-voting common equity held by non-affiliates was $216,521,603.

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

Indicate the number of shares outstanding of each of the issuer s classes of common stock, as of the latest practicable date: 102,556,164 shares of common stock, $0.001 par value per share, were outstanding as of March 9, 2018.

Part III incorporates certain information by reference from the registrant s definitive proxy statement for the 2017 annual meeting of stockholders. The proxy statement with respect to the 2018 annual meeting of stockholders will be filed no later than 120 days after the close of the registrant s fiscal year ended December 31, 2017.

Table of Contents

Table of Contents

EXHIBITS FILED WITH FORM 10-K

Table of Contents

PART I

You are urged to read this Annual Report on Form 10-K (Form 10-K) in its entirety. This Form 10-K contains forward-looking statements that involve risks and uncertainties. Our actual results may differ significantly from the projected results discussed in these forward-looking statements. Factors that may cause such a difference include, but are not limited to, those discussed below and in Item 1A, Risk Factors.

We, our, ours, us, Catalyst, or the Company, when used herein, refers to Catalyst Pharmaceuticals, Inc., a Delaware corporation.

Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements , as that term is defined in the Private Securities Litigation Reform Act of 1995. These include statements regarding our expectations, beliefs, plans or objectives for future operations and anticipated results of operations. For this purpose, any statements contained herein that are not statements of historical fact may be deemed to be forward-looking statements. Without limiting the foregoing, believes , anticipates , proposes , plans , expects , intends , may , and other similar expressions are i identify forward-looking statements. Such statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or other achievements to be materially different from any future results, performances or achievements expressed or implied by such forward-looking statements. Factors that might cause such differences include, but are not limited to, those discussed in the section entitled Item 1A Risk Factors and those discussed in the section entitled Item 7 Management s Discussion and Analysis of Financial Condition and Results of Operations Caution Concerning Forward-Looking Statements.

The successful development and commercialization of our current drug candidates is highly uncertain. We cannot reasonably estimate or know the nature, timing, or estimated expenses of the efforts necessary to complete the development of, or the period in which material net cash inflows are expected to commence due to the numerous risks and uncertainties associated with developing such products, including the uncertainty of:

- our estimates regarding anticipated capital requirements and our need for additional funding;
- the risk that another pharmaceutical company (Jacobus Pharmaceuticals) will receive an approval for its formulation of 3,4-diaminopyridine (3,4-DAP) for the treatment of Lambert-Eaton Myasthenic Syndrome (LEMS), Congenital Myasthenic Syndromes (CMS), or any other indication, before we do;
- whether the clinical studies or trials that are required to be completed before the U.S. Food and Drug Administration (FDA) will accept an NDA submission for Firdapse® for the treatment of either LEMS or CMS will be acceptable to the FDA;
- what additional supporting information, including any additional clinical studies or trials, will be required before the FDA will accept our New Drug Application (NDA) submission for Firdapse® for the treatment of either LEMS or CMS (or any other condition or disease);

whether any NDA that we may submit for Firdapse® will be accepted for filing by the FDA, and if accepted, whether it will be granted a priority review;

Table of Contents

whether, even if the FDA accepts an NDA submission for Firdapse®, such product will be determined to be safe and effective and approved for commercialization for any of the submitted indications;

whether the receipt of breakthrough therapy designation for Firdapse® for LEMS will result in an expedited review of Firdapse® by the FDA or affect the likelihood that the product will be found to be safe and effective;

whether, assuming Firdapse® is approved for commercialization, we will be able to develop or contract with a sales and marketing organization that can successfully market Firdapse® while maintaining full compliance with applicable federal and state laws, rules and regulations;

whether any future trial that we undertake evaluating Firdapse® for the treatment of anti-MuSK antibody positive Myasthenia Gravis (MuSK-MG) or Spinal Muscular Atrophy (SMA) Type 3 will be successful and whether we can obtain the funding required to conduct such trials;

whether as part of the FDA review of any NDA that we may submit for filing for Firdapse®, the tradename Firdapse®, which is the tradename used for the same product in Europe, will be approved for use for the product in the United States;

whether CPP-115 will be determined to be safe for humans;

whether CPP-115 will be determined to be effective for the treatment of infantile spasms;

whether any bioequivalence study of our version of vigabatrin (CPP-109) compared to Sabril® that we submit as part of an Abbreviated New Drug Application (ANDA) for this product will be acceptable to the FDA;

whether any ANDA that we submit for a generic version of Sabril® will be accepted by the FDA for review and approved (and the timing of any such approval);

the scope, rate of progress and expense of our clinical trials and studies, pre-clinical studies, proof-of-concept studies, and our other drug development activities;

our ability to complete our trials and studies on a timely basis and within the budgets we establish for such trials and studies and whether our trials and studies will be successful;

the ability of our third-party suppliers and contract manufacturers to maintain compliance with current Good Manufacturing Practices (cGMP);

whether our estimates of the size of the market for our drug candidates will turn out to be accurate;

the pricing of our products that we may be able to achieve if we are granted the ability to commercialize our drug candidates; and

changes in the healthcare industry occasioned by any future repeal and replacement of the Affordable Care Act, in laws relating to the pricing of drug products, or in the healthcare industry generally.

Table of Contents

Our current plans and objectives are based on assumptions relating to the development of our current drug candidates. Although we believe that our assumptions are reasonable, any of our assumptions could prove inaccurate. In light of the significant uncertainties inherent in the forward-looking statements we have made herein, which reflect our views only as of the date of this report, you should not place undue reliance upon such statements. We undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise. Our current plans and objectives are based on assumptions relating to the development of our current drug candidates. Although we believe that our assumptions are reasonable, any of our assumptions could prove inaccurate. The significant uncertainties inherent in the forward-looking statements we have made herein, which reflect our views only as of the date of this report, suggest that you should not place undue reliance upon such statements. We undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

Item 1. Business

Overview

We are a biopharmaceutical company focused on developing and commercializing innovative therapies for people with rare, debilitating, chronic neuromuscular and neurological diseases. We currently have three drug candidates in development.

Firdapse®

In October 2012, we licensed the North American rights to Firdapse®, a proprietary form of amifampridine phosphate, or chemically known as 3,4-diaminopyridine phosphate, from BioMarin Pharmaceutical Inc. (BioMarin). In August 2013, we were granted breakthrough therapy designation by the U.S. Food and Drug Administration (FDA) for Firdapse® for the treatment of patients with Lambert-Eaton Myasthenic Syndrome, or LEMS, a rare and sometimes fatal autoimmune disease characterized by muscle weakness. Further, the FDA has previously granted Orphan Drug Designation for Firdapse® for the treatment of patients with LEMS, Congenital Myasthenic Syndromes, or CMS, and Myasthenia Gravis (MG).

The chemical entity, amifampridine (3,4-diaminopyridine, or 3,4-DAP), has never been approved by the FDA for any indication. Because amifampridine phosphate (Firdapse®) has been granted three separate Orphan Drug designations for the treatment of LEMS, CMS and MG by the FDA, the product is also eligible to receive seven years of marketing exclusivity upon approval of amifampridine for any or all of these indications. Further, if we are the first pharmaceutical company to obtain approval for marketing an amifampridine product, of which there can be no assurance, we will be eligible to receive five years of marketing exclusivity with respect to the use of this product for any indication, running concurrently with the seven years of orphan marketing exclusivity described above (if both exclusivities are granted).

We previously sponsored a multi-center, randomized, placebo-controlled Phase 3 trial evaluating Firdapse® for the treatment of LEMS. This Phase 3 trial, which involved 38 subjects, was designed as a randomized withdrawal trial in which all patients were treated with Firdapse® during a 7 to 91-day run-in-period followed by treatment with either Firdapse® or placebo over a two-week randomization period. The co-primary endpoints for this Phase 3 trial were the comparison of changes in patients randomized to continue Firdapse® versus those who transitioned to placebo that occurred in both the Quantitative Myasthenia Gravis Score (QMG), which measures muscle strength, and subject global impression score (SGI), on which the subjects rate their global impression of the effects of a study treatment during the two-week randomization period. In September 2014, we reported positive top-line results from this Phase 3

trial, and the successful results of this study were published in 2016 in *Muscle & Nerve* (Muscle Nerve, 2016, 53(5):717-725).

Table of Contents

During 2014, we established an expanded access program (EAP) to make Firdapse® available to any patients diagnosed with LEMS, CMS, or Downbeat Nystagmus in the United States, who meet the inclusion and exclusion criteria, with Firdapse® being provided to patients for free until sometime after new drug application (NDA) approval, should we receive such approval (of which there can be no assurance). We continue to inform neuromuscular physicians on the availability of the Firdapse® EAP and also to work with various rare disease advocacy organizations to inform patients and other physicians about the program.

On December 17, 2015, we announced completion of the submission of an NDA for Firdapse® for the treatment of LEMS and CMS. However, on February 17, 2016, we announced that we had received a refusal-to-file (RTF) letter from the FDA regarding our NDA submission. In early April 2016, we met with the FDA to obtain greater clarity regarding what would be required by the FDA to accept the Firdapse® NDA for filing. Following the receipt of the formal minutes of that meeting, on April 26, 2016, we issued a press release reporting that the FDA had advised us that in addition to the results of our previously submitted multi-center, randomized, placebo-controlled Phase 3 trial, we would need to submit positive results from a second adequate and well-controlled study in patients with LEMS. Additionally, there was a requirement for us to perform three abuse liability studies for Firdapse®.

In October 2016, we announced that we had reached an agreement with the FDA under a Special Protocol Assessment (SPA) for the protocol design, clinical endpoints, and statistical analysis approach to be taken in our second Phase 3 study evaluating Firdapse® for the symptomatic treatment of LEMS. A SPA is a process by which sponsors ask the FDA to evaluate the protocol of a proposed clinical trial to determine whether it adequately addresses scientific and regulatory requirements for the purpose identified by the sponsor. A SPA agreement indicates FDA concurrence with the adequacy and acceptability of specific critical elements of protocol design, endpoints and analysis. Additionally, it provides a binding agreement with FDA s review division that critical design elements of a pivotal trial adequately address the scientific and regulatory objectives in support of a regulatory submission for drug approval. However, even if a clinical trial is conducted pursuant to a SPA, it does not mean that the NDA will meet the standard for approval. Moreover, the FDA may rescind a SPA agreement when the division director determines that a substantial scientific issue essential to determining the safety or efficacy of the product has been identified after the trial has begun.

Our second Phase 3 trial evaluating Firdapse® for the treatment of LEMS (designated as LMS-003) was conducted at sites in Miami, Florida and Los Angeles, California. This double-blind, placebo-controlled withdrawal trial had the same co-primary endpoints as our first Phase 3 trial evaluating Firdapse® for the treatment of LEMS. Further, the FDA allowed us to enroll patients from our expanded access program as study subjects in this second trial. Enrollment in this trial, which included 26 subjects, was completed in October 2017. Details of the Phase 3 clinical trial are available on www.clinicaltrials.gov (NCT02970162).

On November 27, 2017, we reported positive top-line results from the LMS-003 trial. This trial had two prospectively defined co-primary endpoints. The first of these, quantitative myasthenia gravis score (QMG), achieved a statistically significant p-value of 0.0004, and the second, subject global impression (SGI), achieved a statistically significant p-value of 0.0003. More importantly, a clinically significant difference of 6.4 points was observed between the Firdapse® and placebo groups for the QMG endpoint. Firdapse® was well tolerated and showed a similar safety profile to that seen in earlier studies. All p-values reported are based on the entire intent to treat (ITT) population of patients that enrolled in this trial.

The prospectively defined secondary endpoint for the physician s clinical global impression of improvement (CGI-I) achieved statistical significance (p-value 0.0020). Further, the exploratory endpoints of triple timed up and go (3TUG, p-value 0.0112) and the evaluation of the QMG-Limb domains endpoint (p-value 0.0010) were also statistically significant. The exploratory endpoint of most bothersome symptom (MBS) (p-value 0.0572) was not significant, but

showed a trend.

Table of Contents

We were also required to conduct three pre-clinical abuse liability studies under the FDA guidance for Assessment of Abuse Potential of Drugs that was finalized in January 2017 (Self-Administration, Physical Dependence and Drug Discrimination). All three studies have now been completed, and results indicate that amifampridine phosphate does not exhibit abuse potential in these assessment models.

On February 12, 2018, after receipt of the minutes of our recently held Type C meeting with the FDA, we issued a press release reporting on the results of the meeting. Prior to the meeting, we had provided the FDA with our preliminary data package for our proposed NDA resubmission, including the positive top-line results from our LMS-003 trial, as well as the FDA-required abuse liability studies that we recently completed demonstrating that Firdapse® does not have abuse liability potential. The minutes of the meeting reflect the FDA s advice to us that our proposed filing package will be sufficient for resubmission of an NDA for Firdapse®, and we currently anticipate resubmitting our NDA for Firdapse® for LEMS to the FDA by the end of the first quarter of 2018. Notwithstanding, there can be no assurance that any NDA that we submit for Firdapse® for LEMS will be accepted for filing or approved.

Our original NDA submission for Firdapse® included data and information (including data from a currently ongoing investigator treatment IND) providing evidence supporting the benefits of Firdapse® for treating certain types of CMS, and requested that CMS be included in our initial label for Firdapse®. To provide additional support for our submission of an NDA for Firdapse® for the treatment of CMS, in October 2015 we initiated a small blinded clinical trial at four academic centers of up to 10 subjects in the pediatric CMS population, ages 2 to 17. However, after considering comments from the FDA about this study, we determined to enroll both adult and pediatric subjects with CMS in this trial and to expand the number of subjects to be evaluated in the trial to an aggregate of approximately 20 subjects. We are currently conducting this study at five sites around the United States, and we are currently working on adding several additional sites outside the United States. Details of this trial are available on www.clinicaltrials.gov (NCT02562066).

Based on currently available information, we expect to complete enrollment in this trial before the end of 2018 and to report top-line results from this trial in the first quarter of 2019. If the results of the trial are successful, we hope to add the CMS indication to our labeling for Firdapse®. There can be no assurance that any trial we perform for Firdapse® for the treatment of CMS will be successful or whether any NDA or NDA supplement that we may submit for Firdapse® for the treatment of CMS in the future will be filed by the FDA for review and approved.

In February 2016, we announced the initiation of an investigator-sponsored, randomized, double-blind, placebo-controlled, crossover Phase 2/3 clinical trial evaluating the safety, tolerability and potential efficacy of Firdapse® as a symptomatic treatment for patients with anti-MuSK antibody positive Myasthenia Gravis (MuSK-MG). MuSK-MG is a particularly severe form of myasthenia gravis that affects about 3,000 to 4,800 patients in the U.S., for which there are no approved effective therapies (and therefore it is an unmet medical need). Seven patients participated in this proof-of-concept trial. We provided study drug, placebo, and financial support for this study.

On March 15, 2017, we reported top-line results from this trial. Both of the co-primary efficacy endpoints of change from baseline (CFB) in total Quantitative Myasthenia Gravis (QMG) score (p=0.0003) and CFB in total Myasthenia Gravis Activities of Daily Living (MG-ADL) score (p=0.0006) were statistically and clinically significant in this trial. Several secondary efficacy measures also achieved statistical significance. Amifampridine phosphate was well tolerated in this population of patients.

5

Table of Contents

On August 30, 2017, we announced that we had reached an agreement with the FDA on a SPA for the protocol design, clinical endpoints, and statistical analysis approach to be taken in our proposed Phase 3 registration trial evaluating the safety and efficacy of amifampridine phosphate treatment in patients with MuSK-MG. The protocol that the FDA has reviewed is for a multi-site, international (U.S. and Italy), double-blind, placebo-controlled, clinical trial that is targeted to enroll approximately 60 subjects diagnosed with MuSK-MG. The trial will employ a primary endpoint of Myasthenia Gravis Activities of Daily Living (MG-ADL) and a secondary endpoint of Quantitative Myasthenia Gravis Score (QMG). At the FDA s request, the trial will also enroll up to 10 generalized myasthenia gravis patients who will be assessed with the same clinical endpoints, but achieving statistical significance in this subgroup of patients is not required and only summary statistics will be provided.

We initiated this trial in January 2018 and expect to begin enrolling subjects in this trial during the first half of 2018. We anticipate that it will take about 12 months to complete the enrollment for the trial and we expect to report top-line results from this trial in the first half of 2019. Details of this trial are available on www.clinicaltrials.gov (NCT03304054).

On November 21, 2017, we announced the initiation of a company-sponsored, proof-of-concept clinical trial evaluating safety, tolerability and efficacy of Firdapse® as a symptomatic treatment for patients with Spinal Muscular Atrophy (SMA) Type 3. The study is being conducted by a team of researchers led by Lorenzo Maggi, MD, and Giovanni Baranello, MD, of the Fondazione Istituto Neurologico Carlo Besta in Milan, Italy, a major referral center for SMA patients. The study is designed as a randomized (1:1), double-blind, 2-period, 2-treatment, crossover, outpatient proof-of-concept study to evaluate the safety, tolerability and potential efficacy of amifampridine in ambulatory patients diagnosed with SMA Type 3. The study is planned to include approximately 12 patients, and we anticipate reporting top-line results from the study in the second half of 2019.

There can be no assurance that any trial that we initiate to evaluate Firdapse® for MuSK-MG or SMA Type 3 will be successful. Further, there can also be no assurance that the FDA will ever approve Firdapse® for these indications.

Finally, we may seek to evaluate Firdapse® for the treatment of other treatment-refractory types of MG or other rare, similar neuromuscular diseases, although we have not yet begun to develop clinical programs for these other indications, and all such programs are subject to the availability of funding. There can be no assurance that Firdapse® will be an effective treatment for other treatment-refractory types of MG or for any other rare, similar neuromuscular diseases.

Prior to the receipt of the RTF letter, we had actively been taking steps to prepare for the commercialization of Firdapse® in the United States. However, in light of the receipt of the RTF letter, in the first quarter of 2016 we put most of our commercialization activities on hold in order to conserve cash. During the fourth quarter of 2017, we restarted the development of our commercialization plans for Firdapse®. We are also continuing to work with several rare disease advocacy organizations to help increase awareness of LEMS, CMS and MuSK-MG, and to provide awareness and outreach support for the physicians who treat these rare diseases and the patients they treat.

CPP-115

We are developing CPP-115, a GABA aminotransferase inhibitor that, based on our preclinical studies to date, we believe is a more potent form of vigabatrin, and may have fewer side effects (e.g., visual field defects) than those associated with vigabatrin. We are hoping to develop CPP-115 for the treatment of refractory infantile spasms. CPP-115 has been granted Orphan Drug Designation by the FDA for the treatment of infantile spasms and Orphan Medicinal Product Designation in the European Union, or EU, for West syndrome (a form of infantile spasms).

Table of Contents

We are currently refining our development plans for this product. We are also working with one or more potential investigators who have expressed an interest in evaluating our product for particular indications (particularly infantile spasms).

Finally, we are continuing our efforts to seek a partner to work with us in furthering the development of CPP-115. However, no agreements have been entered into to date.

There can be no assurance that we will ever successfully commercialize CPP-115.

Generic Sabril®

In September 2015, we announced the initiation of a project to develop generic versions of Sabril® (vigabatrin) in two dosage forms: tablets and powder sachets. Sabril® is marketed by Lundbeck Inc. in the United States in both dosage forms for the treatment of infantile spasms and refractory complex partial seizures. There can be no assurance that we will be successful in these efforts or that any abbreviated new drug applications (ANDAs) that we submit for vigabatrin will be accepted for review or approved.

We are also continuing our efforts to seek a partner to work with us in furthering the development of generic Sabril®. However, no agreements have been entered into to date.

There can be no assurance that we will ever successfully commercialize a generic version of Sabril®.

Capital Resources

At December 31, 2017, we had cash and investments of approximately $84.0 million. Based on our current financial condition and forecasts of available cash, we believe that we have sufficient funds to support our operations through 2019 (without considering revenues and cash receipts that may be received in 2019 if we are successful in obtaining an approval of Firdapse® and launching the product in 2019, of which there can be no assurance). There can be no assurance that we will ever be in a position to commercialize any of our drug candidates or that we will obtain any additional funding that we require in the future. See Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations Liquidity and Capital Resources below for further information on our liquidity and cash flow.

Our Strategy

Our goal is to develop and commercialize novel prescription drugs targeting rare (orphan) diseases with an initial focus on neuromuscular and neurological diseases and disorders. Specifically, we intend to:

Pursue approval of Firdapse® for LEMS, CMS and MuSK-MG. We are continuing our efforts to seek approval to commercialize Firdapse® for LEMS. We are also taking steps that we hope will allow us to include CMS and MuSK-MG in the labeling of Firdapse®.

Seek additional orphan drug indications for Firdapse®. We intend to take steps to evaluate Firdapse® as a treatment for additional neuromuscular indications, including SMA Type 3.

Seek a partner for CPP-115 and generic Sabril®. We are seeking partners to work with us in furthering the development of CPP-115 and generic Sabril®. However, no agreements have been entered into to date.

Seek to acquire additional products. We continue to seek to acquire additional relatively late stage orphan drug opportunities to add to our product portfolio. However, no agreements have been entered into to date to acquire additional products and any such product acquisitions would be subject to the availability of funding.

Table of Contents

Firdapse®

Product overview

Firdapse® is Catalyst s and BioMarin s (depending on market region) registered trade name for amifampridine phosphate tablets. Amifampridine is the WHO (World Health Organization) registered INN (International Nonproprietary Name) and United States Adopted Name (USAN) for the chemical entity, 3,4-diaminopyridine, often abbreviated as 3,4-DAP or DAP. Firdapse® contains the phosphate salt of amifampridine, hence the name amifampridine phosphate. We will refer to our drug by its proposed trade name in the United States (Firdapse®), by the INN/USAN (amifampridine), or by the specific salt in our product (amifampridine phosphate), throughout this Form 10-K.

In addition to the positive results we reported from our Phase 3 trials of amifampridine phosphate described below, clinical efficacy information for the symptomatic treatment of LEMS patients with amifampridine have been derived from several published randomized, double-blind, placebo-controlled studies and one published randomized, double-blind, active-control study in patients with LEMS. The data from the randomized controlled studies generally show statistically significant improvements across a number of measures of neurological function, including Quantitative Myasthenia Gravis (QMG) score and compound muscle action potential (CMAP), which have been demonstrated to be clinically relevant in patients with LEMS. Results of these studies suggest that amifampridine is more effective for the symptomatic treatment of LEMS compared with placebo or active investigational comparator (pyridostigmine). Additionally, data from multiple published uncontrolled investigations and case reports support the long-term benefits of treatment with amifampridine in patients with LEMS. In some cases, removal of patients from drug can lead to a recurrence of underlying symptoms, but with reintroduction of amifampridine improvement of muscle function is regained. Amifampridine has been recommended as the first-line symptomatic treatment for LEMS by the European Federation of Neurological Societies (now known as the European Academy of Neurology). In December 2009, amifampridine phosphate received marketing approval from the European Commission (with the trade name Firdapse®) for the symptomatic treatment of patients with LEMS.

Safety data from clinical data published over the last 30 years in patients with LEMS or other neurological disorders treated with amifampridine show that amifampridine is well tolerated at doses £80 mg per day. Among the 1,279 patients or healthy subjects assessed in the literature, the most frequently reported adverse events (AEs) were perioral and peripheral paresthesias (unusual sensations like pins and needles), and gastrointestinal disorders (abdominal pain, nausea, diarrhea, and epigastralgia (pain around the upper part of the stomach)). These events were typically mild or moderate in severity, and transient, seldom requiring dose reduction or withdrawal from treatment.

Lambert-Eaton Myasthenic Syndrome

Lambert-Eaton Myasthenic Syndrome, or LEMS, is a rare autoimmune neuromuscular disorder characterized primarily by muscle weakness of the limbs. The disease is caused by an autoimmune reaction where antibodies are formed against voltage-gated calcium channels on nerve endings, which damages the channels. These calcium channels are responsible for the transport of charged calcium atoms that activate the biochemical machinery responsible for releasing acetylcholine. Acetylcholine is the neurotransmitter responsible for causing muscles to contract and the failure to release enough of this neurotransmitter results in muscle weakness in LEMS patients. Additionally, LEMS is often associated with an underlying malignancy, most commonly small-cell lung cancer (SCLC), and in some individuals, LEMS is the first symptom of such malignancy.

8

Table of Contents

LEMS generally affects the extremities, especially the legs. As LEMS most affects the parts of limbs closest to the trunk, difficulties with climbing stairs or rising from a sitting position are commonly reported. Physical exercise and high temperatures tend to worsen the symptoms. Other symptoms often seen include weakness of the muscles of the mouth, throat, and eyes. Individuals affected with LEMS also may have a disruption of the autonomic nervous system, including dry mouth, constipation, blurred vision, impaired sweating, and/or hypotension.

LEMS is managed by treating the symptoms or treating the underlying autoimmune attack on voltage gated calcium channels. Unapproved treatments include steroids, azathioprine and intravenous immunoglobulin, which work by suppressing the immune system; and pyridostigmine and amifampridine, which enhance neuromuscular transmission. Plasma exchange has also been used to attempt to remove antibodies from the body. Firdapse® is a symptomatic treatment and does not alter the underlying autoimmune condition. As a voltage gated potassium blocker, Firdapse® prevents charged potassium atoms from leaving the nerve cells, which prolongs the period of depolarization. This allows more charged calcium atoms to enter the nerves, which enables the nerves to release acetylcholine and causes muscles to contract and to restore lost muscle strength in LEMS patients.

Based on currently available information, we estimate that there are approximately 3,000 LEMS patients in the United States. However, until an amifampridine product is finally approved by the FDA and awareness of the disease is increased, it is unlikely that the total number of LEMS patients in the United States can be determined with better certainty (as is typical of rare diseases), and the actual number of patients in the United States with LEMS may be higher or lower than our estimate. Some of the factors that affect the size of the population with a rare disease such as LEMS include, without limitation, the number of patients actually diagnosed with the disease, the number of patients who were misdiagnosed with other diseases (such as MG) before it is determined that they have the disease, and the number of patients who have the disease whose doctors do not become aware of the availability of a treatment for the disease until after a product is approved or, even if they are aware of the product, are unwilling or unable to prescribe the product until it is approved and generally available in the commercial marketplace. Additionally, while there is an antibody test that positively identifies patients with LEMS, we believe that the test is not particularly well known or utilized at this time by many neurologists. Further, we believe that many patients with small cell lung cancer, or SCLC, some of whom also have LEMS, are not being treated for LEMS because many of the oncology medical professionals who treat SCLC patients are generally not familiar with how to diagnose and treat LEMS. All of these factors are likely to affect the ultimate number of patients, either up or down, who are indicated and in need of treatment with an amifampridine product.

Congenital Myasthenic Syndromes

Congenital Myasthenic Syndromes are rare neuromuscular disorders comprising a spectrum of genetic defects and are characterized by fatigable weakness of skeletal muscles with onset at or shortly after birth or early childhood; in rare cases symptoms may not manifest themselves until later in childhood. Certain types of CMS are thought to be hereditary (autosomal recessive), while others have no known cause. The severity and course of the genetic disease types are variable, ranging from minor symptoms to progressive disabling weakness; symptoms may be mild, but sudden severe exacerbations of weakness or even sudden episodes of respiratory insufficiency also occur.

Many patients with CMS may respond to unapproved pharmacologic intervention, including cholinesterase inhibitors, amifampridine (i.e. 3,4-DAP), ephedrine, fluoxetine or quinidine, and albuterol, alone or in combinations. The particular therapy is dictated by the diagnosed CMS type, as drugs beneficial in treating one type of CMS can be detrimental in patients with another type of CMS.

9

Table of Contents

Congenital myasthenic syndrome(s) is rare, estimated at around one-tenth that of MG, which in itself is rare. Based on currently available information, we estimate that there are between 1,000 and 1,500 CMS patients in the United States.

Myasthenia Gravis

Myasthenia Gravis is a chronic autoimmune neuromuscular disorder that is characterized by fluctuating weakness of the voluntary muscle groups. The prevalence of MG in the United States is estimated to be about 20/100,000 population (equating to an estimate of approximately 64,000 patients in the United States). However, according to the Myasthenia Gravis Foundation of America, MG is probably under diagnosed and the prevalence may be higher. For example, patients with MuSK-MG may have focal or regional weakness and muscle atrophy that are more suggestive of motor neuron or muscle membrane (myopathy) disease. MG occurs in all races, both genders, and at any age. MG is not thought to be directly inherited (although it occasionally occurs in more than one member of the same family), nor is it contagious.

The voluntary muscles of the entire body are controlled by nerve impulses that arise in the brain. These nerve impulses travel down the nerves to the place where the nerves meet the muscle fibers. Nerve fibers do not actually connect with muscle fibers. There is a space between the nerve ending and muscle fiber; this space is called the neuromuscular junction. When the nerve impulse originating in the brain arrives at the nerve ending, it releases a chemical called acetylcholine. Acetylcholine travels across the space to the muscle fiber side of the neuromuscular junction where it attaches to many receptor sites. The muscle contracts when enough of the receptor sites have been activated by the acetylcholine. In MG, there can be as much as an 80% reduction in the number of these receptor sites. The reduction in the number of receptor sites is caused by an antibody that destroys or blocks the receptor site. Antibodies are proteins that play an important role in the immune system. They are normally directed at foreign proteins called antigens that attack the body. Such foreign proteins include bacteria and viruses. Antibodies help the body to protect itself from these foreign proteins. For reasons not well understood, the immune system of the person with MG makes antibodies against the receptor sites of the neuromuscular junction. Abnormal antibodies can be measured in the blood of many people with MG. The antibodies destroy the receptor sites more rapidly than the body can replace them. Muscle weakness occurs when acetylcholine cannot activate enough receptor sites at the neuromuscular junction.

Anti-MuSK antibody positive MG

About 15% of MG patients test negative for the acetylcholine receptor antibody. These patients have seronegative (SN) MG. Approximately 40-50% of these patients with SNMG (equating to an estimate of approximately 4,500 patients in the United States) test positive for antibodies against muscle-specific receptor tyrosine kinase (MuSK), a surface membrane component essential in the development of the neuromuscular junction. These patients are identified as having MuSK-MG. Anti-MuSK antibodies identify a clinically distinguishable, more severe form of MG. The disease is characterized by a prominent weakness of the neck, oro-bulbar and sometimes respiratory musculature. Although many patients with MuSK-MG are presently treated with standard MG treatments such as anticholinesterase inhibitors or immunosuppressants, such patients do not generally respond adequately to these treatments.

Table of Contents

Spinal Muscular Atrophy

Spinal Muscular Atrophy is a spectrum of genetic disorders of the Survival Motor Neuron (SMN) protein that affects the function of the neuromuscular junction. The pathogenesis may, in part, progress due to the lack of retrograde signaling from dysfunctional neuromuscular junctions leading to nerve damage and ultimately nerve cell death. As a spectrum of genetic disorders of the SMN protein, the condition varies in severity and the disease has been classified into Types (SMA Types 1 through 4), based primarily on clinical symptoms of the disease. The overall incidence of SMA is believed to be 1 in 6,000 to 10,000 live births, with over half of the cases diagnosed as SMA Type 1. Due to the poor prognosis of SMA Type 1 patients, the actual prevalence is lower, since well over half of the SMA patients are Type 1 and have a very short life span. Due to the heterogeneity of the disease and the variations in life expectancy, prevalence is difficult to determine and not well defined for the different types of SMA. Current estimates place the prevalence of SMA Types 2 and 3 at about 1.5 per 100,000 people, with the majority of these being SMA Type 3 due to the longer life span of SMA Type 3 patients. Based on currently available data, Catalyst estimates the prevalence of SMA Type 3 in the United States to be between 2,500 and 3,500 patients.

SMA Type 3 (sometimes called Kugelberg-Welander disease) includes clinically heterogeneous patients. They typically reach all major motor milestones in childhood and independent walking by adulthood. However, during infancy they typically have proximal muscular weakness. Some might need wheelchair assistance in childhood, whereas others might continue to walk and live productive adult lives with minor muscular weakness. Patients who lose ambulation often develop scoliosis and other medical problems related to poor mobility and muscle tone, such as obesity and osteoporosis. Two subgroups of severity have been suggested based on the probability of being able to walk by age 10 and on the subsequent probability of losing the ability to walk by age 40. Significant differences in losing the ability to walk have been observed in relation to those with an onset of weakness before (SMA 3a) and after (SMA 3b) age 3.

License Agreement with BioMarin for Firdapse®

On October 26, 2012, we licensed the exclusive North American rights to Firdapse® pursuant to a License Agreement between us and BioMarin (the BioMarin License Agreement). BioMarin holds the worldwide rights to Firdapse® and sells the product in the EU. We believe that we remain in compliance with the BioMarin License Agreement.

Under the BioMarin License Agreement, we have agreed to make certain payments:

Royalties: We have agreed to pay (i) royalties to BioMarin for seven years from the first commercial sale of Firdapse® equal to 7% of net sales (as defined in the BioMarin License Agreement) in North America for any calendar year for sales up to $100 million, and 10% of net sales in North America in any calendar year in excess of $100 million; and (ii) royalties to the third-party licensor of the rights sublicensed to us for seven years from the first commercial sale of Firdapse ® equal to 7% of net sales (as defined in the license agreement between BioMarin and the third-party licensor) in any calendar year.

Milestone Payments. Under our license agreement with BioMarin, we have agreed to pay certain milestone payments that BioMarin is obligated to pay to both a third-party licensor of the rights that have been sublicensed to us and to the former stockholders of Huxley Pharmaceuticals (Huxley) under an earlier stock purchase agreement between BioMarin and the former Huxley stockholders. These

milestones aggregate (i) approximately $2.6 million due upon acceptance by the FDA of a filing of an NDA for Firdapse® for the treatment of LEMS or CMS (approximately $150,000 of which will be due to the third party licensor and approximately $2,425,000 of which will be due to the former Huxley stockholders), and (ii) approximately $7.2 million due upon the unconditional approval by the FDA of an NDA for Firdapse® for the treatment of LEMS (approximately $3.0 million of which will be due to the third party licensor and approximately $4.2 million of which will be due to the former Huxley stockholders). However, under BioMarin s agreement with the former Huxley stockholders (and under our license agreement with BioMarin), BioMarin s obligation to pay the milestone payments due to the former Huxley stockholders (and our corresponding obligation to pay such milestone payments) expressly expires if these milestones have not been not satisfied by April 20, 2018.

BioMarin has recently advised us that the former Huxley stockholders may take legal action seeking payment of the milestone payments due to them from BioMarin if these milestones are achieved after April 20, 2018, notwithstanding the express termination date in the agreements. BioMarin has also advised us that we could become involved in any such legal action. While it is too early to determine how this matter will affect us, based on currently available information we do not believe that this matter will have a material adverse effect on our financial position or results of operations.

Table of Contents

Cost Sharing Payments. In the BioMarin License Agreement, we agreed to share in the cost of certain post-marketing studies of Firdapse® that were being conducted by BioMarin, and, as of December 31, 2017, we had fulfilled our commitment to BioMarin regarding all such payments.

Breakthrough therapy designation

Firdapse® for LEMS has been granted Breakthrough Therapy Designation by the FDA. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

A Breakthrough Therapy Designation conveys all of the fast track program features, as well as more intensive FDA guidance on an efficient drug development program. The FDA also has an organizational commitment to involve senior management in such guidance. The Breakthrough Therapy Designation is a distinct status from use of surrogate endpoints and priority review, which can also be granted to the same drug if relevant criteria are met.

Orphan drug designation

The FDA has granted Orphan Drug Designation for amifampridine phosphate for the treatment of LEMS, CMS and MG, making the drug eligible to be granted seven-year marketing exclusivity for these indications if we are the first pharmaceutical company to obtain approval of an NDA for a product containing amifampridine as the active moiety for the treatment of LEMS, CMS or MG. In addition, the FDA has also granted Jacobus Pharmaceutical s Orphan Drug Designation request for 3,4-diaminopyridine for the treatment of LEMS, which means that if Jacobus Pharmaceuticals were to be the first pharmaceutical company to obtain approval of an NDA for a product containing amifampridine as the active moiety for the treatment of LEMS, we would not be able to obtain FDA approval for that indication for seven years.

Our first Phase 3 clinical trial

As part of our License Agreement with BioMarin, we took over a Phase 3 clinical trial that BioMarin had previously begun in the United States and Europe evaluating Firdapse® for the treatment of LEMS. The trial was designed as a randomized double-blind, placebo-controlled discontinuation trial in approximately 36 LEMS patients. After patients were treated with amifampridine phosphate for at least 91 days, they were randomly assigned to either continue on amifampridine phosphate or be discontinued to placebo over a 2-week period. They were then returned to open label amifampridine phosphate treatment for a two-year follow-up period.

On September 29, 2014, we reported top-line results from this trial. A summary of the results is as follows:

Primary endpoints:

The primary endpoint of change in quantitative myasthenia gravis score, or QMG, at day 14 reached statistical significance (p=0.0452), with a worsening of 2.2 points observed in the placebo group and a worsening of 0.4 points observed in the treatment group.

The primary endpoint of change in subject global impression, or SGI, at day 14 was highly statistically significant (p=0.0028), with a worsening of 2.6 points observed in the placebo group and a worsening of 0.8 points observed in the treatment group.

Table of Contents

Secondary endpoints:

The secondary endpoint for the physician s clinical global impression of improvement, or CGI-I, reached statistical significance (p=0.0267), with a worsening at day 14 of 1.1 points between the placebo group and the treatment group.

The secondary endpoint of change in walking speed at day 14 was not statistically significant.

Patient tolerance of Firdapse®:

Firdapse® was generally safe and well tolerated. During the 91-day open label run-in period, treatment emergent adverse events occurred more frequently in treatment-naïve patients than in previously treated patients (approximately 10% of treatment naïve patients withdrew during this part of the study). During the placebo-controlled portion of the study, side effects occurring more frequently in the Firdapse® group were benign and consisted primarily of perioral and digital paresthesia and infections. No patients withdrew during this period.

All subjects who were randomized into the trial elected to continue with Firdapse® in the two-year safety follow-up phase of the trial.

The results of the Phase 3 trial were first presented in October 2014 at the 139th Annual Meeting of the American Neurological Association (ANA). They have subsequently been presented at the 2014 and 2015 annual meeting of the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) and at the 2015 meeting of the American Academy of Neurology (AAN). The results were also published in 2016 in *Muscle & Nerve* (Muscle Nerve, 2016, 53(5):717-725).

First NDA submission and Refusal-to-File Letter

On July 22, 2015, we announced that we had initiated a rolling submission of an NDA for Firdapse® for the treatment of LEMS and CMS, and on December 17, 2015, we announced the completion of that submission. On February 17, 2016, we announced that we had received an RTF letter from the FDA regarding our NDA submission. The RTF letter stated that after a preliminary review, the FDA has found that our application was not sufficiently complete and requested additional supporting information. Additionally, there was a requirement for us to perform three abuse liability studies for Firdapse®. The letter did not comment on the acceptability of the submitted clinical data, and no judgment was made in the letter on the efficacy or safety of Firdapse®.

On April 26, 2016, we announced that we met with the FDA to discuss the FDA s RTF letter. During that meeting, the FDA advised us that in addition to the results of our first Phase 3 trial, we would need to submit positive results from a second adequate and well-controlled study in patients with LEMS.

Our second Phase 3 clinical trial (LMS-003)

Our second Phase 3 trial evaluating Firdapse® for the treatment of LEMS (designated as LMS-003) was conducted at sites in Miami, Florida and Los Angeles, California. The double-blind, placebo-controlled withdrawal trial had the

same co-primary endpoints as our first Phase 3 trial evaluating Firdapse® for the treatment of LEMS. Further, the FDA allowed us to enroll patients from our expanded access program as study subjects in this second trial. This second Phase 3 trial was conducted under a Special Protocol Assessment (SPA) with the FDA for the protocol design, clinical endpoints, and statistical analysis approach to be taken in the trial. Details of the LMS-003 trial are available on www.clinicaltrials.gov (NCT02970162). Enrollment in this trial, which included 26 subjects, was completed in October 2017.

Table of Contents

On November 27, 2017, we reported positive top-line results from this trial. This trial had two prospectively defined co-primary endpoints. The first of these, quantitative myasthenia gravis score (QMG), achieved a statistically significant p-value of 0.0004, and the second, subject global impression (SGI), achieved a statistically significant p-value of 0.0003. More importantly, a clinically significant difference of 6.4 points was observed between the Firdapse® and placebo groups for the QMG endpoint. Firdapse® was well tolerated and showed a similar safety profile to that seen in earlier studies. All p-values reported are based on the entire intent to treat (ITT) population of patients that enrolled in this trial.

The prospectively defined secondary endpoint for the physician s clinical global impression of improvement (CGI-I) achieved statistical significance (p-value 0.0020). Further, the exploratory endpoints of triple timed up and go (3TUG, p-value 0.0112) and the evaluation of the QMG-Limb domains endpoint (p-value 0.0010) were also statistically significant. The exploratory endpoint of most bothersome symptom (MBS) (p-value 0.0572) was not significant, but shows a trend.

Recent Type C meeting with the FDA and anticipated resubmission of an NDA for Firdapse®

On February 12, 2018, after receipt of the minutes of our recently held Type C meeting with the FDA, we issued a press release reporting on the results of the meeting. Prior to the meeting, we had provided the FDA with our preliminary data package for our proposed NDA resubmission, including the positive top-line results from our LMS-003 trial, as well as the FDA-required abuse liability studies that we recently completed demonstrating that Firdapse® does not have abuse liability potential. The minutes of the meeting reflect the FDA s advice to us that our proposed filing package will be sufficient for resubmission of an NDA for Firdapse®, and we currently anticipate resubmitting our NDA for Firdapse® for LEMS to the FDA by the end of the first quarter of 2018. Notwithstanding, there can be no assurance that any NDA that we submit for Firdapse® for LEMS will be accepted for filing or approved.

Expanded access program

We currently operate an expanded access program (EAP) that makes Firdapse® available to all patients diagnosed with LEMS, CMS, or Downbeat Nystagmus in the United States who meet the inclusion and exclusion criteria, with Firdapse® being provided to patients at no cost until sometime after FDA approval, should we receive such approval (of which there can be no assurance). We continue to inform neuromuscular physicians on the availability of the Firdapse® EAP and also to work with various rare disease advocacy organizations to inform patients and other physicians about the program.

MuSK-MG Proof-of-Concept Study

In February 2016, we announced the initiation of an investigator-sponsored, randomized, double-blind, placebo-controlled, crossover Phase 2/3 clinical trial evaluating the safety, tolerability and potential efficacy of Firdapse® as a symptomatic treatment for patients with anti-MuSK antibody positive myasthenia gravis (MuSK-MG). There are no approved effective therapies for MuSK-MG (and therefore it is an unmet medical need). Seven patients participated in this proof-of-concept trial. We provided study drug, placebo, and financial support for this study.

On March 15, 2017, we reported top-line results from this trial. Both of the co-primary efficacy endpoints of change from baseline (CFB) in total Quantitative Myasthenia Gravis (QMG) score (p=0.0003) and CFB in total Myasthenia Gravis Activities of Daily Living (MG-ADL) score (p=0.0006) were statistically and clinically significant in this trial. Several secondary efficacy measures also achieved statistical significance. Amifampridine phosphate was well tolerated in this population of patients.

14

Table of Contents

Ongoing clinical trials

Phase 3 clinical trial evaluating Firdapse® for the treatment of CMS

Our original NDA submission for Firdapse® included data and information (including data from a currently ongoing investigator treatment IND) providing evidence supporting the benefits of Firdapse® for treating certain types of CMS, and requested that CMS be included in our initial label for Firdapse®. To provide additional support for our submission of an NDA for Firdapse® for the treatment of CMS, in October 2015 we initiated a small blinded clinical trial at four academic centers of up to 10 subjects in the pediatric CMS population, ages 2 to 17. However, after considering comments from the FDA, we determined to enroll both adult and pediatric subjects with CMS in this trial and to expand the number of subjects to be evaluated in the trial to an aggregate of approximately 20 subjects. We are currently conducting this study at five sites around the United States, and we are currently adding several additional sites outside the United States. Details of this trial are available on www.clinicaltrials.gov (NCT02562066).

Based on currently available information, we expect to complete enrollment in this trial before the end of 2018 and to report top-line results from this trial in the first quarter of 2019. If the results of the trial are successful, we hope to add the CMS indication to our labeling for Firdapse®. There can be no assurance that any trial we perform for Firdapse® for the treatment of CMS will be successful or whether any NDA or NDA supplement that we may submit for Firdapse® for the treatment of CMS in the future will be filed by the FDA for review and approved.

Phase 3 clinical trial evaluating Firdapse® for the treatment of MuSK-MG

On August 30, 2017, we announced that we had reached an agreement with the FDA on a SPA for the protocol design, clinical endpoints, and statistical analysis approach to be taken in our proposed Phase 3 registration trial evaluating the safety and efficacy of amifampridine phosphate treatment in patients with MuSK-MG. The protocol that the FDA has reviewed is for a multi-site, international (U.S. and Italy), double-blind, placebo-controlled, clinical trial that is targeted to enroll approximately 60 subjects diagnosed with MuSK-MG. The trial will employ a primary endpoint of Myasthenia Gravis Activities of Daily Living (MG-ADL) and a secondary endpoint of Quantitative Myasthenia Gravis Score (QMG). At the FDA s request, the trial will also enroll up to 10 generalized myasthenia gravis patients who will be assessed with the same clinical endpoints, but achieving statistical significance in this subgroup of patients is not required and only summary statistics will be provided.

We initiated this trial in January 2018 and expect to begin enrolling subjects in this trial during the first half of 2018. We anticipate that it will take about 12 months to complete the enrollment for the trial and we expect to report top-line results from this trial in the first half of 2019. Details of this trial are available on www.clinicaltrials.gov (NCT03304054).

Proof-of-concept clinical trial evaluating Firdapse® for the treatment of SMA Type 3

On November 21, 2017, we announced the initiation of a company-sponsored, proof-of-concept clinical trial evaluating safety, tolerability and efficacy of Firdapse® as a symptomatic treatment for patients with Spinal Muscular Atrophy (SMA) Type 3. The study will be conducted by a team of researchers led by Lorenzo Maggi, MD, and Giovanni Baranello, MD, of the Fondazione Istituto Neurologico Carlo Besta in Milan, Italy, a major referral center for SMA patients. The study is designed as a randomized (1:1), double-blind, 2-period, 2-treatment, crossover, outpatient proof-of-concept study to evaluate the safety, tolerability and potential efficacy of amifampridine in ambulatory patients diagnosed with SMA Type 3. The study is planned to include approximately 12 patients, and we anticipate reporting top-line results from this study in the second half of 2019.

15

Table of Contents

Pre-commercialization efforts

Prior to the receipt of the RTF letter, we had been actively taking steps to prepare for the commercialization of Firdapse® in the United States, including the hiring of a Chief Commercial Officer. However, due to the receipt of an RTF letter, the need to complete a second Phase 3 trial evaluating Firdapse® for the treatment of LEMS, and the need to conserve cash, we underwent a reduction-in-force in May 2016 and terminated most of our commercial staff.

During the fourth quarter of 2017, we restarted the development of our commercialization plans for Firdapse ®. We are currently refreshing our previous market assumptions for launch planning and developing a comprehensive marketing plan, a comprehensive medical communications plan and distribution and reimbursement assistance plans. We currently expect to market the product to approximately 750 neuromuscular physicians around the U.S., along with general neurologists, with a sales force of up to 20 specialized sales representatives and up to four medical science liaisons (MSLs). While we have not yet hired our sales force, we are beginning to initiate the hiring of our commercial team.

We continue to work with several rare disease advocacy organizations to help increase awareness of LEMS, CMS and MuSK-MG and to provide awareness and outreach support for the physicians who treat these rare diseases and the patients they treat.

Future pricing of and access to Firdapse®

We have not yet established our pricing for Firdapse®. However, the independent market research that we have conducted to date indicates that we should be able to obtain typical orphan disease pricing for our product and that our product will likely be widely reimbursed by private and public payors for the indicated small populations of LEMS, CMS, and MuSK-MG. There can be no assurance, however, as to the pricing of our product that we may be able to obtain or as to whether payors will agree to cover our product.

The pricing of pharmaceutical products, in general, and of specialty drugs, in particular, has been a topic of concern in the U.S. Congress, where hearings have been held on the topic, and a topic of recent statements made by the President of the United States. There can be no assurance as to how this scrutiny on pricing of pharmaceutical products will impact future pricing of our products, of orphan drugs generally, or of pharmaceutical products generally.

While our proposed pricing for Firdapse® has not been established, we recognize the importance of access to our medicines and, if Firdapse® is approved by the FDA, we expect to work with insurers to gain broad patient access in the U.S. market for the small patient populations of LEMS and CMS. We also expect to introduce and support comprehensive patient assistance programs and charitable access programs to assist eligible patients.

There is a vocal group of neuromuscular physicians who have raised public concerns in a letter to the editor of a medical journal, and some LEMS patients and neuromuscular physicians who have raised public concerns in interviews quoted in articles published in the press, that LEMS patients may not be able to get amifampridine treatment if we receive an approval of our product. Their overarching concern appears to be that our product will be priced too high as an orphan drug if we are the first pharmaceutical company to receive an FDA approval for an amifampridine product, thereby giving us the seven-year orphan drug exclusivity and the five-year new chemical entity exclusivity for our product. Stories about their concerns have been published in several national publications and some in the press have sought to tie their expectations about the anticipated pricing of Firdapse® to stories about perceived abusive price increases of drug products by other pharmaceutical companies. This vocal group has also questioned the appropriateness of the provisions of the Orphan Drug Act that would grant us exclusivity if our product were to be the first amifampridine product approved by the FDA and whether this exclusivity should be eliminated

from the law. We have directly responded to these concerns in a letter to the editor in this same medical publication. However, there can be no assurance as to the ultimate impact of these activities on us or our products or the extent to which these issues will be raised again in the future.

Table of Contents

Third-Party Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of coverage and adequate reimbursement by third party payors, such as state and federal governments, including Medicare and Medicaid, managed care providers, private commercial insurance plans and pharmacy benefit management (PBM) plans. Decisions regarding the extent of coverage and the amount of reimbursement to be provided for Firdapse® are expected to be made on a plan-by-plan, and in some cases, on a patient-by-patient basis. Particularly given the rarity of LEMS and CMS, we anticipate that securing coverage and appropriate reimbursement from third-party payors will require targeted education. To that end, we expect to hire a dedicated team of field-based market access account managers and reimbursement experts focused on ensuring that clinically-qualified patients have access to our product.

Intellectual property protections for Firdapse®

Under the BioMarin License Agreement, we licensed two pending patents and certain trademarks for Firdapse®. One of the licensed patents is a pending composition of matter patent that, if issued, will protect Firdapse® until February 2027, which includes five years of patent term extension that is expected under the Patent Term Restoration Act. This application was initially rejected following an appeal to the Patent Trial and Appeal Board. The application was refiled with new claims. The new claims were the subject of an office action in which the claims were rejected. A response to the rejection was filed and a final rejection was issued. The application was refiled and is under a final rejection, to which a response is in progress. There can be no assurance that this patent will be issued. The second patent claims methods of administering Firdapse®. Substantive examination has begun on this patent application and a final rejection has been issued, to which a response is in progress. We may also pursue other patents in order to seek to protect the exclusivity of the drug, dosage forms and methods of administration.

No drug product containing amifampridine for any indication has been approved by the FDA. Therefore, our version of amifampridine, if we are the first to obtain approval of the product in the U.S., will be eligible for five-year new chemical entity exclusivity, which provides a five-year period of marketing exclusivity for all indications.

We have licensed the Firdapse® trademark from BioMarin. A trademark application for Firdapse® was allowed, but did not register due to the inability to show use of the mark in interstate shipment. The application was refiled and a Statement of Use was submitted and accepted by the Trademark Office, and the mark was registered in March 2015.

In January 2014, the FDA provisionally approved Firdapse® as a proprietary name for amifampridine phosphate tablets. This provisional approval by the FDA would not prevent the agency from rejecting the name Firdapse® at a later date as part of the NDA review and approval process.

Table of Contents

CPP-115

Current status of our development efforts for CPP-115

We are developing CPP-115, a GABA aminotransferase inhibitor that, based on our preclinical studies to date, we believe is a more potent form of vigabatrin, and may have fewer side effects (e.g., visual field defects) than those associated with vigabatrin. We are hoping to develop CPP-115 for the treatment of refractory infantile spasms. CPP-115 has been granted Orphan Drug Designation by the FDA for the treatment of infantile spasms and Orphan Medicinal Product Designation in the European Union, or EU, for West syndrome (a form of infantile spasms).

We are currently refining our development plans for this product. We are also working with one or more potential investigators who have expressed an interest in evaluating our product for particular indications (particularly infantile spasms).

We are also continuing our efforts to seek a partner to work with us in furthering the development of CPP-115. However, no agreements have been entered into to date.

There can be no assurance that we will ever successfully commercialize CPP-115.

Product Overview

In August 2009, we licensed the exclusive worldwide rights to commercialize certain composition of matter patents relating to a new class of novel GABA aminotransferase inhibitors and derivatives of vigabatrin. We intend to develop these compounds for a broad range of neurological illnesses that could benefit from the inhibition of GABA aminotransferase. CPP-115 is our lead compound from this group of composition of matter patents.

The development efforts of CPP-115 were led by Dr. Richard B. Silverman, the Patrick G. Ryan/Aon Professor of Chemistry at Northwestern University (Northwestern). Dr. Silverman, who holds 75 patents, is the inventor of pregabalin, also known as Lyrica®, which is marketed by Pfizer. His goal in inventing the compound that became CPP-115 was to mimic the mechanism of action of vigabatrin, while making it both more potent and specific.

CPP-115 works by the same mechanism of action as vigabatrin; that is, the inhibition of GABA aminotransferase, which leads to increased brain GABA levels that reduce epileptogenesis. Due to these similarities, we believe that these two drugs will likely share certain biochemical features related to absorption, metabolism, and elimination, and our pre-clinical studies of CPP-115 to date support our expectations. However, based upon our pre-clinical studies of CPP-115 to date, we expect that there will be a significant reduction, and possibly elimination, of visual field defects (VFDs) from the use of CPP-115 compared to vigabatrin. However, there can be no assurance that this will ultimately prove to be the case.

Further, based on animal testing to date, CPP-115 has been shown to be at least 200 times more potent than vigabatrin in both in-vitro and animal model studies. The increased potency could enable the development of dosage forms potentially administrable by other routes of administration compared with the marketed oral, immediate release formulation of vigabatrin, Sabril®. Further, based on non-clinical testing completed to date, CPP-115 appears to have superior specificity to GABA aminotransferase and we believe, will have a better side effect profile (e.g. less VFDs) compared with Sabril®.

18

Table of Contents

Mechanism of action for CPP-115

We believe that CPP-115 will be an effective treatment for refractory infantile spasms because it increases endogenous GABA levels in the brain through the inhibition of GABA-aminotransferase (GABA-AT). GABA-AT is responsible for the eventual breakdown of GABA and helps to balance its inhibitory effects.

CPP-115 is a GABA analog that is readily absorbed and promptly available to the nervous system, producing effects that last for many hours after a single dose. Due to the fact that this drug is not receptor active , its administration does not appear to affect the baseline levels of dopamine, nor those variations in dopamine levels caused by normal stimuli.

Epilepsy and Infantile Spasms

Epilepsy is a brain disorder in which clusters of nerve cells, or neurons, in the brain sometimes signal abnormally. In epilepsy, the normal pattern of neuronal activity becomes disturbed, causing strange sensations, emotions, and behavior or sometimes convulsions, muscle spasms, and loss of consciousness. Epilepsy is a disorder with many possible causes. Anything that disturbs the normal pattern of neuron activity - from illness to brain damage to abnormal brain development - can lead to seizures. Epilepsy may develop because of an abnormality in brain wiring, an imbalance of nerve signaling chemicals called neurotransmitters, imbalance of sensitivity to neurotransmitters, or some combination of these factors. We intend to focus our development efforts for CPP-115 on its use as a treatment for refractory infantile spasms.

An infantile spasm is a specific type of seizure seen in an epilepsy syndrome of infancy and childhood. The onset of infantile spasms is usually in the first year of life, typically between 4-8 months. The seizures primarily consist of a sudden bending forward of the body with stiffening of the arms and legs; some children arch their backs as they extend their arms and legs. Spasms tend to occur upon awakening or after feeding, and often occur in clusters of up to 100 spasms at a time. Infants may have dozens of clusters and several hundred spasms per day. Infantile spasms usually stop by age five, but may be replaced by other seizure types.

In complex partial seizures, consciousness is altered. Patients may exhibit automatisms (automatic repetitive behavior) such as walking in a circle, sitting and standing, or smacking their lips together. Often accompanying these symptoms are the presence of unusual thoughts, such as the feeling of déjà vu, uncontrollable laughing, fear, visual hallucinations, and experiencing unusual unpleasant odors. These symptoms are thought to be caused by abnormal discharges in the temporal lobe.

According to the Epilepsy Foundation, there are about 3.0 million epilepsy patients in the United States, with approximately 150,000 new cases diagnosed in the U.S. each year. Worldwide, 65 million people are estimated to have epilepsy. The incidence of epilepsy appears to depend somewhat on the age of the individual. The risk of epilepsy from birth through age 20 is approximately 1%. Within this group, incidence is highest during the first year of life and increases somewhat at the onset of puberty. From age 20 to 55 it decreases again, but increases after age 55.

Anti-epileptic drugs work through a variety of mechanisms, including inhibition of sodium ion channels and the enhancement of GABA mechanisms. Although the different types of epilepsy vary greatly, in general, available medications can only control seizures in about two-thirds of patients. CPP-115, like vigabatrin, is a GABA-AT inhibitor, and we are developing it for refractory infantile spasms. Based on the historic use of vigabatrin in treating epilepsy, we believe that CPP-115 may ultimately work best as an adjunct therapy to existing drugs.

19

Table of Contents

Vigabatrin has been marketed for decades in over 30 countries by Lundbeck and Sanofi-Aventis and their predecessors and licensees under the brand names Sabril®, Sabrilex® and Sabrilan® (hereinafter referred to as Sabril®) as an adjunct (add-on) treatment for adult epilepsy and as a primary treatment for the management of infantile spasms. The composition of matter patents for Sabril® in the U.S. expired many years ago. On August 21, 2009, the FDA approved two NDAs for Sabril® for the treatment of infantile spasms and as an adjunctive therapy for adult patients with refractory complex partial seizures who have failed treatments with several other anti-epileptic drugs. The NDAs are for different formulations of Sabril® and both NDAs are held by Lundbeck. Due to the risks of visual field damage associated with vigabatrin, Sabril® was approved under an FDA-mandated Risk Evaluation and Mitigation Strategy (REMS) program and is only available through a special restricted distribution program approved by the FDA. In 2016, the FDA authorized changes to the REMS program for Sabril® to make it less onerous and to make it easier for patients to obtain their medication.

In chronic use for the treatment of epilepsy, vigabatrin has been generally well tolerated with lower than average neurological side effects compared to other approved epilepsy therapies. The most common side effects reported have been drowsiness and fatigue. However, one clearly established adverse side effect is the development of peripheral visual field defects, or VFDs. These VFDs are manifest as a constriction of the peripheral field of vision (i.e., tunnel vision). VFDs occur in approximately 33% of users when cumulative dosage levels of vigabatrin approach approximately 1,500 grams.

Our previous clinical and non-clinical studies of CPP-115

On November 1, 2010, we announced key results for our initial series of safety and efficacy evaluations in a number of animal and in-vitro laboratory studies. These results included superior visual safety of CPP-115, compared to vigabatrin, pharmacokinetic data supporting oral administration of CPP-115, pharmacologic target specificity, metabolic profile, and an absence of genotoxic, cardiovascular, respiratory, and liver enzyme side effects. It was also shown to be effective in multiple animal models for epilepsy and cocaine addiction.

On May 22, 2012, we reported positive results from a Phase 1a double-blind, placebo-controlled clinical trial evaluating the safety, tolerability and pharmacokinetic profile of CPP-115. The study evaluated single ascending doses ranging from 5 mg to 500 mg (a dose greater than ten times the predicted effective dose of 15-30 mg/day derived from animal data) of CPP-115 solution administered orally to 55 healthy volunteers. CPP-115 was found to be well tolerated with no side effects, rapidly absorbed and eliminated, and exhibited linear, dose dependent pharmacokinetics.

In December 2015 we announced top line results from a Phase 1b double-blind, placebo controlled safety and tolerance study of CPP-115 in six normal healthy adult male volunteers. The results showed significant increases in brain levels of the surrogate marker for potential efficacy, gamma-aminobutyric acid (GABA), a mechanism known to effectively treat epilepsy and infantile spams. The main adverse effect of prolonged elevated brain GABA, somnolence, was also observed.

While the primary objective of this study was to obtain safety and tolerance data for CPP-115 administered over 14 days, brain GABA levels were measured as a surrogate marker of potential efficacy, since CPP-115 is a second generation GABA aminotransferase inhibitor. Specifically, this study examined GABA levels in both the POC (Parietal-Occipital Cortex), a grey matter rich region thought to be associated with epilepsy, and which was previously studied for vigabatrin. The maximum brain GABA increases, in both brain regions, ranged from about 150% to over 200% of baseline levels, as measured by magnetic resonance spectroscopy (MRS).

20

Table of Contents

Previous clinical and pre-clinical studies of CPP-115 undertaken by others

An animal study reporting positive pre-clinical efficacy in a rat multiple hit model in which the use of CPP-115 was evaluated for the treatment of infantile spasms was published in the January 2014 issue of the journal, *Epilepsia*, The study was authored by Stephen W. Briggs, Tomonori Ono, MD, PhD, Solomon L. Moshe, MD and Aristea S. Galanopoulou, MD, PhD of the Saul R. Korey Department of Neurology, Dominick P. Purpura Department of Neuroscience, Laboratory of Developmental Epilepsy, The Comprehensive Epilepsy Center (CEC) at Montefiore Medical Center / Albert Einstein College of Medicine of Yeshiva University, Bronx, New York. The study concluded that (i) CPP-115 suppresses spasms in the multiple-hit model of infantile spasm, with onset of effect as early as the day after the first dose; (ii) the therapeutic doses of CPP-115 were well tolerated in developing rat pups; and (iii) CPP-115 showed efficacy for a longer duration at lower doses that were better tolerated than the previously tested therapeutic vigabatrin doses.

In September 2016, the Journal of Epilepsy & Behavior Case Reports published a case report of a child treated with CPP-115 in an investigator-sponsored, investigational new drug protocol. Based on treatment with CPP-115, this particular child experienced a significant reduction of seizures, with no evidence of retinal dysfunction. According to the case report, prior to treatment with CPP-115, the patient had failed ten drugs and the ketogenic diet, and had approximately 100 seizures per day. One year after starting CPP-115 and coming off of clobazam and vigabatrin, the patient s reported seizures have seen a marked reduction in frequency and his cognition and behavior have improved.

Northwestern University License Agreement

On August 27, 2009, we entered into a license agreement with Northwestern University (Northwestern), under which we acquired worldwide rights to commercialize new GABA aminotransferase inhibitors and derivatives of vigabatrin which had been discovered and patented by Northwestern. Under the terms of the license agreement, Northwestern granted us an exclusive worldwide license to United States composition of matter patents related to the new class of inhibitors and a patent application relating to derivatives of vigabatrin. This includes U.S. patent number 6,794,413 covering the composition of matter for CPP-115. We have designated the lead compound to be developed under this license as CPP-115.

Under our license agreement with Northwestern, we will be responsible for continued research and development of any resulting drug candidates. We have the right to terminate the agreement in whole or in part upon written notice. As of December 31, 2017, we have paid Northwestern upfront payments, milestone fees and maintenance and patent fees aggregating $424,885 and we are obligated to pay certain additional fees and milestone payments in future years relating to our clinical development activities under this license or payable upon passage of time (the next milestone payment, in the amount of $300,000, is due on the earlier of completion of the first Phase 3 clinical trial of CPP-115 or August 27, 2018). We are also obligated to pay Northwestern royalties on any products resulting from the license agreement. We also have the right to enter into sub-license agreements, and if we do, a royalty on any sub-license fees will be payable to Northwestern.

Patent protection for CPP-115

In addition to the exclusively licensed U.S. Patent 6,794,413, in March 2015, the U.S. Patent & Trademark Office (US PTO) issued patent 8,969,413 for the method of use patent for CPP-115 for neurological and psychological uses. This patent will expire in 2032, subject to potential extensions allowed under the patent term restoration act. A continuation application was filed to capture additional methods of using CPP for neurological and psychological conditions. This continuation application is undergoing substantive examination. Patents for the same coverage remain pending in the European Patent Office, Japan and Canada. There can be no assurance that the claims of this patent will be allowed, or

if allowed, that such claims will provide adequate patent protection for CPP-115.

Table of Contents

Generic Sabril®

In September 2015, we announced the launch of a program to develop our version of vigabatrin (CPP-109) as a generic version of Sabril®, which is marketed in the United States by Lundbeck. Lundbeck s exclusivity for Sabril® expired on April 26, 2017.

As part of our development of this product, we have obtained the reference listed drug and the active pharmaceutical ingredient, entered into an exclusive supply agreement for the vigabatrin active pharmaceutical ingredient with a manufacturer that has submitted a DMF to the FDA, validated the manufacturing process, and prepared a number of batches of vigabatrin for us on a commercial scale in the past, developed and validated quality control and stability test methods, and collected stability data showing that CPP-109 has an acceptable shelf life in two container closure systems. We are also taking the steps that will be required for us to obtain the rights to commercialize generic versions of this product.

There can be no assurance that we will be successful in these efforts or that any ANDA that we submit for vigabatrin will be accepted for review or approved. There can also be no assurance that any bioequivalence studies that we submit to the FDA in support of an ANDA for this product will be acceptable to the FDA. Finally, any approved generic version of vigabatrin that we are approved to commercialize will, consistent with Sabril®, only be available subject to an FDA-mandated Risk Evaluation and Mitigation Strategy (REMS) program.

We are continuing our efforts to seek a partner to work with us in furthering the development of generic Sabril®. However, no agreements have been entered into to date.

Intellectual Property Rights

Protection of our intellectual property and proprietary technology is a strategic priority for our business. We rely on a combination of patent, trademark, copyright and trade secret laws along with institutional know-how and continuing technological advancement, to develop and maintain our competitive position. Our ability to protect and use our intellectual property rights in the future development and commercialization of our products, operate without infringing the proprietary rights of others, and prevent others from infringing our proprietary rights, is crucial to our future success. See Item 1A. Risk Factors Risks Related to Our Intellectual Property.

Manufacturing and Supply

We have no plans to build or acquire the manufacturing capability needed to manufacture any of our research materials or commercial products. We expect that our drug products and drug substances will be prepared by contractors with suitable capabilities for these tasks and that we will enter into appropriate supply agreements with these contractors at appropriate times in the development and commercialization of our products. Because we will use contractors to manufacture and supply our products, we will be reliant on such contractors. Further, the contractors selected would have to be inspected by the FDA and found to be in substantial compliance with federal regulations in order for a drug application for one of our drug candidates to be approved, and there can be no assurance that the contractors we select would pass such an inspection.

Firdapse®

We have entered into agreements with a supplier of the active pharmaceutical ingredient (API) contained in Firdapse® for future requirements and we have contracted with third-party contract manufacturers who will manufacture Firdapse® tablets for us assuming Firdapse® is approved for commercialization.

22

Table of Contents

Any NDA that we submit for Firdapse® must include a manufacturing plan. If the manufacturing plan and data are insufficient, any NDA we submit will not be approved. Before an NDA can be approved, our manufacturers must also demonstrate compliance with FDA s current Good Manufacturing Practices (cGMPs) regulations and policies. Further, even if we receive approval of an NDA for Firdapse®, if our manufacturers do not follow cGMPs in the manufacture of our products, it may delay product launches or shipments and adversely affect our business.

Since we contract with third parties to manufacture our products, if the FDA approves an NDA for Firdapse®, our contract manufacturers will be required to comply with all applicable environmental laws and regulations that affect the manufacturing process. As a result, we do not believe that Catalyst will have any significant direct exposure to environmental issues.

CPP-115

We have entered into a contract to manufacture the API sufficient to meet the needs of our development plans for CPP-115. While we believe that we have ordered and obtained sufficient API for our planned upcoming studies, there can be no assurance of this.

Generic Sabril®

In preparation for the potential future marketing of our version of vigabatrin as a generic version of Sabril®, we have entered into supply agreements for the required API. Additionally, our contract manufacturer of CPP-109 tablets previously developed a manufacturing process for vigabatrin tablets and prepared several commercial scale batches. Our current contract manufacturer also has, based on their experience with CPP-109 tablets, the necessary experience and capability to produce generic vigabatrin for oral solution product. Additionally, we have entered in to an agreement to package vigabatrin for oral solution. Finally, while we have not entered into a contract for commercial production of this product, we believe that our current contract manufacturer and packagers have the capability to produce the product for us for commercial distribution.

Sales and Marketing

We have not yet obtained regulatory approval for any of our drug candidates.

Until the receipt of an RTF letter regarding our first NDA for Firdapse® for the treatment of LEMS, we had begun to hire a sales staff, including a Chief Commercial Officer. However, due to the receipt of an RTF letter and the Company s need to conserve funds, the Company underwent a reduction-in-force in May 2016 and terminated most of its commercial staff.

During the fourth quarter of 2017, we restarted the development of our commercialization plans for Firdapse ®. We are currently refreshing our previous market assumptions for launch planning and developing a comprehensive marketing plan, a comprehensive medical communications plan and distribution and reimbursement assistance plans. We currently expect to market the product to approximately 750 neuromuscular physicians around the U.S., along with general neurologists, with a sales force of up to 20 specialized sales representatives and up to four medical science liaisons (MSLs). While we have not yet hired our sales force, we are beginning to initiate the hiring of our commercial team.

We continue to work with several rare disease advocacy organizations to help increase awareness of LEMS, CMS and MuSK-MG and to provide awareness and outreach support for the physicians who treat these rare diseases and the patients they treat.

23

Table of Contents

In the future, we may also consider entering into arrangements with other pharmaceutical or biotechnology companies for the marketing and sale of Firdapse® in Canada or Mexico, where we have also licensed the product.

Competition

The pharmaceutical industry is intensely competitive, and any product candidate developed or licensed by us would likely compete with currently marketed and potentially new drugs and therapies even though they are not indicated for these conditions. There are many pharmaceutical companies, biotechnology companies, public and private universities, government agencies and research organizations that compete with us in developing various approaches to the treatment of orphan diseases. Many of these organizations have substantially greater financial, technical, marketing and manufacturing resources than we have.

Firdapse® for LEMS

LEMS is currently treated with unapproved drugs and therapies including steroids, azathioprine, other immunosuppressants and intravenous immunoglobulin, which work by suppressing the immune system, and pyridostigmine. Plasma exchange has also been used in an attempt to remove antibodies from the body. Further, one other product, guanidine HCl tablets, was approved many years ago (during a period when drugs were not required to be reviewed by the FDA for both safety and effectiveness) for use in the treatment of LEMS. However, this drug has significant side effects and is not currently viewed as an effective treatment for LEMS. Notwithstanding, drugs may be prescribed by physicians for the treatment of LEMS whether or not they are considered effective.

Another pharmaceutical company, Jacobus Pharmaceutical, has completed a clinical trial studying the safety and efficacy of its own formulation of amifampridine for the treatment of LEMS. Jacobus Pharmaceutical is a privately held company and there is little public information available about their development plans. While there can be no assurance, we believe that Firdapse® is further along in development than this other company s version of amifampridine. Under the Orphan Drug Act of 1983, the first pharmaceutical product to get approval for an indication receives the orphan exclusivity under the statute. If this other pharmaceutical company is able to receive approval of an NDA for its formulation of amifampridine for the treatment of LEMS before we are able to receive approval of Firdapse® for the same indication, we would be barred from marketing Firdapse® in the United States during the seven-year orphan exclusivity period, which would have a severe adverse effect on our results of operations. In addition, if this other company were to receive five-year new chemical entity exclusivity for amifampridine for any indication prior to approval of Firdapse®, and FDA determined that our NDA was a 505(b)(2) NDA, we would be barred from marketing Firdapse® in the United States during this five-year exclusivity period for any indication.

Further, we are aware that Jacobus Pharmaceutical has been making its 3,4-DAP product available to LEMS patients under compassionate use Investigational New Drug applications (INDs) for a number of years and, based on current information, we believe that approximately 200 LEMS patients may currently be receiving the drug under their program. If we are the first to obtain an approval for this product and its associated exclusivity and patent protection, we may not be able to stop Jacobus Pharmaceutical from continuing to supply its existing patients under compassionate use INDs.

Finally, we are aware that amifampridine has been available from compounding pharmacies for many years and may remain available, even if we are able to obtain FDA approval of Firdapse®. Compounded amifampridine, if it remains available, is likely to be substantially less expensive than Firdapse®. The Food and Drug Administration Modernization Act of 1997 included a new section, which clarified the status of pharmacy compounding under Federal law. Under Section 503A, drug products that are compounded by a pharmacist or physician for an individual patient may be entitled to exemptions from three key provisions of the act: (1) the adulteration provision of section

501(a)(2)(B) (concerning FDA s cGMP regulations); (2) the misbranding provision of section 502(f)(1) (concerning the labeling of drugs with adequate directions for use); and (3) the new drug provision of section 505 (concerning the approval of drugs under new drug or abbreviated new drug applications).

Table of Contents

To qualify for these statutory exemptions, a compounded drug product must satisfy several legal requirements. One of these requirements restricted the universe of bulk drug substances that a compounder may use; i.e., that every bulk drug substance used in compounding: (1) must comply with an applicable and current USP or NF drug monograph, if one exists, as well as the current USP chapters on pharmacy compounding; (2) if such a monograph does not exist, the bulk drug substance must be a component of an FDA-approved drug; or (3) if a monograph does not exist and the bulk drug substance is not a component of an FDA-approved drug, it must appear on a list of bulk drug substances that may be used in compounding (i.e., the bulk substances list). While the advertising provisions in Section 503A were ruled unconstitutional in part of the United States by the Supreme Court in 2002, the FDA has in the last five years aggressively regulated and exercised oversight over the practice of pharmacy compounding since a compounding incident at the New England Compounding Center in Massachusetts sickened hundreds and killed over 60 individuals. In 2013, Congress removed the unconstitutional advertising provisions in Section 503A when it passed the Drug Quality and Security Act of 2013 (DQSA), Title I (The Compounding Quality Act). The DQSA also created outsourcing facilities under Section 503B of the Federal Food, Drug, and Cosmetic Act, which are drug compounders that voluntarily register with FDA and may produce compounded formulations for office use (at least one of which must be sterile), but must comply with FDA s cGMP regulations and other requirements set forth in Section 503B. Section 503B outsourcing facilities may also only compound from bulk substances if the product is on FDA s drug shortage list, or the substance is on FDA s Section 503B list of bulk substances that may be used in compounding (Bulk Substances List 1).

While the FDA has been aggressively enforcing Section 503A since its re-enactment, compounders still may attempt to compound copies of approved drug products, under Section 503A, so long as the prescriber makes a change to the compounded formulation that produces for that patient a significant difference between the commercially available drug and the compounded version. Compounders may also copy commercially available products if they do not do so in regular or inordinate amounts. In January 2018, FDA published a Final Guidance document titled, Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act. This Final Guidance sets forth FDA s enforcement policy concerning those compounders that make essentially copies of commercially available drug products. FDA has defined the term regular or inordinate in the Final Guidance to mean: a drug product that is essentially a copy of a commercially available drug product is compounded regularly or in inordinate amounts if it is compounded more frequently than needed to address unanticipated, emergency circumstances, or in more than the small quantities needed to address unanticipated, emergency circumstances. FDA has further stated it will not take enforcement action, considering all the facts and circumstances, against a compounder that compounds less than four essentially copies of a commercially available drug product in a calendar month.

The FDA s Pharmacy Compounding Advisory Committee at its meeting on May 6-7, 1999 voted 7-4 against inclusion of 3,4-DAP on the bulk drugs list, largely based on the safety concerns and the commitment of Jacobus Pharmaceutical to make the drug available under compassionate use INDs, while pursuing FDA approval. Therefore, since 3,4-DAP does not meet the requirements codified in Section 503A described above, the individual or firm that compounds a drug product containing 3,4-DAP may be subject to a warning letter, seizure of product, injunction, and/or criminal prosecution for violations of the FD&C Act. After the re-enactment of Section 503A, and the enactment of new Section 503B of the DQSA, certain entities nominated 3,4 DAP as a bulk substance to be used in compounding under both reenacted section 503A and under the newly enacted Section 503B. As of October 2015, FDA included 3,4-DAP in its interim Bulk Substance List 3 under both Section 503A and Section 503B which list includes bulk drug products that may not currently be used in compounding because there is insufficient clinical evidence to support their use. Although 3,4-DAP has not yet been presented to FDA s Pharmacy Compounding Advisory Committee that was re-established with the passage of the DQSA, the entities that nominated the substance will be required to show additional data establishing safety and/or clinical need for the drug pursuant to FDA s guidelines for bulk substance nominations in order for the drug substance to move to Bulks List 1 (i.e., bulk

substances that may be used in compounding).

Table of Contents

We intend to take all available steps to try to enforce our marketing proprietary rights if we are the first company to obtain an approval for this product. We cannot determine with certainty what impact these factors will have on the market for our product. However, while there can be no assurance, we expect that despite these factors, we will be able to successfully market our product.

Generic Sabril®

Sabril® is marketed by Lundbeck in the United States for infantile spasms and for refractory complex partial seizures. Lundbeck s sales of Sabril® (tablets and sachets) were approximately $193 million in 2016 and $250 million in 2017. No generic version of Sabril® tablets has been approved to date in the United States, although a generic version of the powder form was recently launched by Par (Endo).

Factors affecting competition generally

In general, our ability to compete will depend in large part upon:

- our ability to complete clinical development and obtain regulatory approvals for our drug candidates;
- the demonstrated efficacy, safety and reliability of our drug candidates;
- the timing and scope of regulatory approvals;
- product acceptance by physicians and other health care providers;
- protection of our proprietary rights and the level of generic competition;
- the speed at which we develop drug candidates;
- our ability to supply commercial quantities of a product to the market;
- our ability to obtain reimbursement from private and/or public insurance entities for product use in approved indications;
- our ability to recruit and retain skilled employees; and
- the availability of capital resources to fund development and commercialization activities, including the availability of funding from the federal government.

26

Table of Contents

Regulatory Matters

Government regulation and product approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, record-keeping, promotion, storage, advertising, distribution, marketing and export and import of products such as those we are developing. Our drugs must be approved by the FDA through the NDA process before they may be legally marketed in the United States.

In the United States, drugs are subject to rigorous regulation by the FDA under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations, as well as other federal and state statutes. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA s refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of pre-clinical laboratory tests, animal studies and formulation studies according to the FDA s good laboratory practice, or GLP, regulations;

- submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin and which must include approval by an institutional review board, or IRB, at each clinical site before the trials are initiated;

- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use conducted in compliance with federal regulations and good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors;

- submission to, and acceptance by, the FDA of an NDA;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practice, or cGMP, regulations to assure that the facilities, methods and controls are adequate to preserve the drug s identity, strength, quality and purity;

- potential FDA audit of the non-clinical and clinical trial sites that generated the data in support of the NDA; and

FDA review and approval of the NDA.

Table of Contents

United States drug development process

Once a pharmaceutical candidate is identified for development it enters the pre-clinical testing stage. Pre-clinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. Prior to beginning human clinical trials, an IND sponsor must submit an IND to the FDA. The IND sponsor must submit the results of the pre-clinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some pre-clinical or non-clinical testing may continue even after the IND is submitted. In addition to including the results of the pre-clinical studies, the IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated, if the trial lends itself to an efficacy evaluation. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30 day time period, raises concerns or questions about the conduct of the trial. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may, at any time, impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of one or more qualified investigators in accordance with federal regulations and GCP.

Clinical trials must be conducted under protocols detailing the objectives of the trial and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND. Further, an Institutional Review Board (IRB) at each institution participating in the clinical trial must review and approve each protocol before any clinical trial commences at that institution. All research subjects must provide informed consent, and informed consent information must be submitted to the IRB for approval prior to initiation of the trial. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if adverse events or other certain types of other changes occur.

Human clinical trials are typically conducted in three phases. A fourth, or post-approval, phase may include additional clinical studies. These phases generally include the following, and may be sequential, or may overlap or be combined:

Phase 1 clinical trials involve the initial introduction of the drug into human subjects. These studies are designed to determine the safety of usually single doses of the compound and determine any dose limiting intolerance, as well as evidence of the metabolism and pharmacokinetics of the drug in humans.

Phase 2 clinical trials usually involve studies in a limited patient population to evaluate the safety and efficacy of the drug for specific, targeted indications, to determine dosage tolerance and optimal dosage, and to identify possible adverse effects and safety risks.

In Phase 3, if a compound is found to be potentially effective and to have an acceptable safety profile in Phase 2 (or occasionally Phase 1) studies, the Phase 3 studies will be conducted to further confirm clinical efficacy, optimal dosage and safety within an expanded population which may involve geographically diverse clinical trial sites. Generally, but not always, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Phase 4 clinical trials are studies required of or agreed to by a sponsor that are conducted after the FDA has approved a product for marketing. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase 4 clinical trial requirement. Failure to promptly conduct Phase 4 clinical trials where necessary could result in withdrawal of approval for products approved under accelerated approval regulations.

Table of Contents

While Phase 1, Phase 2, and Phase 3 tests are generally required for approval of an NDA, certain drugs may not require one or more steps in the process depending on other testing and the situation involved. Additionally, the FDA, an IRB, or the sponsor may stop testing at any time if results show patients being exposed to unnecessary health risks or overly dangerous side effects.

In addition, the manufacturer of an investigational drug in a Phase 2 or Phase 3 clinical trial for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access to such investigational drug.

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

Special factors with respect to clinical trials and pre-clinical studies conducted by others

The primary focus of our product development efforts is on our own clinical trials and pre-clinical studies. However, we have in the past supported and will continue in the future to support pre-clinical studies and clinical trials and studies by academic investigators (including members of our scientific advisory committee and academic institutions with which they are affiliated) of the use of our drug candidates that we believe might further the understanding or increase the value of our drug candidates.

In some cases, in the past, we have provided unrestricted sponsorship funds for such studies and we may do so again in the future. In other cases, we have provided, and may in the future provide, alternative assistance to the investigator, most typically providing drug substance or dosage form as well as matching placebo. We expect to continue supporting investigator-sponsored studies in the future to the extent that they meet criteria acceptable to us. In all cases, we seek to assist investigators in designing their studies so that such studies are most appropriately conducted and, to the extent possible, to make sure that these investigator studies potentially complement, and do not adversely impact, our activities.

United States review and approval process

FDA approval of an NDA is required before marketing of the product may begin in the United States. The NDA must include the results of product development, pre-clinical studies and clinical studies, together with other detailed information, including information on the chemistry, manufacture and composition of the product. The FDA has 60 days from its receipt of the NDA to review the application to ensure that it is sufficiently complete for substantive review before accepting it for filing. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is 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 submission of an NDA is also subject to the payment of a substantial application fee (for FDA fiscal year 2018 this fee is $2,421,495), although a waiver of such fee may be obtained under certain limited circumstances, including when the drug that is subject of the application has received Orphan Drug Designation for the indication sought. Further, the sponsor of an approved NDA is subject to an annual program fee, which for FDA fiscal year 2018 is $304,162 per prescription drug product. Beginning in fiscal year 2018, this annual program fee replaces the annual product and establishment fees. User fees typically increase annually. The approval process is

lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured to determine whether its manufacturing is cGMP compliant to assure and preserve the product s identity, strength, quality, purity and stability.

Table of Contents

If the FDA s evaluation of the NDA submission or manufacturing facilities is not favorable, the FDA will issue a complete response letter. The complete response letter outlines the deficiencies in the submission and often requires additional testing or information in order for the FDA to reconsider the application. Even after submitting this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. With limited exceptions, the FDA may withhold approval of a NDA regardless of prior advice it may have provided or commitments it may have made to the sponsor.

Special Protocol Assessments

An SPA is a process in which sponsors may request to meet with the FDA to reach agreement on the design and size of certain clinical trials, clinical studies, or animal trials to determine if they adequately address scientific and regulatory requirements. As part of this process, sponsors submit specific questions about protocol design and scientific and regulatory requirements. After the FDA completes the review of an SPA request, the FDA may issue a SPA Letter, including an assessment of the protocol, agreement or non-agreement with the proposed protocol, and answers to the sponsor s relevant questions.

An SPA agreement indicates concurrence by the FDA with the adequacy and acceptability of specific critical elements of overall protocol design (e.g., entry criteria, dose selection, endpoints, and planned analyses). These elements are critical to ensuring that the trial conducted under the protocol has the potential to support a future submitted application s ability to meet regulatory requirements for approval. Feedback on these issues provides the greatest benefit to sponsors in planning late-phase development strategy. However, an SPA agreement does not indicate FDA concurrence on every protocol detail. Further, the FDA may rescind an SPA if the director of the FDA reviewing division determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the trial began. Thus, an SPA is not binding on the FDA if, for example, the Agency identifies a safety concern related to the product or its pharmacological class, if the FDA or the scientific community recognizes a paradigm shift in disease diagnosis or management, if the relevant data or assumptions provided by the sponsor in the SPA submission are found to be false or misstated, or if the sponsor fails to follow the protocol that was agreed upon with the FDA. The FDA retains significant latitude and discretion in interpreting the terms of an SPA agreement and the data and results from the applicable clinical trial.

Because an SPA provides for the evaluation of protocols for trials that have not been initiated, the conduct and results of the subsequent trial are not part of the evaluation. Therefore, the existence of an SPA agreement does not guarantee that the FDA will accept an NDA, or that the trial results will be adequate to support approval. Those issues are addressed during the review of a submitted application; however, it is hoped that trial quality will be improved by the SPA process.

Table of Contents

Post-approval requirements and consideration

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. As a condition of NDA approval, the FDA may also require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for the healthcare professionals, and other Elements To Assure Safe Use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug.

Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control as well as drug manufacture, packaging, and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

The Hatch-Waxman Amendments

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims covering the applicant s product or approved methods of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA s Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown to be bioequivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, pre-clinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

31

Table of Contents

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA s Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the new product will not infringe the already approved product s listed patents, or that such patents are invalid, is called a Paragraph IV certification. 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 of 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.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity or NCE, which is a drug that contains no active moiety that has been approved by FDA in any other NDA, that drug receives five years of marketing exclusivity during which FDA cannot receive any ANDA seeking approval of a generic version of that drug. A drug may obtain a three-year period of exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for the previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the applicant. During this period of exclusivity, FDA cannot approve an ANDA for a generic drug that includes the change.

An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

Section 505(b)(2) New Drug Applications

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2), or 505(b)(2), NDA, which enables the applicant to rely, in part, on FDA s previous approval of a similar product, or published literature, in support of its application.

505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference. If the Section 505(b)(2) applicant can establish that reliance on FDA s prior findings of safety and effectiveness or published literature is scientifically appropriate, it may eliminate the need to conduct certain pre-clinical or clinical studies of the new product.

32

Table of Contents

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 product 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.

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. A Section 505(b)(2) NDA may be eligible for three years of marketing exclusivity to the same extent that a Section 505(b)(1) NDA is.

Abbreviated new drug applications

Generic drugs may enter the market after the approval of an ANDA. The ANDA development process typically does not require new pre-clinical or clinical studies, but it does typically require one or more bioequivalence studies to show that the ANDA drug is bioequivalent to the previously approved brand name reference listed drug. Bioequivalence studies compare the bioavailability of the proposed drug product with that of the approved listed product containing the same active ingredient. Bioavailability is a measure of the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action. A demonstration of bioequivalence means that the rate and extent of absorption of the ANDA drug is not significantly different from the rate and extent of absorption of the brand name reference listed drug when administered at the same molar dose under similar experimental conditions.

As noted above, generic drug products are generally introduced to the marketplace at the expiration of patent protection and non-patent market exclusivity for the reference listed drug. However, if an ANDA applicant is the first ANDA applicant to submit an ANDA containing a Paragraph IV certification, that ANDA may be eligible for a period of generic marketing exclusivity on approval. This exclusivity, which under certain circumstances must be shared with other ANDA applicants with Paragraph IV certifications, lasts for 180 days, during which the FDA cannot grant final approval to other ANDA sponsors of an application for a generic equivalent to the same reference drug. Under certain circumstances, eligibility for 180-day exclusivity may be forfeited.

Various types of changes to an approved ANDA must be requested in a prior approval supplement. In addition, some changes may only be approved only after new bioequivalence studies are conducted or other requirements are satisfied. In addition, the ANDA applicant must demonstrate that manufacturing procedures and operations conform to FDA cGMP requirements. Facilities, procedures, operations and/or testing of products are subject to periodic inspection by the FDA and other authorities. In addition, the FDA conducts pre-approval and post-approval reviews and inspections to determine whether the systems and processes are in compliance with cGMP and other FDA regulations.

There are also user fees for ANDA applicants, sponsors, and manufacturers. For fiscal year 2018, the application fees are $171,823 per ANDA application and the facility fees are $211,087 per domestic final dosage form facility, $226,087 per foreign final dosage form facility, $45,367 per domestic active pharmaceutical ingredient facility, and $60,367 per foreign active pharmaceutical ingredient facility. In addition, there is a new annual program fee based on the size of the generic drug applicant. These user fees typically increase each fiscal year.

Table of Contents

Other regulatory requirements

In addition to regulation by the FDA and certain state regulatory agencies, we are also subject to a variety of foreign regulations governing clinical trials and the marketing of other products. Outside of the United States, our ability to market a product depends upon receiving a marketing authorization from the appropriate regulatory agencies. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from country to country. In any country, however, we will only be permitted to commercialize our products if the appropriate regulatory agency is satisfied that we have presented adequate evidence of safety, quality and efficacy. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must be obtained prior to the commencement of marketing of the product in those countries. The regulatory approval and oversight process in other countries includes all of the risks associated with regulation by the FDA and certain state regulatory agencies as described above.

Under the European Union regulatory system, applications for drug approval may be submitted either in a centralized or decentralized manner. Under the centralized procedure, a single application to the European Medicines Agency leads to an approval granted by the European Commission which permits marketing of the product throughout the European Union. The decentralized procedure provides for mutual recognition of nationally approved decisions and is used for products that do not comply with requirements for the centralized procedure. Under the decentralized procedure, the holders of national marketing authorization in one of the countries within the European Union may submit further applications to other countries within the European Union, who will be requested to recognize the original authorization based on an assessment report provided by the country in which marketing authorization is held.

Pharmaceutical pricing and reimbursement

In both US and foreign markets, our ability to commercialize our products successfully, and to attract commercialization partners for our products, depends in significant part on the availability of adequate financial coverage and reimbursement from third-party payors, including, in the United States, governmental payors such as Medicare and Medicaid, managed care organizations, private commercial health insurers and PBMs. Third party payors are increasingly challenging the prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic or other studies in order to further demonstrate the value of our products. Even with the availability of such studies, our products may be considered less safe, less effective or less cost-effective than alternative products, and third-party payors may not provide coverage and reimbursement for our drug candidates, in whole or in part.

Political, economic and regulatory influences are subjecting the health care industry in the United States to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could significantly affect our business, including the Patient Protection and Affordable Care Act of 2010 (the Affordable Care Act). In fact, there continue to be efforts in Congress to repeal the Affordable Care Act and replace it with another law and President Trump has stated that he supports repeal of all or portions of the Affordable Care Act. As a result, there is great uncertainty as to what changes will be made to U.S. healthcare laws and there can be no assurance how changes to those laws may affect our business.

We anticipate that in the US, Congress, state legislatures, and private sector entities will continue to consider and may adopt healthcare policies intended to curb rising healthcare costs. These cost containment measures could include:

controls on government-funded reimbursement for drugs;

34

Table of Contents

controls on healthcare providers;

controls on pricing of pharmaceutical products;

challenges to the pricing of drugs or limits or prohibitions on reimbursement for specific products through other means;

reform of drug importation laws;

entering into contractual agreements with payors; and

expansion of use of managed-care systems in which healthcare providers contract to provide comprehensive healthcare for a fixed cost per person.

We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted may have a material adverse effect on our business prospects.

Further, the pricing of pharmaceutical products generally, and particularly the pricing of orphan drugs, has recently received scrutiny from the press, from members of Congress in both parties, and from President Trump. Some members of the medical community have also weighed in in the press on the potential pricing of orphan drugs generally and our product specifically. The impact of this scrutiny on us and on the pricing of orphan drugs and other pharmaceutical products generally cannot be determined with any certainty at this time.

Orphan Drug Exclusivity and Pediatric Exclusivity Designation

Some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983 (ODA), the FDA may grant Orphan Drug Designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. In the United States, Orphan Drug Designation must be requested before submitting an application for marketing approval. An Orphan Drug Designation does not shorten the duration of the regulatory review and approval process. The grant of an Orphan Drug Designation request does not alter the standard regulatory requirements and process for obtaining marketing approval. Safety and efficacy of a compound must be established through adequate and well-controlled studies. If a product which has been granted Orphan Drug Designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to an orphan drug exclusivity period, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as where an alternative product demonstrates clinical superiority to the product with orphan exclusivity. In addition, holders of exclusivity for orphan drugs are expected to assure the availability of sufficient quantities of their orphan drugs to meet the needs of patients. Failure to do so could result in the withdrawal of marketing exclusivity for the drug.

The orphan drug exclusivity contained in the ODA has been the subject of recent scrutiny from the press, from some members of Congress and from some in the medical community. There can be no assurance that the exclusivity granted in ODA to orphan drugs approved by the FDA will not be modified in the future, and as to how any such change might affect our products, if approved.

Table of Contents

Pediatric exclusivity is another type of non-patent exclusivity in the U.S. 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 five-year and three-year non-patent and seven-year orphan exclusivities. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly responds 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. If the FDA determines that information relating to the use of the new drug in the pediatric population may produce health benefits in the population, the clinical study is deemed to fairly respond to the FDA s request and the reports of FDA-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 covering 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 approve another application relying on the NDA sponsor s data.

The European Orphan Drug Regulation is considered for drugs intended to diagnose, prevent or treat a life-threatening or very serious condition afflicting five or fewer per 10,000 people in the EU, including compounds that for serious and chronic conditions would likely not be marketed without incentives due to low market return on the sponsor s development investment. The medicinal product considered should be of significant benefit to those affected by the condition. Benefits of being granted Orphan Medicinal Product