CATABASIS PHARMACEUTICALS INC
Form 10-K
March 14, 2019

Use these links to rapidly review the document

Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2018

or

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

For the transition period from to
Commission File Number: 001-37467

Catabasis Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**26-3687168**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
One Kendall Square Bldg. 1400E, Suite B14202 Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code **(617) 349-1971**

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

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

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

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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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. ý

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

Large accelerated filer o	Accelerated filer o	Non-accelerated filer ý	Smaller reporting company ý
			Emerging growth company ý

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

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

Aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last sale price for such stock on June 30, 2018: $63,319,764.

As of March 7, 2019, there were 11,495,742 shares of the registrant's Common Stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2019 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. The registrant intends to file such proxy statement with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this Annual Report on Form 10-K relates.

Table of Contents

TABLE OF CONTENTS

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

These forward-looking statements include, among other things, statements about:

- our expectations regarding our ability to successfully conduct the PolarisDMD trial, and our expectations regarding the timing and results of such trial, including reporting top-line results of this trial in the second quarter of 2020 and the potential consistency of data produced by this trial with prior results from our MoveDMD® trial, as well as any new data and analyses relating to the safety profile and potential clinical benefits of edasalonexent;
- our plans to identify, develop and commercialize novel therapeutics based on our SMART Linker drug discovery platform;
- ongoing and planned clinical trials for edasalonexent and other product candidates, whether conducted by us or by any future collaborators, including the timing of initiation of these trials and of the anticipated results;
- our plans to enter into collaborations for the development and commercialization of product candidates;
- the potential benefits of any future collaboration;
- our ability to receive research and development funding and achieve anticipated milestones under any future collaborations;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional products or product candidates with significant commercial potential;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

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

Table of Contents

results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

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

REFERENCES TO CATABASIS

Except as otherwise indicated herein or as the context otherwise requires, references in this Annual Report on Form 10-K to "Catabasis," "the Company," "we," "us," and "our" refer to Catabasis Pharmaceuticals, Inc. and its consolidated subsidiary.

Table of Contents

PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics. Our lead product candidate is edasalonexent, formerly known as CAT-1004, an oral small molecule that inhibits NF-κB, or nuclear factor kappa-light-chain-enhancer of activated B cells, in development for the treatment of Duchenne muscular dystrophy, or DMD. We believe edasalonexent has the potential to be a foundational therapy for all patients affected by DMD regardless of the underlying dystrophin mutation. DMD is an ultimately fatal genetic disorder involving progressive muscle degeneration. The United States Food and Drug Administration, or FDA, has granted orphan drug, fast track and rare pediatric disease designations to edasalonexent for the treatment of DMD. The European Commission, or EC, has granted orphan medicinal product designation to edasalonexent for the treatment of DMD.

We initiated a global Phase 3 trial of edasalonexent for the treatment of DMD in September 2018, which we refer to as the PolarisDMD trial. The PolarisDMD trial is designed to evaluate the efficacy and safety of edasalonexent for registration purposes, with top-line results expected in the second quarter of 2020. Our goal is to submit a New Drug Application, or NDA, for edasalonexent for the treatment of DMD in early 2021. PolarisDMD is currently enrolling patients with enrollment expected to be completed in 2019. The trial design was informed by discussions with the FDA, as well as input from treating physicians, families of boys affected by DMD and patient advocacy organizations.

The PolarisDMD trial is a randomized, double-blind, placebo-controlled trial, and we anticipate enrolling approximately 125 patients between the ages of four and seven (up to eighth birthday), regardless of mutation type, who have not been on steroids for at least six months. The primary efficacy endpoint is change in North Star Ambulatory Assessment, or NSAA, score after 12 months of treatment with edasalonexent compared to placebo. Key secondary endpoints are the age-appropriate timed function tests: time to stand, 4-stair climb and 10-meter walk/run. Assessments of growth, cardiac and bone health are also included in the trial.

This month, we are initiating a new open-label extension trial called the GalaxyDMD trial, in which we plan to enroll all of the boys currently participating in the MoveDMD open-label extension, and which will also provide the boys who complete the 12-month PolarisDMD trial with the opportunity to receive open-label edasalonexent treatment. The GalaxyDMD trial is designed to provide longer term safety data to support registration filings.

Our MoveDMD Phase 1/2 trial enrolled ambulatory boys four to seven years old with a genetically confirmed diagnosis of DMD who were steroid naive or had not used steroids for at least six months prior to the trial. Boys enrolled in the trial were not limited to any specific dystrophin mutations and the 31 boys in the trial had 26 different dystrophin mutations. The MoveDMD trial was designed to be conducted in three sequential parts, Phase 1 and Phase 2, both of which are completed, and an open-label extension, which is on-going. In Phase 1 of the MoveDMD trial, we assessed the safety, tolerability and pharmacokinetics of edasalonexent in 17 patients, following seven days of dosing, and we reported in January 2016 that all three doses of edasalonexent tested were generally well tolerated with no safety signals observed and there were no serious adverse events and no drug discontinuations. In the Phase 2 portion of the trial, we assessed the effects of edasalonexent using magnetic resonance imaging, or MRI, T2 as an early biomarker at 12 weeks, and announced in January 2017 that the primary efficacy endpoint of average change from baseline to week 12 in the MRI T2 composite measure of lower leg muscles for the pooled edasalonexent treatment groups compared to placebo was not met, although we observed directionally positive results in the 100/mg/kg/day edasalonexent treatment group that were not statistically significant. Subsequently, in the open-label extension of the

Table of Contents

MoveDMD trial, we observed statistically significant improvement in the rate of change in lower leg composite MRI T2 through 12, 24, 36 and 48 weeks on 100 mg/kg of edasalonexent treatment compared to the off-treatment control period.

We have completed key efficacy and safety assessments from the MoveDMD trial. In the ongoing open-label extension of the MoveDMD trial through 72 weeks of oral 100 mg/kg/day edasalonexent treatment, we observed preserved muscle function and consistent improvements in all four assessments of muscle function: NSAA score, time to stand, 4-stair climb and 10-meter walk/run, compared to the rates of change in the control period for boys prior to receiving edasalonexent treatment. Additionally, supportive changes in non-effort-based measures of muscle health were seen, supporting the durability of edasalonexent treatment effects. Specifically, we observed in the 100 mg/kg/day treatment group, that all four muscle enzymes tested (creatine kinase, alanine aminotransferase, aspartate aminotransferase and lactate dehydrogenase) were significantly decreased compared to baseline following edasalonexent treatment at 12 weeks and later time points through 72 weeks ($p<0.05$). Through 72 weeks of treatment, edasalonexent continued to be well tolerated with no safety signals observed in the MoveDMD trial. Boys treated with edasalonexent continued to follow age-appropriate growth curves with age-appropriate increases in weight and height and overall body mass index trended down to age-normative values. We also observed that the heart rate of the boys significantly decreased toward age-normative values through over a year and a half period of edasalonexent treatment.

In addition to edasalonexent, we have developed CAT-5571 as a potential treatment for cystic fibrosis, or CF. CAT-5571 is an oral small molecule that is designed to activate autophagy, a mechanism for recycling cellular components and digesting pathogens, which is important for host defenses and is depressed in CF. We have completed investigational new drug, or IND, application-enabling activities for CAT-5571.

As of December 31, 2018, we owned six issued U.S. patents with composition of matter and method of use claims directed to edasalonexent and four issued U.S. patents with composition of matter and method of use claims directed to CAT-5571. These patents are expected to expire between 2029 and 2030, without taking into account potential patent term extensions. In addition, our patent portfolio includes over 70 issued foreign patents, three pending U.S. patent applications, four pending international patent applications, and 17 pending foreign patent applications.

Our Product Candidates

Edasalonexent

We designed edasalonexent to inhibit NF-κB, a protein that is activated in DMD and that drives inflammation, fibrosis and muscle degeneration, and suppresses muscle regeneration. We have reported results from Phase 1, Phase 2 and the ongoing open-label extension of the MoveDMD trial through administration of edasalonexent for up to 72 weeks, as described further below under " Edasalonexent Clinical Development". The FDA has granted edasalonexent orphan drug, fast track and rare pediatric disease designations for the treatment of DMD. The EC has granted orphan medicinal product designation to edasalonexent for the treatment of DMD.

Overview of DMD

DMD is a rare pediatric disorder involving progressive muscle degeneration that eventually leads to death. DMD is caused by various mutations in the dystrophin gene that result in a lack of functional dystrophin in muscle fibers, which renders muscle fibers more susceptible to mechanical stress. Dystrophin is a protein that resides in the membrane of muscle cells and is critical to the structural and membrane stability of muscle fibers in skeletal, diaphragm, and cardiac muscle. When muscles contract or stretch during normal use, the absence of normally functioning dystrophin results in activation of the NF-κB pathway, triggering inflammation in the muscles, initiating muscle degeneration, and reducing

Table of Contents

the ability of muscles to regenerate. As muscle damage progresses, connective and adipose tissues replace muscle fibers, resulting in inexorable muscle weakness.

DMD occurs almost exclusively in males, occurring in approximately 1 in 3,500 live male births. Based on this incidence rate, we estimate that DMD affects a total of approximately 15,000 patients in the United States and approximately 19,000 patients in the European Union, or EU.

Children with DMD typically begin to show symptoms of disease between ages two and five, when they develop a waddling gait, frequently fall and have difficulty rising from the floor. Progressive weakness then develops in the voluntary muscles in the arms, legs and trunk. This muscle weakness is accompanied by fixations, or contractures, of joints, such as knees, hips and elbows. By age eight, most patients have difficulty ascending stairs. Patients typically lose walking ability between the ages of ten and fourteen and, by about twelve years of age, most people with DMD are unable to walk and need to use a power wheelchair on a regular basis. Patients' cardiac and respiratory muscles are also adversely affected, typically requiring use of ventilators in their late teens. Progressive weakening of cardiac and respiratory muscles of DMD patients eventually results in death, generally in the patient's mid-twenties.

The Role of NF-κB in Duchenne Muscular Dystrophy

NF-κB plays an important role in regulating skeletal muscle health and appears to be especially important in regulating skeletal muscle mass in chronic diseases such as DMD. NF-κB is a key link between loss of dystrophin and disease progression in DMD, and NF-κB has a fundamental role in skeletal and cardiac muscle disease in DMD. Activated NF-κB promotes the degradation of specific muscle proteins and leads to the induction of pro-inflammatory mediators such as cytokines, including tumor necrosis factor alpha, or TNF-α, interleukin 6, or IL-6, and interleukin-1 beta, or IL-1β; chemokines; cell adhesion molecules; and tissue degrading enzymes, such as matrix metallopeptidase 9, or MMP-9. In addition, activated NF-κB suppresses muscle stem cell differentiation that is required for muscle regeneration by preventing satellite stem cells from differentiating into myoblasts, progenitor cells that differentiate, to give rise to muscle cells. Activation of NF-κB is observed in muscle tissues of patients with DMD prior to the onset of other clinical manifestations, and activated NF-κB is persistently elevated in the immune cells and regenerative muscle fibers of patients with DMD. Moreover, evidence exists that mechanical stress activates NF-κB in muscles and increases levels of activated NF-κB by a factor of three to four times. Muscles with increased mechanical stress, such as quadriceps and hamstrings, show the most rapid progression of disease.

Unaddressed Market Opportunity

There are currently only two therapies approved in the United States for the treatment of DMD: the Sarepta Therapeutics, Inc., or Sarepta, drug EXONDYS 51®, also known as eteplirsen, an exon skipping therapy targeting the skipping of exon 51, that was granted accelerated approval by the FDA, and PTC Therapeutics' EMFLAZA®, also known as deflazacort, a glucocorticoid, which is indicated for the treatment of DMD in patients five years of age and older. Corticosteroid therapy, including treatment with prednisone, is often prescribed to treat the inflammation underlying DMD and to delay loss of ambulation. In DMD patients, corticosteroids have demonstrated efficacy, which is believed to be driven by reductions in activated NF-κB. However, because corticosteroids primarily act through another pathway called the glucocorticoid receptor-mediated pathway, they can cause significant complications including growth suppression, excessive weight gain, behavioral changes, reduction in bone strength and compromise of the immune system. Over time, corticosteroids induce chronic myopathy in many diseases through induction of muscle protein breakdown, which ultimately leads to muscle damage. DMD patients treated with corticosteroids typically show an initial improvement in measures of muscle function but then resume a progressive decline. Approximately half of DMD patients treated with steroids lose the ability to walk by age thirteen and the vast majority are in

Table of Contents

wheelchairs by age sixteen. DMD patients typically live until their mid-twenties, despite the availability of corticosteroids.

In addition to the FDA-approved DMD therapies in the United States, there are several treatments for DMD that currently are being reviewed by the FDA or are approved or under review in the EU or are expected to be under review by regulatory agencies in the near future. For example, Sarepta announced in February 2019 that the rolling NDA for golodirsen, its phosphorodiamidate morpholino oligomer, or PMO, based, exon-53 skipping candidate, has been accepted by the FDA. Golodirsen has been granted priority review by the FDA and the Prescription Drug User Fee Act, or PDUFA, date for a decision is August 19, 2019. Also, PTC Therapeutics' ataluren is conditionally approved in the EU and several other countries for treatment of nonsense mutation DMD, or nmDMD, in ambulatory patients aged two years and older, under the trade name Translarna . In the third quarter of 2018, PTC Therapeutics filed in the EU for an extension of the existing label for Translarna to include non-ambulatory DMD patients. PTC Therapeutics is conducting additional clinical trials with ataluren in nmDMD in the United States and is in discussions with the FDA as to the regulatory approval pathway.

EXONDYS 51, golodirsen and ataluren target mechanisms to increase levels of dystrophin in muscles. Each of these agents addresses a specific type of genetic mutation in order to produce a partially functional dystrophin protein. The therapeutic goal of these product candidates is to reduce disease severity and extend survival in those DMD patients who are candidates for therapy with these agents. Based on the prevalence of the specific mutations that EXONDYS 51, golodirsen and ataluren are designed to address, they would be expected to be effective in an aggregate of approximately 34% of DMD patients. We believe that DMD patients, including those treated with these dystrophin-targeted therapies, will continue to require treatments to reduce muscle inflammation and degeneration and enhance muscle regeneration.

Edasalonexent for the Treatment of Duchenne Muscular Dystrophy

Based on the mechanism of action by which edasalonexent suppresses NF-κB and the results that we have seen in preclinical models of DMD, we believe that edasalonexent has the potential to combine reduction of inflammation and muscle degeneration with positive effects on muscle regeneration, all of which may allow patients to retain muscle function longer. In addition, we believe that edasalonexent has the potential to be an effective therapy in all DMD patients, regardless of the underlying mutation, and to provide significant benefit to patients, both as monotherapy and when used in combination with other therapies, including dystrophin-targeted therapies. If we receive marketing approval, we intend to commercialize edasalonexent in North America ourselves and commercialize edasalonexent outside of North America either ourselves or with a collaborator.

Edasalonexent Clinical Development

PolarisDMD Phase 3 Trial of Edasalonexent in Patients with DMD

We initiated a global Phase 3 trial for the treatment of DMD in September 2018, which we refer to as the PolarisDMD trial. The PolarisDMD trial is designed to evaluate the efficacy and safety of edasalonexent for registration purposes, with top-line results expected in the second quarter of 2020. PolarisDMD is currently enrolling patients with sites open for enrollment in the United States, Canada and Australia. Additional PolarisDMD clinical trial sites are expected to open in the United States, Australia, Canada, Europe and Israel in the next few months. In total, the PolarisDMD trial is expected to include approximately 40 clinical trial sites globally with enrollment expected to be completed in 2019. The trial design was informed by discussions with the FDA, as well as input from treating physicians, families of boys affected by DMD and patient advocacy organizations.

Table of Contents

The PolarisDMD trial is a randomized, double-blind, placebo-controlled trial, and we anticipate enrolling approximately 125 patients between the ages of four and seven (up to eighth birthday), regardless of mutation type, who have not been on steroids for at least six months. Boys may be eligible to enroll in the trial if they are on a stable dose of EXONDYS 51, one of two therapies approved for the treatment of DMD in the United States. The primary efficacy endpoint is change in NSAA score after 12 months of treatment with edasalonexent compared to placebo. Key secondary endpoints are the age-appropriate timed function tests: time to stand, 4-stair climb and 10-meter walk/run. Assessments of growth, cardiac and bone health are also included. Enrolled boys are being randomized in a 2:1 ratio with two boys receiving edasalonexent for every boy that receives placebo, and we expect that after the initial 12-month treatment period all boys will be offered the opportunity to receive edasalonexent in an open-label extension.

MoveDMD Phase 1/2 Trial of Edasalonexent in Patients with DMD

Our MoveDMD Phase 1/2 trial enrolled 31 ambulatory boys four to seven years old with a genetically confirmed diagnosis of DMD who were steroid naive or had not used steroids for at least six months prior to the trial. Boys enrolled in the trial were not limited to any specific dystrophin mutations and the boys in the trial had 26 different dystrophin mutations. The MoveDMD trial was designed to be conducted in three sequential parts, Phase 1 and Phase 2, both of which are completed, and an open-label extension, which is on-going. In Phase 1 of the MoveDMD trial, we assessed the safety, tolerability and pharmacokinetics of edasalonexent in 17 patients, following seven days of dosing, and we reported in January 2016 that all three doses of edasalonexent tested were generally well tolerated with no safety signals observed and there were no serious adverse events and no drug discontinuations. In the Phase 2 portion of the trial, we assessed the effects of edasalonexent using MRI T2 as an early biomarker at 12 weeks, and announced in January 2017 that the primary efficacy endpoint of average change from baseline to week 12 in the MRI T2 composite measure of lower leg muscles for the pooled edasalonexent treatment groups compared to placebo was not met, although we observed directionally positive results in the 100/mg/kg/day edasalonexent treatment group that were not statistically significant and subsequently observed positive MRI T2 results in the open-label extension of the MoveDMD trial described further below.

We have completed key efficacy and safety assessments from the MoveDMD trial. In the open-label extension of the MoveDMD trial through 72 weeks of oral 100 mg/kg/day edasalonexent treatment, we reported in October 2018 that we have observed preserved muscle function and consistent improvements in all four assessments of muscle function: NSAA score, time to stand, 4-stair climb and 10-meter walk/run, compared to the rates of change in the control period for boys prior to receiving edasalonexent treatment. Additionally, supportive changes in non-effort-based measures of muscle health were seen, supporting the durability of edasalonexent treatment effects. Specifically, we observed statistically significant improvement in the rate of change in lower leg composite MRI T2 through 12, 24, 36 and 48 weeks on 100 mg/kg of edasalonexent treatment compared to the off-treatment control period. MRI T2 is closely associated with functional outcomes in DMD supported by data from ImagingDMD, the largest natural history database of MRI assessments in boys with DMD.

The relative proportion of fat in muscle, which is referred to as fat fraction and is correlated with functional ability, can also be determined by magnetic resonance spectroscopy, or MRS. Improvements in the MRS fat fraction rate of change through 48 weeks of edasalonexent treatment compared to the off-treatment control period were observed in both soleus and vastus lateralis leg muscles, which are strongly correlated with ambulatory function.

Additional supportive measures of muscle health also reinforce the positive edasalonexent treatment effects observed in the 100 mg/kg/day treatment group. All four muscle enzymes tested (creatine kinase, alanine aminotransferase, aspartate aminotransferase and lactate dehydrogenase) were

Table of Contents

significantly decreased compared to baseline following edasalonexent treatment at 12 weeks and later time points through 72 weeks ($p<0.05$), consistent with a positive impact on muscle health and supportive of a positive impact from treatment with edasalonexent. Biomarker results showed that C-reactive protein, or CRP, was significantly decreased with edasalonexent at 12, 24, 36 and 48 weeks compared to baseline in the 100 mg/kg/day treatment group ($p<0.001$). CRP is a well-characterized blood test marker that provides a global assessment of inflammation and is elevated in boys affected by DMD. The significant decrease observed in CRP supports a conclusion that the biological activity of edasalonexent in inhibiting NF-κB can decrease inflammation.

Edasalonexent was well tolerated in the MoveDMD trial with no clinical safety signals observed to date through 2 years of treatment. The majority of adverse events, or AEs, have been mild in nature with no serious AEs. The most common treatment-related AEs were gastrointestinal, primarily mild and transient diarrhea and, in Phase 2, vomiting. There were no treatment-related serious adverse events, no drug discontinuations and no dose reductions. Boys treated with edasalonexent grew an average of 2.1 inches taller per year and gained 2.9 pounds per year, and their overall body mass index decreased from 70th percentile of unaffected boys to the 55th percentile over 72 weeks of treatment, approaching the average body mass index for unaffected boys.

Additionally, boys with DMD in the age range enrolled in the trial typically have resting tachycardia, a heart rate that exceeds the normal resting rate, and we observed that the heart rate of the boys treated with edasalonexent significantly decreased toward age-normative values over a year and a half period of edasalonexent treatment.

In the MoveDMD trial, two boys received edasalonexent and eteplirsen for an average of 1 year. The combination was well tolerated with no safety signals. Edasalonexent has previously been shown to increase dystrophin expression in combination with exon-skipping therapy in mdx mice, supporting the potential of edasalonexent to enhance dystrophin-targeted therapies such as eteplirsen and other therapies in development.

Edasalonexent Research Collaborations

In November 2018, we announced a collaboration with University of Texas Southwestern, or UT Southwestern, to explore the potential of edasalonexent to improve cardiac function in DMD and Becker muscular dystrophy, or BMD. This is a one-year preclinical collaboration with Pradeep Mammen, MD, FACC, FAHA, founder and Medical Director of the Neuromuscular Cardiomyopathy Clinic at UT Southwestern Medical Center as well as Co-Director of the National Institute of Health Sponsored UT Southwestern Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Center. Cardiomyopathy is the leading cause of mortality in DMD and BMD. Preclinical and clinical data support the potential for cardiac benefits with edasalonexent in DMD and BMD.

In September 2016, we announced a pre-clinical joint research collaboration with Sarepta to explore a combination drug treatment approach for DMD. In the collaboration, increased dystrophin protein expression was seen with an exon-skip modality in combination with edasalonexent in a mouse model of DMD.

Edasalonexent Orphan Drug, Fast Track and Rare Pediatric Disease Designations

The FDA has granted edasalonexent orphan drug, fast track and rare pediatric disease designations for the treatment of DMD. A product may be designated by the FDA as an "orphan drug" if it is intended to treat a rare disease or condition affecting fewer than 200,000 individuals in the United States. If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the FDA will not approve another sponsor's marketing application for the same product for the same use or indication before the expiration of seven years, except in certain limited circumstances. The FDA fast track process is designed to expedite the

Table of Contents

development and review of drugs to treat serious or life-threatening conditions and demonstrate the potential to address unmet medical needs. Companies that receive fast track designation are allowed to submit NDAs on a rolling basis, expediting the FDA review process, and benefit from more frequent communication with the FDA to discuss all aspects of clinical development. In addition, drugs that receive fast track designation are eligible for accelerated approval and priority review if certain criteria are met. The FDA's rare pediatric disease designation gives us the potential to receive a priority review voucher if edasalonexent is approved. However, the rare pediatric disease program is set to expire in September 2020.

The EC has granted orphan medicinal product designation to edasalonexent for the treatment of DMD. Similar to the FDA orphan drug designation, the EC may designate a product as an orphan medicinal product if it is intended for the treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons. In Europe, marketing authorization for an orphan medicinal product generally leads to up to a ten-year period of market exclusivity if the product candidate is granted marketing authorization in the EU.

Edasalonexent Expansion Indication Opportunities

In addition to our work in DMD, we are evaluating other diseases where the inhibition of NF-κB may be beneficial for further therapeutic applications of edasalonexent. There are a number of other rare diseases where NF-κB is believed to play an important role, such as BMD, which is a type of muscular dystrophy and is characterized by slowly progressive muscle weakness of the legs and pelvis.

CAT-5571

CAT-5571 is a conjugate that contains cysteamine, a naturally occurring molecule that is a degradation product of the amino acid cysteine, and DHA, based on our proprietary Safely Metabolized And Rationally Targeted linker, or SMART Linker, drug discovery platform. We are developing CAT-5571 as a potential oral treatment for CF. CAT-5571 is a small molecule that is designed to activate autophagy, a mechanism for recycling cellular components and digesting pathogens, which is important for host defenses and is depressed in CF. We have completed IND application-enabling activities for CAT-5571. We intend to further develop our CAT-5571 program through selective collaborations with leading biotechnology and pharmaceutical companies.

Cystic Fibrosis

CF is a rare, chronic, genetic, life-shortening orphan disease that affects over 70,000 patients worldwide, predominantly in the Caucasian population. In CF, a malfunctioning cystic fibrosis transmembrane conductance regulator ion channel impairs chloride secretion, with deleterious effects on multiple organs, and particularly devastating effects on pulmonary, intestinal and pancreatic function. Patients affected with CF are also predisposed to respiratory failure caused by persistent lung infections, notably bacteria and most commonly *P. aeruginosa,* that are difficult to treat with standard antibiotics. CF patients have frequent pulmonary exacerbations due to their inability to clear the persistent lung infections. Advancement in research and treatments have extended the life expectancy for those living with CF, however, there is currently no cure.

Sales and Marketing

Given our stage of development, we have not yet established a commercial organization or distribution capabilities, nor have we entered into any collaboration or co-promotion arrangements. If we are able to progress our edasalonexent program, we intend to commercialize edasalonexent in North America ourselves and commercialize edasalonexent outside of North America either ourselves or with a collaborator.

Table of Contents

Manufacturing and Supply

Our product candidates are small molecule compounds manufactured from component raw materials. The omega-3 fatty acid materials that we use as bioactives are purified from natural sources by established pharmaceutical fine chemicals manufacturers. The other bioactive and linker raw materials that we use are also readily available from established pharmaceutical intermediate manufacturers. The components are conjugated to form the SMART Linker product candidate using well understood, conventional chemistries.

We currently have no manufacturing facilities and limited personnel with manufacturing experience. We rely on contract manufacturers to produce both drug substance and drug product required for our clinical trials. We plan to continue to rely upon contract manufacturers and, potentially, collaborators to manufacture commercial quantities of our products, if approved.

Competition

The development and commercialization of new drugs is highly competitive. If we successfully develop and commercialize any of our product candidates, we and any future collaborators will face competition from pharmaceutical and biotechnology companies worldwide. Many of the entities developing and marketing potentially competing products have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing. Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop.

The key competitive factors affecting the success of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

Edasalonexent for Duchenne Muscular Dystrophy

There are currently only two therapies approved in the United States for the treatment of DMD. Sarepta's drug EXONDYS 51 was approved by the FDA for the treatment of DMD under the accelerated approval pathway in September 2016 for patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. In addition, in February 2017, the FDA granted approval of PTC Therapeutics' drug EMFLAZA, for the treatment of DMD in patients five years and older. PTC Therapeutics has subsequently submitted an sNDA to expand the EMFLAZA label to include two-to-five year old DMD patients in the United States and has stated that it expects a response from the FDA in 2019. Outside of the United States, PTC Therapeutics' drug ataluren, also known as Translarna, has been conditionally approved within the EU Member States, Iceland, Liechtenstein, Norway, Israel and South Korea for the treatment of nmDMD in ambulatory patients aged two years and older. PTC Therapeutics is also currently running confirmatory Phase 2/3 clinical trials with ataluren in nmDMD in the United States and has stated that it plans to re-submit an NDA to FDA pending the outcomes of these trials. Although not previously approved for the treatment of DMD, corticosteroid therapy, including prednisone, is considered standard of care and is often prescribed to treat the inflammation underlying DMD and to delay loss of ambulation.

A number of companies are developing therapies to treat DMD in patients with specific mutations in the dystrophin gene. In addition to EXONDYS 51, Sarepta has two additional exon-skipping therapies for DMD in Phase 3 clinical development. These agents, golodirsen (SRP-4053) and casimersen (SRP-4045), target skipping of exons 53 and 45, respectively. Sarepta has submitted a rolling NDA to the FDA for golodirsen with an August 19, 2019 PDUFA date. Daiichi-Sankyo is developing an exon-skipping product candidate for DMD patients with out-of-frame deletion mutations amenable

Table of Contents

to exon 45 skipping and announced in February 2016 that it began its first Phase 1/2 clinical trial for its product candidate, DS-5141b, in Japan. NS Pharma has a compound, NS-065/NCNP-01, in Phase 2 clinical development in the United States and Japan for patients with mutations amenable to exon 53 skipping. NS-065/NCNP-01 received orphan drug designation in the United States and was granted Fast Track designation by the FDA. Based on the prevalence of the specific mutations that these product candidates being developed by Sarepta, Daiichi-Sankyo and NS-Pharma are designed to address, they would be expected to have the potential to be effective in an aggregate of approximately 16% of DMD patients. In addition, Wave Life Sciences Ltd., or Wave, initiated a Phase 1 clinical trial in DMD in November 2017 for its exon 51 skipping candidate, suvodirsen (WVE-210201). Wave has stated that it plans to initiate a Phase 2/3 clinical trial in DMD with suvodirsen in 2019.

In addition to exon-skipping therapies, other companies have alternative therapeutic approaches to the treatment of DMD in late stage clinical development. Other alternative therapeutic approaches in later stage clinical trials include Italfarmaco S.p.A.'s Phase 3 trial in ambulant DMD boys for givinostat, a histone deacetylase inhibitor. F. Hoffman-La Roche Ltd., or Roche, has a myostatin inhibitor in a Phase 2/3 clinical trial for DMD. Additionally, ReveraGen is testing vamololone, a putative dissociative steroid, in a Phase 2b clinical trial. Mallinckrodt is also running a large Phase 2 trial in DMD boys aged four to eight years old for cosyntropin, or MNK-1411, and Santhera has announced that it plans to re-submit marketing authorization applications for idebenone for the treatment of DMD in patients with respiratory function decline and not taking concomitant glucocorticoids to EMA and the FDA in 2019. A number of companies also have products candidates in earlier clinical development for DMD, including Akashi Therapeutics, Astellas, Capricor Therapeutics, Cardero Therapeutics, EspeRare, Fibrogen, Phrixus Pharmaceuticals, and Taiho Pharmaceuticals. If successfully developed, some of these alternative therapeutic approaches may be applicable to all DMD patients regardless of underlying mutation status. Additionally, several gene therapy programs targeting the dystrophin gene have entered clinical development, including Solid Biosciences SGT-001, Pfizer's PF-06939926, and Sarepta's GALGT2 and micro-dystrophin programs being conducted in collaboration with Nationwide Children's Hospital.

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business, including pursuing and maintaining patent protection intended to cover the composition of matter of our product candidates, their methods of use, related technologies and other inventions that are important to our business. In addition to patent protection, we also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection, including certain aspects of our SMART Linker drug discovery platform.

Our commercial success depends in part upon our ability to obtain and maintain patent and other proprietary protection for commercially important technologies, inventions and know-how related to our business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable intellectual property rights of others.

The patent positions for biotechnology and pharmaceutical companies like us are generally uncertain and can involve complex legal, scientific and factual issues. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our product candidates will be protected or remain protectable by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

As of December 31, 2018, our patent estate included over 10 issued U.S. patents, over 70 issued foreign patents, over three pending U.S. patent applications, four pending international patent applications, and 17 pending foreign patent applications.

Table of Contents

With regard to edasalonexent, we have six issued U.S. patents with composition of matter and method of use claims covering edasalonexent and its use. The issued U.S. patents are expected to expire in 2029, without taking a potential patent term extension into account. In addition, we have patents that have been granted in various countries and regions including Australia, Canada, China, Europe, India, Israel, Japan, Korea, Mexico and New Zealand, which are expected to expire in 2029, without taking potential patent term extensions into account, and at least five pending patent applications in various other countries in North and South America, which, if issued, are expected to expire in 2029, without taking potential patent term extensions into account.

With regard to CAT-5571, we have four issued U.S. patents with composition of matter and method of use claims covering CAT-5571 and its use, which are scheduled to expire in 2030, without taking potential patent term extensions into account. We also have 10 patent applications pending in the United States and in other regions including North America, South America, Europe, Asia and Australia, with claims covering CAT-5571 and related compounds and their use, including their use in the treatment of cystic fibrosis.

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

In the United States, the term of a patent covering an FDA-approved drug may be eligible for a patent term extension under the Hatch-Waxman Act as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years beyond the expiration of the patent but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering edasalonexent and CAT-5571, may be entitled to patent term extensions. If our product candidates receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved product candidates. We also intend to seek patent term extensions in any jurisdictions where they are available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we also rely on trade secret protection for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection, including, for example, certain aspects of our manufacturing processes and conjugate selection methodologies. However, trade secrets can be difficult to protect. Although we take steps to protect our proprietary information, including restricting access to our premises and our confidential information, as well as entering into agreements with our employees, consultants, advisors and potential collaborators, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the EU, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, sales, reimbursement, distribution, pricing, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along

Table of Contents

with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities, including state agencies.

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

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of an NDA;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information,

Table of Contents

analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as chronic toxicity and carcinogenicity assessments, may continue after the IND is submitted.

Companies usually must complete some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity and must also develop additional information about the chemistry and physical characteristics of the investigational product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the candidate product and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted, to demonstrate that the candidate product does not undergo unacceptable deterioration over its shelf life.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a partial or full clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with FDA certain regulatory requirements in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with GCP, including review and approval by an

Table of Contents

independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board, or DSMB, or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on its ClinicalTrials.gov website.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or treatment IND application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act, or FDARA, later amended) a requirement that drug and biologic companies that sponsor one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. Sponsors are required to make such policies publicly available upon the earlier of

Table of Contents

initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018 the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

Phase 1. The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

Phase 2. The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Phase 4. Post-approval studies, which are conducted following initial approval, are typically conducted to gain additional experience and data from treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has

Table of Contents

been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency 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.

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

FDARA established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2019 is $2,588,478 for an application requiring clinical data. The sponsor of an approved NDA is

Table of Contents

also subject to an annual program fee, which for fiscal year 2019 is $309,915. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed