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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 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, 2019

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.)
100 High Street Floor 28 Boston, Massachusetts	**02110**
(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	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.001 par value per share	**CATB**	**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 ☒ 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 ☒ No

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

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 ☒	Smaller reporting company ☒ Emerging growth company ☒

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

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

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 28, 2019, the last trading day before June 30, 2019: $73,359,556

As of March 2, 2020, there were 17,897,172 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 2020 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.

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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 fourth quarter of 2020, the goal of filing of a New Drug Application in 2021, 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 expectations regarding our ability to successfully conduct the GalaxyDMD open-label extension trial, including the anticipated announcement of data from this trial;
- our plans to evaluate edasalonexent in a Phase 2 clinical trial in non-ambulatory patients with supportive funding from Duchenne UK;
- our plans to explore the potential of edasalonexent as a therapy in indications other than DMD;
- our plans to identify, develop and commercialize novel therapeutics based on our Safety Metabolized and Rationally Targeted linker, or SMART Linker™, drug discovery platform;
- other 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 the anticipated announcement of 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, including the likelihood of support for edasalonexent, if approved, by physicians, patient advocates and patients, and the likelihood of coverage and reimbursement by third-party payers;
- 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 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.

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, an oral small molecule that inhibits NF-kB, 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 a randomized, double-blind, placebo-controlled trial, and is designed to evaluate the efficacy and safety of edasalonexent for registration purposes. 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. We announced in September 2019 that the Phase 3 PolarisDMD trial completed enrollment and exceeded our target enrollment of 125 boys. We enrolled 131 boys between the ages of four and seven, up to their eighth birthday, regardless of mutation type, who had not been on steroids for at least six months. We expect to report top-line results from the Phase 3 PolarisDMD trial in the fourth quarter of 2020. Our goal is to submit a New Drug Application, or NDA, for edasalonexent for the treatment of DMD in 2021.

Our previous trial, the MoveDMD Phase 1/2 trial, enrolled ambulatory boys four to seven years old, up to their eighth birthday, with DMD who had not used steroids for at least six months prior to the trial. The MoveDMD trial was conducted in three sequential parts, Phase 1, Phase 2, and an open-label extension. 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. In the open-label extension of the 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 with improvement through 72 weeks on 100 mg/kg of edasalonexent treatment compared to the off-treatment control period. We also 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, through 72 weeks of edasalonexent treatment 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 consistency and durability of edasalonexent treatment effects. Edasalonexent continued to be well tolerated with no safety signals observed in the MoveDMD trial. We also observed that the heart rate of the boys significantly decreased toward age-normative values with over a year and a half period of edasalonexent treatment.

We initiated an open-label extension trial in March 2019, which we refer to as the GalaxyDMD trial. The remaining boys that were participating in the MoveDMD trial open-label extension transitioned to the GalaxyDMD trial and their eligible siblings were also able to enroll. In addition, when boys complete the 12-month Phase 3 PolarisDMD trial, they are given the option to receive open-label edasalonexent in the GalaxyDMD trial. The GalaxyDMD trial is designed to provide longer term safety data to support registration filings.

In addition, we are exploring the potential of edasalonexent as a therapy in other indications where the inhibition of NF-kB may provide clinical benefit. In August 2019, we entered into a preclinical research collaboration with the Jain Foundation to study edasalonexent in dysferlinopathy, which includes limb-girdle muscular dystrophy type 2B and Miyoshi myopathy, a serious rare disease that causes progressive muscle weakness for which there is currently no approved treatment option. In dysferlinopathy, muscles lack dysferlin and as a result NF-kB is chronically activated. Under our collaboration, we and the Jain Foundation are conducting a preclinical study to evaluate the potential of edasalonexent as a therapeutic intervention for dysferlinopathy by measuring disease progression in dysferlin-deficient mice treated with edasalonexent. Initial results are expected in the first half of 2020.

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, 2019, we owned 6 issued U.S. patents with composition of matter and method of use claims directed to edasalonexent. These patents are expected to expire in 2029 without taking into account potential patent term extensions. We also owned 5 issued U.S. patents with composition of matter and method of use claims directed to CAT-5571. These patents are expected to expire between 2030 and 2035, without taking into account potential patent term extensions. In addition, our patent portfolio includes over 70 issued foreign patents, 3 pending U.S. patent applications, 4 pending International (PCT) patent applications, and 17 pending foreign patent applications.

Our Product Candidates

Edasalonexent

We designed edasalonexent to inhibit NF-kB. In DMD the loss of dystrophin leads to chronic activation of NF-kB, which is a key driver of skeletal and cardiac muscle disease progression. We have reported results from Phase 1, Phase 2 and the 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-kB pathway, triggering inflammation in the muscles, initiating muscle degeneration, and reducing 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 Europe.

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-kB in Duchenne Muscular Dystrophy

NF-kB 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-kB is a key driver of skeletal muscle and cardiac disease progression in DMD. Activated NF-kB 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-a, interleukin 6, or IL-6, and interleukin-1 beta, or IL-1b; chemokines; cell adhesion molecules; and tissue degrading enzymes, such as matrix metallopeptidase 9, or MMP-9. In addition, activated NF-kB 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-kB is observed in muscle tissues of patients with DMD prior to the onset of other clinical manifestations and activated NF-kB is persistently elevated in the immune cells and regenerative muscle fibers of patients with DMD. Moreover, evidence exists that mechanical stress activates NF-kB in muscles and increases levels of activated NF-kB 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 three therapies approved for the treatment of DMD in the United States: EXONDYS 51®, an exon skipping therapy targeting the skipping of exon 51; VYONDYS 53, an exon skipping agent targeting the skipping of exon 53; and EMFLAZA®, a corticosteroid that is indicated for the treatment of DMD in patients two years of age and older. EXONDYS 51 and VYONDYS 53 have been granted accelerated approval and are marketed by Sarepta Therapeutics, or Sarepta. Based on the prevalence of the specific mutations that are amenable to EXONDYS 51 and VYONDYS 53 treatment, they are expected to be appropriate in an aggregate of approximately 21% of DMD patients. EMFLAZA is marketed by PTC Therapeutics. Corticosteroid therapy, including treatment with prednisone, is often prescribed to treat DMD. Corticosteroids primarily act through the glucocorticoid receptor-mediated pathway and they can cause significant complications including growth suppression, excessive weight gain, behavioral changes, reduction in bone strength, compromise of the immune system and have been shown to induce muscle myopathy in other diseases. DMD patients treated with corticosteroids typically show an initial improvement in measures of muscle function but then resume a progressive decline. DMD patients typically only live until their mid-twenties.

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 has initiated a rolling NDA submission for casimersen, its exon 45 skipping agent. NS Pharma

has completed a rolling NDA submission for its exon 53 skipping agent, viltolarsen, and the Prescription Drug User Fee Action date, or PDUFA date, for viltolarsen is in the third quarter of 2020. PTC Therapeutics' TRANSLARNA™ 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, and is approved for the treatment of nmDMD in ambulatory patients aged five years and older in Brazil. PTC Therapeutics is conducting additional clinical trials with TRANSLARNA in nmDMD in the United States.

EXONDYS 51, VYONDYS 53, TRANSLARNA, viltolarsen and casimersen 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 agents is to reduce disease severity and extend survival in those DMD patients who are candidates for therapy with these agents. 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.

In September 2019, we appointed Andrew A. Komjathy as our Chief Commercial Officer in preparation for the potential commercial launch of edasalonexent. As part of our commercialization preparations, we conducted market research, which has indicated high unmet need for therapies to treat DMD. If edasalonexent is approved for the treatment of DMD, we believe, based on market research and our internal assessment, that there is a high likelihood of support for edasalonexent by physicians, patient advocates and patients and support for coverage and reimbursement by third-party payers in the United States, Europe and other markets.

Edasalonexent for the Treatment of Duchenne Muscular Dystrophy

Based on the ability of edasalonexent to inhibit NF-kB 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 United States ourselves and commercialize edasalonexent outside of United States either ourselves or with a partner.

Edasalonexent Clinical Development

Phase 3 PolarisDMD 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 fourth quarter of 2020. Our goal is to submit an NDA for edasalonexent for the treatment of DMD in 2021.

We announced in September 2019 that the Phase 3 PolarisDMD trial completed enrollment and exceeded our target enrollment of 125 boys. We enrolled 131 boys between the ages of four to seven, up to their eighth birthday, regardless of mutation type, who had not been on steroids for at least six months, across all eight countries where the clinical trial is active. Boys on a stable dose of EXONDYS 51 were eligible to enroll. Enrolled boys were randomized in a 2 to 1 ratio with two boys receiving 100 mg/kg/day of edasalonexent for each boy that receives placebo. Following the completion of enrollment, we conducted an analysis of the baseline age and timed function test performance of the patients enrolled in the Phase 3 PolarisDMD trial as compared to the patients enrolled in the Phase 2 MoveDMD trial and found no significant difference in these baseline characteristics of the patient

populations in the two trials, which we believe supports the assumptions we used for powering the Phase 3 PolarisDMD trial.

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 in the trial. 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.

GalaxyDMD Open-Label Extension Trial of Edasalonexent in Patients with DMD

We initiated an open-label extension trial in March 2019, which we refer to as the GalaxyDMD trial. The remaining boys that were participating in the MoveDMD trial open-label extension transitioned to the GalaxyDMD trial and their eligible siblings were also able to enroll. In addition, when boys complete the 12-month Phase 3 PolarisDMD trial, they are given the option to receive open-label edasalonexent in the GalaxyDMD trial and their eligible siblings are also able to enroll. Boys in the GalaxyDMD trial that are amenable are able to initiate co-administration of approved exon skipping therapies. The GalaxyDMD trial is designed to provide longer term safety data to support registration filings.

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, up to their eighth birthday, 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 has been completed and was conducted in three sequential parts, Phase 1 and Phase 2, and an open-label extension. 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.

In the 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. In the 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 statistically significant improvement in the rate of change in lower leg composite MRI T2 through 12, 24, 36 and 48 weeks with improvement through 72 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.

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 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-kB can decrease inflammation.

Edasalonexent was well tolerated in the MoveDMD trial with no clinical safety signals observed to date through more than 60 years of cumulative patient exposure. 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 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. 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 the mdx mouse model of DMD, supporting the potential of edasalonexent to enhance dystrophin-targeted therapies such as EXONDYS 51, VYONDYS 53 and other therapies in development.

Planned Clinical Trials

While our clinical trials to date have focused on younger ambulatory patients, we believe edasalonexent has the potential to be a foundational therapy for all DMD patients. In January 2020, we announced a partnership with Duchenne UK, a charity that seeks to fund and accelerate treatments and a cure for DMD, to evaluate edasalonexent in a Phase 2 clinical trial in non-ambulatory DMD patients. Duchenne UK granted us more than $600,000 in funding to support patient and clinical trial site costs. This planned Phase 2 clinical trial is designed to assess safety and pharmacokinetics of edasalonexent, with exploratory measures of function, including cardiac, skeletal muscle and pulmonary function, in non-ambulatory DMD patients. The older, non-ambulatory patients represent a significant potential market for edasalonexent, with approximately 60% of all DMD patients being 12 years of age and older.

Recent Edasalonexent Research Collaboration

In August 2019, we entered into a preclinical research collaboration with the Jain Foundation, a non-profit foundation whose mission is to cure muscular dystrophies caused by dysferlin protein

deficiency, to study the potential effects of edasalonexent in dysferlinopathy, which includes limb-girdle muscular dystrophy type 2B and Miyoshi myopathy. Dysferlinopathy is a serious rare disease that causes progressive muscle weakness for which there is currently no approved treatment option. In dysferlinopathy, muscles lack dysferlin, which is important for skeletal muscle repair, and as a result NF-kB is chronically activated. Edasalonexent, an oral small molecule designed to inhibit NF-kB, has the potential to slow disease progression in dysferlin-deficient populations. Under our collaboration, we and the Jain Foundation are conducting a preclinical study to evaluate the potential of edasalonexent as a therapeutic intervention for dysferlinopathy by measuring disease progression in dysferlin-deficient mice treated with edasalonexent. Initial results are expected in the first half of 2020.

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 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. A sponsor who receives FDA approval for a drug or biologic for a rare pediatric disease may qualify for a priority review voucher, which the sponsor may also redeem to receive priority review of a subsequent marketing application for a different product. In lieu of using the voucher for one of its own product candidates, a sponsor may also sell that voucher for use by a third party. Current prices for these vouchers are in the range of a hundred million dollars. The current rare pediatric disease priority review voucher program will expire in October 2020, unless Congress renews the program, although a drug designated as a rare pediatric disease treatment can still receive a priority review voucher if the marketing approval application for the drug is submitted and the drug is approved by October 2022.

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-kB may be beneficial for further therapeutic applications of edasalonexent. There are a number of other rare diseases where NF-kB is believed to play an important role, such as dysferlinopathy and also Becker muscular dystrophy, or BMD, which is a type of muscular dystrophy and is characterized by slowly progressive muscle weakness of the legs and pelvis.

CAT-5571

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.

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

While we have hired a Chief Commercial Officer and begun initial planning for a potential commercial launch, given our stage of development, we have not yet hired a sales team or otherwise begun to establish a commercialization infrastructure 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 the United States ourselves and commercialize edasalonexent outside of the United States either ourselves or with a partner.

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 three therapies approved in the United States for the treatment of DMD: Sarepta's drug EXONDYS 51 for patients amenable to exon 51 skipping, VYONDYS 53, also from Sarepta, for patients amenable to exon 53 skipping, and PTC Therapeutics' drug EMFLAZA, for the treatment of DMD. Outside of the United States, PTC Therapeutics' drug 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. TRANSLARNA was granted marketing approval from the Brazilian National Health Surveillance Agency (ANVISA) under rare diseases procedure, for the treatment of ambulatory children age five years and older with nmDMD. PTC Therapeutics is also currently running confirmatory Phase $^{2}/_{3}$ clinical trials with TRANSLARNA in nmDMD in the United States and has stated that it plans to re-submit an NDA pending the outcomes of these trials. Although not previously approved for the treatment of DMD, corticosteroid therapy, including prednisone, is often prescribed to treat DMD.

A number of companies are developing therapies to treat DMD in patients with specific mutations in the dystrophin gene. In addition to EXONDYS 51 and VYONDYS 53, Sarepta has initiated a rolling NDA for casimersen (SRP-4045), an agent which targets skipping of exon 45. Approximately 8% of DMD patients are believed to have mutations amenable to exon 45 skipping. NS Pharma completed a rolling NDA submission in October 2019 for its exon 53 agent, viltolarsen and the PDUFA date is in the third quarter of 2020. An additional 8% of DMD patients are believed to be eligible for therapy with an agent that targets skipping of exon 53. Sarepta has in Phase 2 clinical development another agent that targets skipping of exon 51. This agent, SRP-5051, uses a different RNA chemistry than EXONDYS 51. Daiichi-Sankyo is developing an exon-skipping product candidate for DMD patients with out-of-frame deletion mutations amenable 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. In addition to exon-skipping therapies, other companies have alternative therapeutic approaches to the treatment of DMD in late stage clinical development. Sarepta, Pfizer and Solid BioSciences each have microdystrophin gene therapy programs in Phase 2 clinical development. Sarepta's SRP-9001 and Pfizer's PF-06939926 are expected to initiate Phase 3 clinical trials in mid-2020. Solid's program, SGT-001, is currently on clinical hold by the FDA due to a serious adverse event and the timeline for when and if this program can resume dosing in patients is not known. Sarepta's GALGT2 gene therapy program is being conducted in collaboration with Nationwide Children's Hospital and is in Phase 1/2a clinical development. Each of these programs is designed to be used in DMD patients without antibodies against adeno-associated virus, or AAV, regardless of the underlying mutation in the dystrophin gene.

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. ReveraGen is testing vamorolone, a dissociative steroid, in a Phase 2b clinical trial. Santhera has re-submitted its marketing authorization application for idebenone, also known as PULDYSA, for the treatment of DMD in patients with respiratory function decline and not taking concomitant glucocorticoids to EMA and a decision from the Committee for Medicinal Products for Human Use (CHMP) is expected in mid-2020. Santhera has announced it plans to re-submit an NDA for idebenone pending positive results from the SIDEROS Phase 3 clinical trial. A number of companies also have products candidates in earlier clinical development for DMD including Astellas, Biophytis, Capricor Therapeutics, Cumberland Pharmaceuticals, 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.

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 ours 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, 2019, our patent estate included over 10 issued U.S. patents, over 70 issued foreign patents, 3 pending U.S. patent applications, 4 pending international (PCT) patent applications, and 17 pending foreign patent applications.

With regard to edasalonexent, we have 6 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 5 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 5 issued U.S. patents with composition of matter and method of use claims covering CAT-5571 and its use, which are scheduled to expire between 2030 and 2035, 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 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, 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 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. Similar

requirements for posting clinical trial information are present in the EU (EudraCT) website: https://eudract.ema.europa.eu/ and other countries, as well.

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 sponsors of 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. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of 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 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 applications is subject to an application user fee, which for federal fiscal year 2020 is $2,942,965 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2020 is $325,424. 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 to certain performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required

specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites involved with the conduct of the Phase 3 clinical trials to assure compliance with GCP. If compliance or data integrity is called into question due to inspection finding, this may cause a delay or affect the likelihood of drug approval. Under the FDARA, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may 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 FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

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

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with

respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Finally, with passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. There is limited experience with accelerated approvals by the FDA based on intermediate clinical endpoints. However, the FDA has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long, and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated

approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA may issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA, and other foreign regulatory agencies, have substantial discretion in the approval process.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

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

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with

cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

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

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drug samples at the

federal level and set minimum standards for the regulation of distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Section 505(b)(2) NDAs

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

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

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

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

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

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

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of "competitor generic therapies" or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

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

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

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

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

product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval).

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

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

Pediatric Studies and Exclusivity

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

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting an NDA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different conditions. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Rare Pediatric Disease Priority Review Voucher Program

With enactment of the FDASIA in 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications that meet the criteria specified in the law. This provision is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application.

For the purposes of this program, a "rare pediatric disease" is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare disease or conditions within the meaning of the Orphan Drug Act. A sponsor may choose to request rare pediatric disease designation, but the designation process is entirely voluntary; requesting designation is not a prerequisite to requesting or receiving a priority review voucher. In addition, sponsors who choose not to submit a rare pediatric disease designation request may nonetheless receive a priority review voucher if they request such a voucher in their original marketing application and meet all of the eligibility criteria. Under the Cures Act, the Rare Pediatric Disease Priority Review Voucher program was reauthorized until 2020. However, if a drug is designated before October 1, 2020, it is eligible to receive a voucher if approved before October 2022. In July 2019, FDA updated and issued draft guidance which clarifies the process for requesting designations and vouchers under this program.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality,

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

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on Good Clinical Practice, or GCP, and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the EU. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. The new Clinical Trials Regulation has not yet become effective. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC and replacing any national legislation that was put in place to implement the Directive. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which on-going clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single-entry point, the "EU Portal and Database"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Concerned Member States). Part II is assessed separately by each Concerned Member State. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Concerned Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

As of January 1, 2020, the website of the European Commission reported that the implementation of the new Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020.

As in the United States, similar requirements for posting clinical trial information are present in the EU website: https://eudract.ema.europa.eu/ and other countries. Similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries, as well.

PRIME Designation in the European Union

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products (CHMP) or Committee for Advanced Therapies (CAT) are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Procedures Governing Approval of Drug Products in the European Union

To obtain marketing approval of a product under EU regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the EC that is valid for all EU member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various EU member states where such product has not received marketing approval in any EU member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned

member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

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

Data and Market Exclusivity in the European Union

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

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

Periods of Authorization and Renewals

Marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the EC or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the EU market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Orphan Drug Designation and Exclusivity

Regulation 141/2000 provides that a drug shall be designated as an orphan drug if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Community when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Community and that without incentives it is unlikely that the marketing of the drug in the European Community would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Community or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Regulation 847/2000 sets out criteria and procedures governing designation of orphan drugs in the EU. Specifically, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of "clinically relevant superiority" by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs pursuant to Regulation 141/2000 shall be eligible for incentives made available by the European Community and by the member states to support research into, and the development and availability of, orphan drugs.

Pricing Decisions for Approved Products

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the United Kingdom will not accept high regulatory alignment with the European Union.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the European Union General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged for medical products and services and imposing

controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

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

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

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies. For example, the EU provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

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

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

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created federal criminal laws that prohibit, among other things, knowingly and willingly executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

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

- Foreign Corrupt Practices Act which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

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

- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and

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

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

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

In March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. The Affordable Care Act:

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;

- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

- expanded the types of entities eligible for the 340B drug discount program; and

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

These healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress may consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, Centers for Medicare & Medicaid Services has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. This decision is under review by the U.S. Supreme Court during its current term. The full effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

In addition, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. On December 18, 2019, that court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services, or HHS, will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers;

avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants would be required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Employees

As of December 31, 2019, we had 27 employees, 16 of whom were primarily engaged in research and development activities. A total of 8 employees have Ph.D. degrees. None of our employees is represented by a labor union and we believe our relations with our employees are good.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on June 26, 2008 under the name Catabasis Pharmaceuticals, Inc. Our executive offices are located at 100 High Street, Floor 28, Boston, Massachusetts, 02110, and our telephone number is (617) 349-1971. Our website address is www.catabasis.com. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge on our website located at www.catabasis.com as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission, or the SEC. These reports are also available at the SEC's Internet website at www.sec.gov.

A copy of our Corporate Governance Guidelines, Code of Business Conduct and Ethics and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are posted on our website, www.catabasis.com, under "Corporate Governance".

Item 1A. Risk Factors

We operate in a dynamic and rapidly changing business environment that involves risks and substantial uncertainty. The following discussion addresses risks and uncertainties that could cause, or contribute to causing, actual results to differ from expectations in material ways. In evaluating our business, investors should pay particular attention to the risks and uncertainties described below and in other sections of this Annual Report on Form 10-K and in our subsequent filings with the Securities and Exchange Commission, or SEC. These risks and uncertainties, or other events that we do not currently anticipate or that we currently deem immaterial also may affect our results of operations, cash flows and financial condition. The trading price of our common stock could also decline due to any of these risks, and you could lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

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

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We initiated our Phase 3 PolarisDMD clinical trial of edasalonexent in the third quarter of 2018 and our open-label extension trial GalaxyDMD in March 2019 and expect that our expenses will increase substantially as we conduct these trials. In addition, we may in the future initiate new research, preclinical and clinical development efforts for and seek marketing approval for, other product candidates, and would expect our expenses to increase in connection with each of these activities. If we obtain marketing approval for any of our product candidates, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a future collaborator, and these activities would require substantial additional funding. Furthermore, we have incurred and will continue to incur significant additional costs associated with operating as a public company.

Accordingly, we will need to obtain additional funding in connection with our continuing operations and for costs related to filing a New Drug Application, or NDA, seeking regulatory approvals and commercialization activities for edasalonexent in Duchenne muscular dystrophy, or DMD, and for any of our other product candidates that have successful clinical trials. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our research and development programs or any future efforts to commercialize edasalonexent, our lead product candidate. Any additional funding may not be available to us on acceptable terms, on a timely basis or at all. In the event that we are unable to obtain such funding on acceptable terms and in a timely manner, we may not be able to complete the regulatory approval or commercialization of edasalonexent or the clinical development, regulatory approval or commercialization of any other product candidate.

In addition, while we may seek one or more collaborators for future development of our product candidates or programs or for our platform technology, we may not be able to enter into a collaboration for any of our product candidates or programs or for our platform technology on suitable terms or at all. In any event, our existing cash, cash equivalents and short-term investments will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates. Accordingly, we will be required to obtain substantial additional funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds.

Adequate additional funding may not be available to us on acceptable terms, on a timely basis or at all, impacting our ability to execute on our strategic plans. Our failure to raise capital on acceptable

terms as and when needed would have a material adverse effect on our business, results of operations, financial condition and ability to pursue our business strategy.

We believe that our existing cash, cash equivalents and short-term investments as of December 31, 2019, together with the additional $25.6 million that we have raised to date in 2020 in net proceeds from equity financings will enable us to fund our operating expenses and capital expenditure requirements based on our current operating plan into the third quarter of 2021. Our estimate as to how long we expect our cash, cash equivalents and short-term investments securities to be able to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including:

- any unanticipated costs or expenses related to our Phase 3 PolarisDMD and GalaxyDMD trials, including costs and expenses for any additional research or preclinical or clinical development efforts related to this trial;
- the progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, our product candidates and potential product candidates, including current and future clinical trials;
- our ability to enter into and the terms and timing of any additional collaborations, licensing or other arrangements that we may establish;
- the number and characteristics of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of our product candidates;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the costs of operating as a public company.

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

Significant additional capital will be needed in the future to continue our planned operations. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, our existing stockholders' ownership interest may be substantially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. For example, our June 2018 and February 2019 registered offerings of common stock and common stock warrants and our January 2020 registered offering of common stock were highly dilutive to existing stockholders' ownership interests. Further, exercise of the common stock warrants sold in in our June 2018 and February 2019 offerings

could result in additional dilution upon exercise. Additional debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing additional financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

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

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

Any future indebtedness that we may incur, combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

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

Failure to make payments or comply with other covenants under any debt instruments could result in an event of default and acceleration of amounts due.

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

We have incurred significant annual net operating losses in every year since our inception. We expect to continue to incur significant operating losses for at least the next several years. Our net losses were $26.3 million and $25.9 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $223.6 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations to date primarily through private placements of our preferred stock, registered offerings of our common stock, including our initial public offering, or IPO, our June 2018 and February 2019 registered offerings of common stock and common stock warrants and our January 2020 registered offering of common stock, our at-the-market program, and a secured debt financing, and have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical development programs. Our net losses may fluctuate significantly from quarter

to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We anticipate that our expenses will increase substantially if and to the extent we:

- continue to conduct our Phase 3 PolarisDMD clinical trial and GalaxyDMD open-label extension clinical trial of edasalonexent in DMD;
- initiate our planned Phase 2 clinical trial of edasalonexent in non-ambulatory DMD patients with supportive funding from Duchenne UK;
- initiate and continue research and preclinical and clinical development efforts for edasalonexent and our other product candidates;
- seek to identify and develop additional product candidates;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain marketing approval, if any;
- require the manufacture of larger quantities of product candidates for clinical development and potentially commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel, such as clinical, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development programs.

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

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

We began operations in 2008. Our operations to date have been limited to financing and staffing our company and developing our technology and conducting preclinical research and clinical trials for our product candidates. We have not yet demonstrated an ability to successfully conduct pivotal clinical trials, obtain marketing approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, our investors should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially clinical-stage biopharmaceutical companies such as ours. Predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our third-party research institution collaborators, contract research organizations, contract manufacturing operations, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics such as the novel coronavirus, and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

Our approach to the discovery and development of product candidates has been based on our SMART Linker drug discovery platform, which is unproven, and we do not know whether we will be able to develop any products of commercial value.

We have been focused on discovering and developing novel small molecule drugs by applying our SMART Linker drug discovery platform. We have not yet succeeded and may never succeed in demonstrating efficacy and safety for any of our product candidates in a Phase 3 clinical trial or in obtaining marketing approval thereafter. For example, although we have discovered and evaluated numerous compounds using our SMART Linker drug discovery platform, no product created using the SMART Linker drug discovery platform has ever been approved for sale.

We are dependent on the success of our product candidate edasalonexent. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize this product candidate, either alone or with a collaborator, or if we experience significant delays in doing so, our business would be substantially harmed.

We currently have no products approved for sale and are focusing substantially all of our efforts and financial resources in the development of edasalonexent for the treatment of DMD. Our prospects are substantially dependent on our ability, or that of any future collaborator, to develop, obtain marketing approval for and successfully commercialize edasalonexent. Because our business is almost entirely dependent upon this one product candidate, any setback in obtaining regulatory approval for edasalonexent would have a material adverse effect on our business and prospects.

The success of edasalonexent will depend on several factors, including the following:

- successful completion of our Phase 3 PolarisDMD clinical trial of edasalonexent, as well as any additional clinical trials of edasalonexent, including our ongoing GalaxyDMD open-label extension clinical trial;
- safety, tolerability and efficacy profiles that are satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities;
- the performance of our future collaborators, if any;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials suppliers and manufacturers;
- establishment of arrangements with third-party manufacturers to obtain finished drug products that are appropriately packaged for sale;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protection of our rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors following any marketing approval; and
- our ability to compete with other therapies, including therapies targeting dystrophin, myostatin and inflammatory mediators.

Many of these factors are beyond our control, including the outcome of clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize edasalonexent, on our own or with any future collaborator, or experience delays as a result of any of these or other factors, our business would be substantially harmed.

Our SMART Linker drug discovery platform may fail to help us discover and develop additional potential product candidates.

A significant portion of the research that we have conducted to date and may in the future conduct, involves the development of new compounds using our SMART Linker drug discovery platform. Although, we have suspended efforts to discover additional compounds while we focus our resources on the clinical development of edasalonexent, any drug discovery that we are conducting using our SMART Linker drug discovery platform may not be successful in creating compounds that have commercial value or therapeutic utility. Our SMART Linker drug discovery platform may initially show promise in identifying potential product candidates, yet fail to yield viable product candidates for clinical development or commercialization for a number of reasons, including:

- compounds created through our SMART Linker drug discovery platform may not demonstrate improved efficacy, safety or tolerability;

- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance;
- competitors may develop alternative therapies that render our potential product candidates non-competitive or less attractive; or
- a potential product candidate may not be capable of being produced at an acceptable cost.

Our research programs to identify new product candidates will require substantial technical, financial and human resources, and we may be unsuccessful in our efforts to identify new product candidates. If we are unable to identify suitable additional compounds for preclinical and clinical development, either because our SMART Linker platform is not successful or because we do not develop alternative methods to identify compounds for development, our ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to our financial position and adversely impact our stock price.

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates.

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any NDAs that we submit for our product candidates or may conclude after review of our data that our applications are insufficient to obtain marketing approval of our product candidates. If the FDA does not accept or approve any NDAs we submit, it may require that we conduct additional clinical, nonclinical or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA or application that we submit may be delayed by several years or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any future collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. For example, while we observed positive NF-kB biomarker data in the Phase 1 portion of our MoveDMD Phase 1/2 clinical trial of edasalonexent for the treatment of DMD that demonstrated NF-kB target engagement via statistically significant reduction in NF-kB controlled gene expression for the 67 mg/kg/day and 100 mg/kg/day dosing levels, the primary efficacy endpoint in the Phase 2 portion of the trial, which was average change from baseline to week 12 in the magnetic resonance imaging, or MRI, T2 composite measure of lower leg muscles for the pooled edasalonexent treatment groups compared to placebo, for the same dosing levels was not met. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

The regulatory approval processes for product candidates that target rare diseases, including DMD and cystic fibrosis, are uncertain.

Due to the lack of precedent, broad discretion of regulatory authorities, and a multitude of unique factors that impact the regulatory approval process, the likelihood of the approval of any of our product candidates that target rare diseases, such as DMD or cystic fibrosis, is uncertain, and we may not be able to anticipate, prepare for or satisfy requests or requirements from regulatory authorities, including completing and submitting planned investigational new drug applications and NDAs for our product candidates, in a timely manner, or at all. For example, DMD is a rare disease for which there are only two FDA approved therapeutics. Further, the FDA may determine, after evaluation of our data and analyses, that such data and analyses do not support an NDA submission, filing or approval. Due to this lack of predictability, we may not have the resources necessary to meet regulatory requirements and successfully complete a potentially protracted, expensive and wide-ranging approval process for commercialization of product candidates for rare diseases.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

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

Clinical testing is expensive, time-consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. Further, the clinical development of our product candidates is susceptible to the risk of failure at any stage of drug

development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

In addition to the risk of failure inherent in drug development, certain of the compounds that we are developing and may develop in the future using our SMART Linker drug discovery platform may be particularly susceptible to failure to the extent they are based on compounds that others have previously studied or tested, but did not progress in development due to safety, tolerability or efficacy concerns or otherwise. Our failure to successfully complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business.

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

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Comparable foreign regulatory authorities, such as the European Medicines Agency, or the EMA, impose similar restrictions. We, and any future collaborators, may never receive such approvals. We, and any future collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we, or they, will be able to obtain these approvals.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We have not previously submitted an NDA to the FDA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates. Any inability to complete preclinical and clinical development successfully could result in additional costs to us, or any future collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if (1) we, or any future collaborators, are required to modify our trial designs, such as required modifications with respect to patient populations, endpoints, comparators or trial duration, (2) we, or any future collaborators, are required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we, or they contemplate, (3) we, or any future collaborators, are unable to successfully complete clinical trials of our product candidates or other testing, (4) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or (5) there are unacceptable safety concerns associated with our product candidates, we, or any future collaborators, may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;

- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Adverse events or undesirable side effects caused by, or other unexpected properties of, any of our product candidates may be identified during development that could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, any future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any future collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

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

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

- clinical trials of our product candidates may produce unfavorable or inconclusive results, such as occurred in our MoveDMD Phase 1/2 clinical trial of edasalonexent for the treatment of DMD, where the primary efficacy endpoint was not met;
- we, or any future collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we, or any future collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any future collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any future collaborators, anticipate;
- the cost of planned clinical trials of our product candidates may be greater than we anticipate;
- our third-party contractors or those of any future collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any future collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any future collaborators in a timely manner or at all;
- regulators or institutional review boards may not authorize us, any future collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- we, or any future collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;

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

- regulators or institutional review boards may require that we, or any future collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;

- the FDA or comparable foreign regulatory authorities may disagree with our, or any future collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;

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

- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

In addition, we are currently conducting and may in the future conduct clinical trials outside of the United States. Unforeseen global instability, including political instability, or instability from an outbreak of pandemic or contagious disease, such as the novel coronavirus, in or around the countries in which we conduct our clinical trials, could affect our ability to enroll patients in our clinical trials in these countries, prevent patients already enrolled from completing our clinical trials, and/or cause other trial delays or otherwise adversely impact our clinical trials.

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

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

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

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

The successful completion of any future clinical trial for edasalonexent or any other product candidate for the treatment of DMD will be dependent upon our ability to enroll a sufficient number of patients with DMD. DMD is a rare disease with a small patient population. Further, there are only a limited number of specialist physicians that regularly treat patients with DMD and major clinical centers that support DMD treatment are concentrated in a few geographic regions. Further, these specialized sites typically treat a range of pediatric neuromuscular diseases and, at any point in time, may have constrained resources and capacity to handle clinical trials. In addition, other companies are conducting clinical trials and have announced plans for future clinical trials that are seeking, or are likely to seek, to enroll patients with DMD and patients are generally only able to enroll in a single trial at a time. The small population of patients, competition for these patients and the limited trial sites and their constrained resources may make it difficult for us to enroll enough patients to complete clinical trials for edasalonexent in a timely and cost-effective manner or at all.

The clinical trials that we conduct may also have inclusion criteria that further limit the population of patients that we are able to enroll. For example, further clinical trials for edasalonexent may require that the enrolled boys be between certain ages and not on certain other medications. These inclusion criteria, or other inclusion criteria that are not yet defined, could further limit the available patient pool and present challenges to clinical trial enrollment.

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

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability, or that of any future collaborators, to market the drug could be compromised.

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

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the drug may become less competitive; and
- our reputation may suffer.

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

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

We have never commercialized a product. Even if one of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

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

- the efficacy and safety of the product;
- the potential advantages of the product compared to alternative treatments;

- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- the strength of sales, marketing and distribution support;
- the approval of other new products for the same indications;
- changes in the standard of care for the targeted indications for the product;
- the timing of market introduction of our approved products as well as competitive products;
- availability and amount of reimbursement from government payors, managed care plans and other third-party payors;
- adverse publicity about the product or favorable publicity about competitive products; and
- potential product liability claims.

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

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

We recently hired a Chief Commercial Officer and have taken initial steps towards planning for commercialization of our lead product candidate. However, we have not begun to establish a sales, marketing or distribution infrastructure and have limited experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We plan to use a combination of focused in-house sales and marketing capabilities and third-party collaboration, licensing and distribution arrangements to sell any of our products that receive marketing approval.

We generally plan to seek to retain full commercialization rights for products that we can commercialize with a specialized sales force and to retain co-promotion or similar rights when feasible in indications requiring a larger commercial infrastructure. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any

product launch. If the commercial launch of a product for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

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

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

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

The development and commercialization of new drug products is highly competitive. We expect that we, and any future collaborators, will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to any of our product candidates that we, or they, may seek to develop or commercialize in the future. Specifically, there are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of the key indication of our most advanced program, DMD.

There are currently three therapies approved for the treatment of DMD in the United States: EXONDYS 51®, also known as eteplirsen, an exon skipping therapy targeting the skipping of exon 51; VYONDYS 53, also known as golodirsen, an exon skipping agent targeting the skipping of exon 53; and EMFLAZA®, also known as deflazacort, a glucocorticoid, which is indicated for the treatment of DMD in patients two years of age and older. EXONDYS 51 and VYONDYS 53 have been granted accelerated approval and are marketed by Sarepta Therapeutics, or Sarepta. EMFLAZA is marketed by PTC Therapeutics. Additionally, corticosteroid therapy, including prednisone, is often prescribed off-label to treat the inflammation underlying DMD and to delay loss of ambulation. PTC Therapeutics' TRANSLARNA™ has conditional marketing authorization in the European Union for the treatment of DMD caused by a nonsense mutation. A number of companies are developing additional therapies to treat DMD and are in the process of registration or in late stage clinical development, including Italfarmaco S.p.A., ReveraGen, PTC Therapeutics, Santhera Pharmaceuticals and Sarepta Therapeutics.

Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, have fewer or more tolerable side effects or are less costly than any product

candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

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

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

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

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

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. It is unclear whether the FDA will treat the active ingredients in our product candidates as NCEs and, therefore, afford them five years of NCE data exclusivity if they are approved. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

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

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

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, we, or any future collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement for products can differ significantly from payor to payor.

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

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize any of our product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

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

manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

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

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

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we or any future collaborators commercially sell any product that we may or they may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend resulting litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we maintain general liability insurance of $5.0 million in the aggregate and clinical trial liability insurance of $10.0 million in the aggregate, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we begin selling any product candidate that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Our Dependence on Third Parties

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

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We expect to seek one or more collaborators for the development and commercialization of one or more of our product candidates. For example, conducting clinical trials of CAT-5571 in patients with cystic fibrosis will likely involve significant cost, and we expect that we would conduct any clinical trial of CAT-5571 in patients with cystic fibrosis in collaboration with one or more partners. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the potential differentiation of our product candidate from competing product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product candidate.

Collaborations are complex and time-consuming to negotiate and document. Further, there have been a significant number of business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. In addition, any loan and security agreements or collaboration agreements that we enter into in the future may contain, restrictions on our ability to enter into potential collaborations or to otherwise develop specified compounds.

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

If we enter into collaborations with third parties for the development and commercialization of our product candidates, our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.

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

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

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

We rely on third parties to conduct our clinical trials. If they do not perform satisfactorily, our business could be significantly harmed.

We do not independently conduct clinical trials of any of our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct these clinical trials and expect to rely on these third parties to conduct clinical trials of any other product candidate that we develop. Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new contract research organization begins work. As a result, delays would likely occur, which could materially impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Further, our reliance on these third parties for clinical development activities limits our control over these activities, but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example,

notwithstanding the obligations of a contract research organization for a trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as current Good Clinical Practices, or cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the marketing approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

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

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

We currently have 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 collaboration partners, to manufacture commercial quantities of our products, if approved. Reliance on such third-party contractors entails risks, including:

- manufacturing delays if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;

- the possible termination or nonrenewal of agreements by our third-party contractors at a time that is costly or inconvenient for us;

- the possible breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

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

Any manufacturing problem or the loss of a contract manufacturer could be disruptive to our operations, delay our clinical trials and, if our products are approved for sale, result in lost sales. Additionally, we rely on third parties to supply the raw materials needed to manufacture our product candidates. Any reliance on suppliers may involve several risks, including a potential inability to obtain critical materials and reduced control over production costs, delivery schedules, reliability and quality. Any unanticipated disruption to future contract manufacture caused by problems at suppliers could delay shipment of our product candidates, increase our cost of goods sold and result in lost sales.

Our ability to obtain clinical supplies of our product candidates could also be disrupted if the operations of any of our third-party contract manufacturers are affected by a man-made or natural disaster or other business interruption. There can be no assurance that our supply of research and development, preclinical study, and clinical trial drugs and other materials will not be limited, interrupted, restricted in certain geographic regions, or of satisfactory quality.

If we are at any time unable to provide an uninterrupted supply of our product candidates or, following regulatory approval, any products to patients, we may lose patients, physicians may elect to utilize competing therapeutics instead of our products, and our clinical trials may be adversely affected, which could materially and adversely affect our clinical trial outcomes.

If any of our product candidates are approved by any regulatory agency, we plan to enter into agreements with third-party contract manufacturers for the commercial production and distribution of those products. It may be difficult for us to reach agreement with a contract manufacturer on satisfactory terms or in a timely manner. In addition, we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under current good manufacturing practices, or cGMPs, that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization efforts.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. If our manufacturers cannot successfully manufacture material that conforms to our specifications or the strict regulatory requirements of the FDA and any applicable foreign regulatory

authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate.

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

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

Risks Related to Our Intellectual Property

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary product candidates. If we do not adequately protect our intellectual property, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel product candidates that are important to our business. The patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

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

Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, patents are granted to the party who was the first to file a patent application. However, prior to March 16, 2013, in the United States, patents were granted to the party who was the first to invent the claimed subject matter. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in post-grant review procedures, oppositions, derivations, reexaminations, inter partes review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

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

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

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

While we have obtained composition of matter patents with respect to our most advanced product candidates, we also rely on trade secret protection for certain aspects of technology platform, including certain aspects of our SMART Linker drug discovery platform. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, advisors, contract manufacturers, suppliers and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or

those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

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

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

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates and use our SMART Linker drug discovery platform without infringing the intellectual property and other proprietary rights of third parties. Third parties have U.S. and non-U.S. issued patents and pending patent applications relating to compounds and methods of use for the treatment of DMD, the key indication for our most advanced program. If any third-party patents or patent applications are found to cover our product candidates or their methods of use, we may not be free to manufacture or market our product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our product candidates, including interference proceedings before the USPTO. Third parties may assert infringement claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

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

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or the Leahy-Smith Act, signed into law in September 2011, could increase those uncertainties and costs. The Leahy-Smith Act included a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, for example, via post grant review and inter partes review proceedings at the USPTO. In addition, the Leahy-Smith Act transformed the U.S. patent system into a "first to file" system. The first-to-file provisions, however, only became effective in March 2013. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our or our collaboration partners' patent applications and the enforcement or defense of our or our collaboration partners' issued patents, all of which could harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our product candidates, our competitive position would be adversely affected.

We may not be able to enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents or where any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing with us.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities in those

jurisdictions is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Patent term may be inadequate to protect our competitive position on our products for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including members of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

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

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drug products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, which regulations differ from country to country. We, and any future collaborators, are not permitted to market our product candidates in the United States or in other countries until we, or they, receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Our product candidates are in various stages of development and are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved.

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

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

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

In order to market and sell our products in the European Union and many other jurisdictions, we, and any future collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We, and any future collaborators, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the United Kingdom will not accept high regulatory alignment with the European Union.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our product candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. While we have obtained orphan drug designation from the FDA and orphan medicinal product designation from the European Commission for edasalonexent for the treatment of DMD, we, or any future collaborators, may seek orphan drug designations for other product candidates or in other jurisdictions and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain orphan drug exclusivity for that product candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same drug for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because FDA has taken the position that, under certain circumstances, another drug with the same active moiety can be approved for the same condition. Specifically, the FDA's regulations provide that it can approve another drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

In August 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

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

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

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

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

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

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

Any of our product candidates for which we, or any future collaborators, obtain marketing approval in the future, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such product, among other things, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing

requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy.

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

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

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Under the Cures Act and the Trump Administration's regulatory reform initiatives, the FDA's policies, regulations and guidance may be revised or revoked and that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing

requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump Administration may impact our business and industry. Namely, the Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. An under-resourced FDA could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. In January 2017, President Trump issued an executive order, applicable to all executive agencies including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB in February 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations. Subsequently, on October 9, 2019, the President issued Executive Order 13,892, which is titled "Promoting the Rule of Law Through Transparency and Fairness in Civil Administrative Enforcement and Adjudication." This Order declares that "guidance documents may not be used to impose new standards of conduct on persons outside the executive branch." It is difficult to predict how these various requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

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

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the Affordable Care Act, or ACA, became law in 2010 and includes the following provisions of potential importance to our product candidates:

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

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress may consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. This decision is under review by the U.S. Supreme Court during its current term. The full effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known. In addition, Centers for Medicare & Medicaid Services has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

In addition, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. On December 18, 2019, that court affirmed the lower court's ruling that the individual mandate portion of

the ACA was unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business. It is possible that such initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to amend the ACA is uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop commercialize product candidates.

Further, there have been several recent U.S. congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration has pressed for drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

In addition, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services, or HHS, will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage

importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

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

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

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

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

False Claims Laws. The federal false claims laws impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters, and, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information;

Transparency Requirements. Federal laws require applicable manufacturers of covered drugs, biologics, devices and supplies to report payments and other transfers of value to physicians and teaching hospitals and ownership and investment interests by physicians; and

Analogous State and Foreign Laws. Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, which may be broader in scope, can apply

to our business activities, including sales or marketing arrangements, and claims involving healthcare items or services and are generally broad and are enforced by many different federal and state agencies as well as through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

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

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the European Union General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures

when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could significantly harm our business.

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

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

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

regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

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

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

A fast track designation by the FDA may not actually lead to a faster development, regulatory review or approval process.

If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet needs for this condition, the treatment sponsor may apply for FDA fast track designation. In July 2015, the FDA notified us that we obtained fast track designation for edasalonexent for the treatment of DMD. Fast track designation does not ensure that we will experience a faster development, regulatory review or approval process compared to conventional FDA procedures. Additionally, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

Although FDA has granted rare pediatric disease designation to edasalonexent for the treatment of DMD, that designation will not expedite or ensure approval of edasalonexent nor will it guarantee that we receive a Priority Review Voucher if edasalonexent is approved by the FDA for the treatment of DMD.

The FDA has awarded rare pediatric disease Priority Review Vouchers to sponsors of drug candidates to treat rare pediatric disease products, if the treatment sponsors apply for this designation and meet certain criteria. Under this program, upon the approval of a qualifying NDA or biologics license application, or BLA, for the treatment of a rare pediatric disease, the sponsor of such an application would be eligible for a rare pediatric disease Priority Review Voucher that can be used to obtain priority review for a subsequent NDA or BLA. The Priority Review Voucher may be sold or transferred an unlimited number of times. In September 2015, the FDA notified us that we obtained rare pediatric disease designation for edasalonexent for the treatment of DMD. This designation does not guarantee that an NDA for edasalonexent will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. It also does not ensure expedited review or approval of edasalonexent for the treatment of DMD. With passage of the 21st Century Cures Act in December 2016, the Rare Pediatric Disease Priority Review Voucher program was reauthorized until 2020. In addition, if a product candidate is designated before October 1, 2020, as is the case with edasalonexent, it is eligible to receive a voucher if it is approved before October 2022. However, there is no guarantee that edasalonexent will be approved by that date and, therefore, we may not be in a position to obtain the Priority Review Voucher prior to expiration of the program.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, which we collectively refer to as the Trade Control Laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control Laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control Laws by U.K., U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Risks Related to Employee Matters, Managing Growth and Information Technology

Our future success depends on our ability to retain our senior management and to attract, retain and motivate qualified personnel.

We are highly dependent on members of our senior management, including Jill C. Milne, Ph.D., our President and Chief Executive Officer, Joanne Donovan, M.D., Ph.D., our Chief Medical Officer, Andrew Nichols, Ph.D., our Chief Scientific Officer, Andrew Komjathy, our Chief Commercial Officer, and Noah Clauser, our VP of Finance. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. Recruiting and retaining qualified scientific, clinical, manufacturing, sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees and any difficulties in recruiting and retaining other critical personnel could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

If we are unable to retain our executive officers or other key employees, replacing them may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given

the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

We expect to grow our organization significantly if our Phase 3 trial of edasalonexent for the treatment of DMD is successful, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug manufacturing, regulatory affairs and sales, marketing and distribution, if our Phase 3 trial of edasalonexent for the treatment of DMD is successful and we obtain FDA approval to market edasalonexent for the treatment of DMD in the United States. To manage these growth activities, we would need to implement and improve our managerial, operational and financial systems, expand our facilities and to recruit and train additional qualified personnel. Our management may need to devote a disproportionate amount of its attention to managing these growth activities. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or identify, recruit and train additional qualified personnel. Our inability to manage the expansion of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

Security breaches and other disruptions to our information technology systems could compromise our information, disrupt our business and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect, process and store sensitive data, including intellectual property, as well as our proprietary business information, employee data and personally identifiable information of clinical trial participants. We also rely to a large extent on information technology systems to operate our business. We have outsourced elements of our confidential information processing and information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. The secure maintenance of this information is important to our operations and business strategy. Despite our security measures, our information technology infrastructure, and that of our vendors and third-party providers, may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. We, our vendors and third-party providers could be susceptible to third party attacks on our, and their, information security systems, which attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organized criminal groups, hacktivists, nation states and others. While we have invested in information technology security measures and the protection of confidential information, there can be no assurance that our efforts will prevent service interruptions or security

breaches. Although we are not aware of any material information security incidents to date, we have detected common types of attempts to attack our information technology systems and data using means that have included phishing. Any service interruptions or security breaches of our information technology systems may substantially impair our ability to operate our business and could compromise our networks, or those of our vendors and third-party providers, and the information stored could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation, any of which could adversely affect our business.

Risks Related to Our Common Stock

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

Our shares of common stock began trading on The Nasdaq Global Market, or Nasdaq, in June 2015. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price for our common stock and thereby affect the ability of our stockholders to sell their shares. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

If we were to be delisted from The Nasdaq Stock Market, it could make trading in our stock more difficult.

There are various quantitative listing requirements for a company to remain listed on the Nasdaq, including maintaining a minimum bid price of $1.00 per share. No assurance can be given that we will continue to remain compliant with the minimum bid price requirement or Nasdaq's other continued listing requirements. For example, in August 2018, we received a deficiency letter from the Listing Qualifications Department of Nasdaq notifying us that, for the preceding 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Global Market as required by Nasdaq Listing Rule 5450(a)(1). In order to regain compliance, on December 28, 2018, we effected a one-for-ten reverse split of our common stock Any delisting would likely have a negative effect on the price of our common stock and would impair stockholders' ability to sell or purchase their common stock when they wish to do so.

The price of our common stock is likely to be highly volatile, which could result in substantial losses for our stockholders.

Our stock price is likely to be highly volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our investors may lose some or all of their investments. The market price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of edasalonexent and any of our other product candidates;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our development programs;
- the success of existing or new competitive products or technologies;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;

- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including political instability, or instability from an outbreak of pandemic or contagious disease, such as the novel coronavirus; and
- the other factors described in this "Risk Factors" section.

Additionally, in the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because smaller pharmaceutical and biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until the last day of our fiscal year following the fifth anniversary of our IPO, subject to specified conditions. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We expect to continue to take advantage of some or all of the available exemptions until we cease to be an emerging growth company on January 1, 2021. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company, which would allow us to take advantage of many of the same exceptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of SOX Section 404 and reduced disclosure obligations regarding executive compensation. Investors may find our common stock less attractive as a result of our reliance on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

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

Pursuant to SOX Section 404 we are required to furnish reports by our management on our internal control over financial reporting with our Annual Reports on Form 10-K with the SEC. Commencing January 1, 2021, when we are no longer an emerging growth company, we may also be required to include attestation reports on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. As of January 31, 2020, we had outstanding 12,607,172 shares of common stock. Subsequent to January 31, 2020 we issued an additional 5,290,000 shares of common stock related to our January 2020 registered offering. As of January 31, 2020, we had outstanding warrants to purchase 4,200,000 shares of common stock at an exercise price of $12.00 per share, and 1,991,300 shares of common stock at an exercise price of $6.25 per share. These warrants are fully exercisable and we have registered the issuance of shares upon exercise of these warrants under registration statements. As a result, the shares issuable

upon exercise of these warrants can be freely sold in the public marked upon issuance, subject to volume limitations applicable to affiliates.

The number of shares of common stock underlying our outstanding warrants is significant in relation to our currently outstanding common stock, which could have a negative effect on the market price of our common stock and make it more difficult for us to raise funds through future equity offerings.

As part of our June 2018 equity financing we issued warrants to purchase an aggregate of 4,200,000 shares of common stock at an exercise price of $12.00 per share, all of which are outstanding, and as part of our February 2019 equity financing we issued warrants to purchase an aggregate of 2,000,000 shares of common stock at an exercise price of $6.25 per share, of which warrants to purchase 1,991,300 shares remain outstanding. Upon exercise in full of these outstanding warrants, the shares issuable upon exercise would represent a significant portion of our outstanding common stock. The warrants were fully exercisable upon issuance and remain exercisable for five years from their respective dates of issuance. We have registered the issuance of shares upon exercise of these warrants under a registration statements under the Securities Act of 1933, as amended, and, accordingly, such shares can be freely sold into the public market upon issuance, subject to volume limitations applicable to affiliates. Sales of these shares could cause the market price of our common stock to decline significantly. Furthermore, if our stock price rises, the holders of these warrants may be more likely to exercise their warrants and sell a large number of shares, which could negatively impact the market price of our common stock and reduce or eliminate any appreciation in our stock price that might otherwise occur.

We may also find it more difficult to raise additional equity capital while these warrants are outstanding. At any time during which these warrants are likely to be exercised, we may be unable to obtain additional equity capital on more favorable terms from other sources. In addition, the exercise of these warrants would result in a significant increase in the number of our outstanding shares of common stock, which could have the effect of significantly diluting the interest of our current stockholders, and following such exercise the former holders of such warrants could have significant influence over our company as a result of the shares of common stock they acquire upon such exercise.

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

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. Any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be investors' sole source of gain for the foreseeable future.

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

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

management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

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

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

Our certificate of incorporation designates the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors and officers.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws, or any action asserting a claim against us governed by the internal affairs doctrine. This exclusive forum provision includes actions arising under the Securities Exchange Act of 1934, as amended, and the Securities Act of 1933, as amended. There is uncertainty as to whether a court would enforce such exclusive forum provision in the case of an action arising under the Securities Act of 1933, as amended, and investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder. This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors or officers, which may discourage such lawsuits against us and our directors and officers.

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

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

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our offices are located in Boston, Massachusetts and consist of approximately 11,000 square feet of subleased office space under a lease that expires in July 2022. We also lease approximately 19,000 square feet of office and laboratory space in Cambridge, Massachusetts under a lease that expires in June 2020. We sublease approximately 15,000 square feet of our total leased space in Cambridge to a third party under a sublease which expires in June 2020. We believe that our existing facilities are sufficient for our needs for the foreseeable future.

Item 3. Legal Proceedings

From time to time we may become subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this Annual Report on Form 10-K, we do not believe we are party to any claim or litigation, the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock, $0.001 par value per share, has been publicly traded on the Nasdaq Global Market under the symbol "CATB" since June 25, 2015. Prior to that time, there was no public market for our common stock.

Holders

As of March 2, 2020, there were approximately 33 holders of record of our common stock. This number of holders of record does not include beneficial owners of our common stock whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared nor paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future.

Recent Sales of Unregistered Securities

We did not sell or issue any equity securities that were not registered under the Securities Act of 1933 during the period covered by this Annual Report on Form 10-K.

Purchases of Equity Securities

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

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

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

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics. Our lead product candidate is edasalonexent, an oral small molecule that inhibits NF-kB, 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 a randomized, double-blind, placebo-controlled trial, and is designed to evaluate the efficacy and safety of edasalonexent for registration purposes. 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. We announced in September 2019 that the Phase 3 PolarisDMD trial completed enrollment and exceeded our target enrollment of 125 boys. We enrolled 131 boys between the ages of four and seven, up to their eighth birthday, regardless of mutation type, who had not been on steroids for at least six months. We expect to report top-line results from the Phase 3 PolarisDMD trial in the fourth quarter of 2020. Our goal is to submit a New Drug Application, or NDA, for edasalonexent for the treatment of DMD in 2021.

Our previous trial, the MoveDMD Phase $^{1}/_{2}$ trial, also 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. The MoveDMD trial was conducted in three sequential parts, Phase 1, Phase 2, and an open-label extension. From Phase 1 we reported 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 Phase 2 we announced 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. In the open-label extension, we observed improvement in the rate of change in lower leg composite MRI T2 through 72 weeks on 100 mg/kg of edasalonexent treatment compared to the off-treatment control period. We also 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, through 72 weeks of edasalonexent 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 consistency and durability of edasalonexent treatment effects. Through 72 weeks of treatment, edasalonexent continued to be well tolerated with no safety signals observed in the MoveDMD trial.

We initiated an open-label extension trial in March 2019, which we refer to as the GalaxyDMD trial. The remaining boys that were participating in the MoveDMD trial open-label extension transitioned to the GalaxyDMD trial and their eligible siblings were also able to enroll. In addition, when boys complete the 12-month Phase 3 PolarisDMD trial, they are given the option to receive open-label edasalonexent in the GalaxyDMD trial. The GalaxyDMD trial is designed to provide longer term safety data to support registration filings.

In addition, we are exploring the potential of edasalonexent as a therapy in other indications where the inhibition of NF-kB may provide clinical benefit. In August 2019, we entered into a preclinical research collaboration with the Jain Foundation to study edasalonexent in dysferlinopathy, which includes limb-girdle muscular dystrophy type 2B and Miyoshi myopathy, a serious rare disease that causes progressive muscle weakness for which there is currently no approved treatment option. In dysferlinopathy, muscles lack dysferlin and as a result NF-kB is chronically activated. Under our collaboration, we and the Jain Foundation are conducting a preclinical study to evaluate the potential of edasalonexent as a therapeutic intervention for dysferlinopathy by measuring disease progression in dysferlin-deficient mice treated with edasalonexent. Initial results are expected in the first half of 2020.

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.

Since our inception in June 2008, we have devoted substantially all of our resources to developing our proprietary platform technology, identifying potential product candidates, undertaking preclinical studies and conducting clinical trials for three clinical-stage compounds, building our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, and providing general and administrative support for these operations. To date, we have primarily financed our operations through private placements of our preferred stock, registered offerings of our common stock, including our initial public offering, or IPO, as well as a secured debt financing. From our inception through December 31, 2019, we raised an aggregate of $272.7 million through various private placements of preferred stock, our IPO, debt financing as well as various other registered equity offerings, including underwritten public offerings, at-the-market, or ATM, offerings, and stock option and warrant exercises. Following December 31, 2019, we raised an additional $26.5 million in gross proceeds from an underwritten public offering of common stock in January 2020, or our January 2020 Financing, and an additional $1.1 million in gross proceeds from our ATM offering program.

Financial Overview

Revenue

As of December 31, 2019, we have not generated any revenue from product sales.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our product candidates, which include:

- employee-related expenses including salaries, benefits and stock-based compensation expense;

- expenses incurred under agreements with third parties, including contract research organizations that conduct clinical trials and research and development and preclinical activities on our behalf;
- the cost of consultants;
- the cost of lab supplies and acquiring, developing and manufacturing study materials; and
- facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies.

Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

The following summarizes our most advanced current research and development programs:

- ***Edasalonexent for the treatment of DMD***—Edasalonexent is a conjugate of salicylic acid and the omega-3 fatty acid docosahexaenoic acid, or DHA, a naturally occurring unsaturated fatty acid with anti-inflammatory properties, based on our proprietary Safely Metabolized And Rationally Targeted linker, or SMART Linker, drug discovery platform. We designed edasalonexent to inhibit NF-kB. In DMD the loss of dystrophin leads to chronic activation of NF-kB, which is a key driver of skeletal and cardiac muscle disease progression. We reported results from the Phase 1 portion of the MoveDMD trial in January 2016 and reported top-line safety and efficacy results for the 12-week placebo-controlled Phase 2 portion of the trial in January 2017. In July 2016, we initiated an open-label extension of the MoveDMD trial, and we reported efficacy and safety results from the open-label extension in October 2017, February 2018, April 2018, October 2018, February 2019 and April 2019 reflecting data through 24, 36, 48, 60 and 72 weeks of edasalonexent treatment. In March 2019, we launched the GalaxyDMD open-label extension trial. The remaining boys participating in the MoveDMD trial open-label extension transitioned to the GalaxyDMD trial, which is designed to provide longer term safety data to support registration filings. In September 2018, we initiated the global Phase 3 PolarisDMD trial of edasalonexent for the treatment of DMD, regardless of mutation type, and completed enrollment in September 2019. We expect to report top-line results from the Phase 3 PolarisDMD trial in the fourth quarter of 2020. The Phase 3 trial is designed to evaluate the efficacy and safety of edasalonexent in patients with DMD and is intended to support an application for commercial registration of edasalonexent. When boys complete the 12-month Phase 3 trial, they are given the option to receive open-label edasalonexent in the GalaxyDMD trial.
- ***Edasalonexent for the treatment of Becker Muscular Dystrophy, or BMD***—We are evaluating the potential benefits of edasalonexent treatment in BMD and investigating potential approaches for clinical trials in BMD.
- ***Edasalonexent for the treatment of dysferlinopathy***—We are evaluating the potential benefits of edasalonexent treatment in dysferlinopathy, which includes limb-girdle muscular dystrophy type 2B and Miyoshi myopathy, through a preclinical study in collaboration with the Jain Foundation.
- ***CAT-5571***—CAT-5571 is a SMART Linker conjugate that contains cysteamine, a naturally occurring molecule that is a degradation product of the amino acid cysteine, and DHA. CAT-5571 is a potential oral therapy to treat CF. CAT-5571 is a small molecule 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-enabling activities for CAT-5571.

We typically use our employee, consultant and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, other internal costs or external consultant costs to specific product candidates or development programs. We record our research and development expenses net of any research and development tax incentives we are entitled to receive from government authorities.

The following table summarizes our research and development expenses by program (in thousands):

	Year Ended December 31,	
	2019	2018
Edasalonexent	$ 11,973	$ 7,897
CAT-5571	15	528
Other research and platform programs	—	628
Costs not directly allocated to programs:		
Employee expenses including cash compensation, benefits and stock-based compensation	5,062	6,379
Facilities	303	910
Consultants and professional expenses, including stock-based compensation	602	361
Other	362	339
Total costs not directly allocated to programs	6,329	7,989
Total research and development expenses	$ 18,317	$ 17,042

Since inception of the edasalonexent and the CAT-5571 programs, total direct expenses to support the programs have been $49.4 million and $4.2 million, respectively.

The successful development of our product candidates is highly uncertain. Accordingly, at this time, we cannot reasonably estimate the nature, timing and costs of the efforts that will be necessary to complete the remainder of the development of these product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from edasalonexent or any of our other current or potential product candidates. This is due to our need to raise additional capital to fund further clinical trials of our product candidates and the numerous risks and uncertainties associated with developing medicines, including the uncertainties of:

- establishing an appropriate safety profile with IND-enabling toxicology studies;
- successful enrollment in, and completion of clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others; and
- a continued acceptable safety profile of the products following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect to incur significant research and development costs for the foreseeable future. We expect that our research and development expenses will increase significantly in the near term in connection with the substantial activities required to conduct our Phase 3 PolarisDMD trial and prepare for registration of edasalonexent for the treatment of DMD. We do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, commercial, business development, legal and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that in the near term our general and administrative expenses will remain relatively consistent with their current levels. As we approach the anticipated read out of top-line results from our Phase 3 PolarisDMD trial in the fourth quarter of 2020, we may increase our general and administrative expenditures to hire personnel to support potential commercialization of edasalonexent, dependent on our available capital resources and our prospects for obtaining additional financing.

Restructuring

In April 2018, we announced a strategic shift to focus resources on our lead program edasalonexent. Consequently, we reduced our workforce by 40% during the quarter ended June 30, 2018. Charges for employee severance, employee benefits, consolidation of facilities and contract terminations of $0.9 million were recorded in the year ended December 31, 2018, all of which was paid by December 31, 2019. Of these costs, $0.4 million was recorded in the general and administrative section and $0.5 million was recorded in the research and development section of the accompanying consolidated statement of operations. We also recorded a net gain in other income, net of $0.3 million in connection with the sale or exchange of assets disposed of during the consolidation and relocation of facilities.

Other Income (Expense)

Other income (expense), net consists of gains and losses on sale and disposal of property and equipment, interest income earned on our cash, cash equivalents, and short-term investments, interest expense incurred on debt instruments, amortized deferred financing costs and amortized debt discount and net amortization expense on short-term investments.

Critical Accounting Policies and Significant Judgments and Estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with United States generally accepted accounting principles. We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as critical because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we

make the estimate, and different estimates—which also would have been reasonable—could have been used. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policy is the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by contract research organizations, or CROs, in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to CROs on our estimates of the services received and efforts expended pursuant to contracts with CROs that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our CROs will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting expense amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Results of Operations

Comparison of the Years Ended December 31, 2019 and 2018

The following table summarizes our results of operations for the years ended December 31, 2019 and 2018, together with the dollar change in those items (in thousands):

	Year Ended December 31,		Period-to-Period Change
	2019	2018	
Operating expenses:			
Research and development	18,317	17,042	1,275
General and administrative	8,771	9,329	(558)
Total operating expenses	27,088	26,371	717
Loss from operations	(27,088)	(26,371)	(717)
Other income, net	795	501	294
Net loss	$ (26,293)	$ (25,870)	$ (423)

Research and Development Expenses

Research and development expenses increased by $1.3 million to $18.3 million for the year ended December 31, 2019 from $17.0 million for the year ended December 31, 2018, an increase of 7%. The increase in research and development expenses was attributable to a $4.1 million increase in costs to support our edasalonexent program, and a $0.2 million increase in consulting and professional services. These increases were partially offset by a $0.5 million decrease in costs to support our CAT-5571 program, a $0.6 million decrease in costs to support other research and platform programs, a $0.6 million decrease in the research and development portion of facilities costs associated with subleasing a portion of our office space in Cambridge, and a $1.3 million decrease in employee compensation due to a reduction in our workforce in 2018.

General and Administrative Expenses

General and administrative expenses decreased by $0.6 million to $8.8 million for year ended December 31, 2019 from $9.3 million for the year ended December 31, 2018, a decrease of 6%. The decrease in general and administrative expenses was attributable to a $0.8 million decrease in employee compensation due to recognition of severance expense in 2018 as well as one-time performance bonuses awarded to general and administrative employees in 2018 that were not awarded in 2019, and a $0.4 million decrease in the general and administrative portion of facilities expense. These decreases were partially offset by a $0.4 million increase in consulting and professional services associated with commercialization activities, and a $0.2 million increase in the general and administrative portion of insurance expense.

Other Income (Expense), Net

Other income (expense), net increased by $0.3 million for the year ended December 31, 2019 compared to the year ended December 31, 2018 due to a decrease in interest expense of $0.1 million following to the maturity of our now expired credit facility in September 2018 and an increase of $0.4 million in interest and investment income due to an increase in our interest-bearing assets following our February 2019 financing. These increases were partially offset by a $0.2 million decrease in other income due to the net gain realized on assets sold in consolidation of our facilities in 2018.

Liquidity and Capital Resources

From our inception through December 31, 2019, we raised an aggregate of $272.7 million, through various private placements of preferred stock, our IPO, a secured debt financing as well as various other registered equity offerings, including underwritten public offerings, ATM offerings, and stock option and warrant exercises. As of December 31, 2019, we had $36.2 million in cash, cash equivalents and short-term investments. Subsequent to December 31, 2019, we raised an additional $26.5 million in gross proceeds from the January 2020 Financing and an additional $1.1 million in gross proceeds from our ATM offering program.

We have not generated any revenue from product sales to date. We have incurred significant annual net operating losses in every year since our inception and expect to incur net operating losses in 2020 and for the foreseeable future. As of December 31, 2019, we had an accumulated deficit of $223.6 million. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase significantly if and to the extent that we continue to develop and conduct clinical trials with respect to edasalonexent and other product candidates; initiate and continue research, preclinical and clinical development efforts for our other product candidates and potential product candidates; maintain, expand and protect our intellectual property portfolio; establish a commercial infrastructure to support the marketing and sale of certain of our product candidates; hire additional personnel, such as clinical, regulatory, quality control and scientific personnel; and operate as a public company.

At-the-Market Offerings

We have entered into various sales agreements with Cowen and Company LLC, or Cowen, pursuant to which we could issue and sell shares of our common stock under ATM programs. Cowen was not required to sell any specific amount but acted as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. Shares sold pursuant to these sales agreements were sold pursuant to shelf registration statements, one of which became effective on July 19, 2016, and which was replaced by a new shelf registration statement which became effective May 22, 2019. We have paid Cowen 3% of the gross proceeds from the common stock sold through these sales agreements.

During the year ended December 31, 2019, we sold an aggregate of 1,282,904 shares of common stock pursuant to our ATM programs, at an average offering price of $5.81 per share, for gross proceeds of $7.5 million, resulting in net proceeds of $7.0 million after deducting sales commissions and offering expenses. During the year ended December 31, 2018, we sold an aggregate of 577,195 shares of common stock pursuant to our ATM programs, at an average offering price of $15.27 per share, for gross proceeds of $8.8 million, resulting in net proceeds of $8.4 million after deducting sales commissions and offering expenses.

Subsequent to December 31, 2019, we sold an aggregate of 173,572 shares of common stock through our existing ATM program at an average offering price of $6.29 per share, for gross and net proceeds of $1.1 million after deducting sales commissions and offering expenses. Currently, $43.6 million remains available for sale under this program.

January 2020 Financing

On January 30, 2020, we entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering of an aggregate of 5,290,000 shares of our common stock, at a price to the public of $5.00 per share, including 690,000 shares issued upon the exercise in full by Oppenheimer & Co. Inc. of its overallotment option. This resulted in gross proceeds of $26.5 million, and net proceeds of $24.5 million.

February 2019 Financing

On February 6, 2019, we entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering of 4,000,000 shares of our common stock and accompanying warrants to purchase up to 2,000,000 shares of common stock, at a combined price to the public of $5.00 per unit, for gross proceeds of $20.0 million, and net proceeds of $18.5 million. The warrants were immediately exercisable at an exercise price of $6.25 per share and will expire five years from the date of issuance.

June 2018 Financing

On June 20, 2018, we entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering, of 4,200,000 shares of our common stock, and accompanying warrants to purchase up to 4,200,000 shares of common stock, at a combined price to the public of $10.00 per unit, for gross proceeds of $42.0 million, resulting in net proceeds of $38.9 million. The warrants were immediately exercisable at an exercise price of $12.00 per share and will expire five years from the date of issuance.

Funding Requirements

Our primary uses of capital are for compensation and related expenses, manufacturing costs for pre-clinical and clinical materials, third party clinical trial research and development services, clinical costs, legal and other regulatory expenses, initial commercialization preparations and general overhead.

As of December 31, 2019, we had an accumulated deficit of $223.6 million. We have been primarily involved with research and development activities and have incurred operating losses and negative cash flows from operations since our inception.

As of December 31, 2019, we had available cash, cash equivalents and short-term investments of $36.2 million. We expect that with the additional $25.6 million that we have raised to date in 2020 in net proceeds from equity financings, our existing cash, cash equivalents and short-term investments are sufficient to support our operating expenses into the third quarter of 2021.

Our estimate as to how long we expect our cash, cash equivalents and short-term investments to be able to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including:

- any unanticipated costs or expenses related to our Phase 3 PolarisDMD and GalaxyDMD trials, including costs and expenses for any additional research or preclinical or clinical development efforts related to this trial;
- the progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, our product candidates and potential product candidates, including current and future clinical trials;
- our ability to enter into and the terms and timing of any additional collaborations, licensing or other arrangements that we may establish;
- the number and characteristics of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;

- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;

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

- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;

- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and

- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

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

Cash Flows

Comparison of the Years Ended December 31, 2019 and 2018

The following table provides information regarding our cash flows for the years ended December 31, 2019 and 2018 (in thousands):

	Year Ended December 31,	
	2019	2018
Net cash used in operating activities	$ (26,569)	$ (23,465)
Net cash used in investing activities	(4,082)	(21,905)
Net cash provided by financing activities	25,620	44,295
Net decrease in cash, cash equivalents and restricted cash	$ (5,031)	$ (1,075)

Net Cash Used in Operating Activities

Net cash used in operating activities was $26.6 million for the year ended December 31, 2019 and consisted primarily of a net loss of $26.3 million adjusted for non-cash items, including stock-based compensation expense of $1.5 million, other non-cash items of $0.1 million, and a net increase in operating assets of $1.9 million, which resulted primarily from an increase in prepaid expenses and other current assets as well as decreases in accounts payable and accrued expenses.

Net cash used in operating activities was $23.5 million for the year ended December 31, 2018 and consisted primarily of a net loss of $25.9 million adjusted for non-cash items, including stock-based compensation expense of $1.8 million, depreciation and amortization expense of $0.1 million, other non-cash items of $0.1 million and a net decrease in operating assets of $0.7 million, which resulted primarily from increases in accounts payable and accrued expenses. These were partially offset by a gain on disposal of property and equipment of $0.3 million.

Net Cash Used in Investing Activities

Net cash used in investing activities was $4.1 million for the year ended December 31, 2019 and consisted of purchases of short-term investments of $155.2 million partially offset by proceeds from maturities of short-term investments of $151.1 million. Net cash used in investing activities was $21.9 million for the year ended December 31, 2018 and consisted of purchases of short-term investments of $70.4 million partially offset by proceeds from maturities of short-term investments of $48.1 million and sales of property and equipment of $0.4 million.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $25.6 million during the year ended December 31, 2019, which was primarily attributable to net proceeds of $18.5 million from our February 2019 financing and net proceeds of $7.1 million from our ATM programs. Net cash provided by financing activities was $44.3 million during the year ended December 31, 2018, which was primarily attributable to net proceeds of $38.9 million from our June 2018 financing and net proceeds of $8.3 million from our ATM programs, partially offset by $2.9 million in repayments on our now expired credit facility.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Contractual Obligations

The following table summarizes our significant contractual obligations as of payment due date by period at December 31, 2019:

	Payments due by period			
(In thousands)	Total	Less than 1 Year	1 - 3 Years	More than 3 Years
Operating lease obligations(1)	2,627	1,449	1,178	—
Total contractual cash obligations	$ 2,627	$ 1,449	$ 1,178	$ —

(1) Represents future minimum lease payments under our non-cancelable operating leases. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

We enter into agreements in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes. We have not included these payments in the table of contractual obligations above since the contracts are cancelable at any time by us, generally upon 60 days' prior written notice to the CRO, and therefore we believe that our non-cancelable obligations under these agreements are not material.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of December 31, 2019, we had cash, cash equivalents and short-term investments of $36.2 million and, as of December 31, 2018, we had cash, cash equivalents and short-term investments of $37.6 million. Our cash equivalents as of December 31, 2019 consisted of corporate debt securities and money market funds and, as of December 31, 2018, consisted of corporate debt securities, money market funds and U.S. reverse repurchase agreements. Our short-term investments as of December 31, 2019 consisted of commercial paper, corporate debt securities and U.S. reverse repurchase agreements and, as of December 31, 2018, consisted of corporate debt securities and U.S. reverse repurchase agreements. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio and interest income.

As of December 31, 2019 and December 31, 2018, we had no material liabilities denominated in foreign currencies.

Item 8. Financial Statements and Supplementary Data

The consolidated financial statements together with the report of our independent registered public company accounting firm, required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those consolidated financial statements is found in Item 15 of this Annual Report on Form 10-K.

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

There has been no change of accountants nor any disagreements with accountants on any matter of accounting principles or practices or financial disclosure required to be reported under this Item.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, or the Exchange Act) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

As of December 31, 2019, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of December 31, 2019, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

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

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

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2019. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in Internal Control—

Integrated Framework (2013). Based on its assessment, our management believes that, as of December 31, 2019, our internal control over financial reporting was effective based on those criteria.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting due to an exemption established by the Jumpstart Our Business Startups Act of 2012 for "emerging growth companies".

Changes in Internal Control over Financial Reporting

During the three months ended December 31, 2019, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is set forth under the captions "Election of Directors," "Directors," "Corporate Governance," "Executive Officers," "Corporate Governance—Code of Ethics" and "Compensation Governance—Audit Committee Financial Expert" in our definitive proxy statement for our 2020 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2019, and is incorporated into this Annual Report on Form 10-K by reference.

We are also required under Item 405 of Regulation S-K to provide information concerning delinquent filers of reports under Section 16 of the Securities and Exchange Act of 1934, as amended. If applicable, this information will be set forth under the caption "Delinquent Section 16(a) Reports" in our definitive proxy statement for the 2020 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission no later than 120 days after the end of our fiscal year and is incorporated herein by reference.

We have adopted a code of ethics, our Code of Business Conduct and Ethics, that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, and persons performing similar functions. Our Code of Business Conduct and Ethics, as well as our corporate governance guidelines and the charters for the audit, compensation, nominating and corporate governance, and science and technology committees of our Board of Directors, are each accessible under the "Corporate Governance" heading of the "Investors" section of our website, http://www.catabasis.com. We also intend to disclose in the same location on our website, any amendments to, or waivers from, our Code of Business Conduct & Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

Item 11. Executive Compensation

The information required by this Item is set forth under the captions "Executive Officers," "Executive Compensation—Compensation Discussion and Analysis," "Corporate Governance—Compensation Committee Interlocks and Insider Participation," "Compensation Committee Report" and "Director Compensation" in our definitive proxy statement for our 2020 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2019, and is incorporated into this Annual Report on Form 10-K by reference.

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

Securities Authorized for Issuance under Equity Compensation Plans

The following table contains information about our equity compensation plans as of December 31, 2019:

Plan category	Number of securities to be issued upon exercise of outstanding stock options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders	785,832(1)	$ 16.48	637,965(2)
Equity compensation plans not approved by security holders	—	—	—
Total	785,832	$ 16.48	637,965

(1) Consists of stock options outstanding as of December 31, 2019 under our Amended and Restated 2008 Equity Incentive Plan, as amended, and our Amended and Restated 2015 Stock Incentive Plan.

(2) Consists of shares issuable under our Amended and Restated 2015 Stock Incentive Plan and our 2015 Employee Stock Purchase Plan, but does not reflect an automatic increase that was effective as of January 1, 2020 of 36,470 shares under the 2015 Employee Stock Purchase Plan. Our 2015 Employee Stock Purchase Plan provides for further annual increases, to be added as of the first day of each fiscal year, from January 1, 2020 until, and including, January 1, 2026, in an amount equal to the least of 36,470 shares of our common stock, 1% of the total number of shares of our common stock outstanding on the first day of the applicable year, and an amount determined by our board of directors.

The other information required by this Item is set forth under the caption "Security Ownership of Certain Beneficial Owners and Management" in our definitive proxy statement for our 2020 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2019 and is incorporated into this Annual Report on Form 10-K by reference.

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

The information required by this Item is set forth under the captions "Corporate Governance—Board Independence" and "Director Compensation—Transactions with Related Persons" in our definitive proxy statement for our 2020 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2019 and is incorporated into this Annual Report on Form 10-K by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item is set forth under the caption "Independent Registered Public Accounting Firm" in our definitive proxy statement for our 2020 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2019 and is incorporated into this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a)(1) Financial Statements

The financial statements listed below are filed as part of this Annual Report on Form 10-K and are incorporated herein by reference.

(a)(2) Financial Statement Schedules

All financial schedules have been omitted because the required information is either presented in the consolidated financial statements filed as part of this Annual Report on Form 10-K or the notes thereto or is not applicable or required.

(a)(3) Exhibits

The exhibits required for this Annual Report on Form 10-K by Item 601 of Regulation S-K and Item 15(b) of Form 10-K are listed in the following Exhibit Index:

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the Securities and Exchange Commission on July 1, 2015)
3.2	Certificate of Amendment to Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the Securities and Exchange Commission on December 31, 2018)
3.3	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the Securities and Exchange Commission on July 1, 2015)
4.1	Specimen stock certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on June 11, 2015)
4.2	Form of Common Stock Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the Securities and Exchange Commission on June 20, 2018)
4.3	Form of Common Stock Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the Securities and Exchange Commission on February 6, 2019)
4.4	Description of Registered Securities
10.1	Warrant to purchase shares of Series B Preferred Stock issued on August 27, 2014 by the Registrant to Square 1 Bank (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.2	Warrant to purchase shares of Series B Preferred Stock issued on August 27, 2014 by the Registrant to Midcap Financial SBIC, L.P. (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.3*	Amended and Restated 2008 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.4*	Form of Incentive Stock Option Agreement under Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)

Exhibit Number	Description of Exhibit
10.5*	Form of Nonstatutory Stock Option Agreement under Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.6	Amended and Restated 2015 Stock Incentive Plan (incorporated by reference to Exhibit 99.1 to the Registrant's Registration Statement on Form S-8 (File No. 333-229643) filed with the Securities and Exchange Commission on February 13, 2019)
10.7*	Form of Incentive Stock Option Agreement under 2015 Stock Incentive Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on June 3, 2015)
10.8*	Form of Nonstatutory Stock Option Agreement under 2015 Stock Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on June 3, 2015)
10.9*	2015 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.22 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on June 3, 2015)
10.10	Second Amended and Restated Investors' Rights Agreement, dated as of March 17, 2015, among the Registrant and the other parties thereto, as amended June 10, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on June 11, 2015)
10.11*	Amended and Restated Employment Agreement, dated as of April 7, 2010, by and between the Registrant and Jill C. Milne, as amended (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.12*	Catabasis Pharmaceuticals, Inc. Executive Severance Benefits Plan effective April 15, 2016 (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the Securities and Exchange Commission on April 19, 2016)
10.13*	Form of Indemnification Agreement by and between the Registrant and each of its executive officers and directors (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.14	Indenture of Lease, dated as of December 17, 2010, by and between the Registrant and RB Kendall Fee, LLC, as amended (incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.15	Second Amendment of Lease, dated as of July 16, 2015, by and between the Registrant and DWF IV One Kendall, LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the Securities and Exchange Commission on November 11, 2015)

Exhibit Number	Description of Exhibit
10.16	Third Amendment of Lease, dated as of November 3, 2016, by and between the Registrant and DWF IV One Kendall, LLC (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the Securities and Exchange Commission on November 7, 2016)
10.17	Fourth Amendment of Lease, dated August 7, 2017, by and between Registrant and ARE-MA REGION NO. 59, LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the Securities and Exchange Commission on August 10, 2017)
10.18	Sublease Agreement, dated as of September 14, 2018, by and between Inzen Therapeutics, Inc. and the Registrant (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the Securities and Exchange Commission on October 16, 2018)
10.19	Sublease Agreement, dated as of September 9, 2019, by and between Allied Minds, LLC and the Registrant (Incorporated by reference to Exhibit 10.1 to the to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the Securities and Exchange Commission on November 7, 2019).
10.20	Warrant to purchase shares of Series B Preferred Stock issued on March 31, 2015 to Square 1 Bank (incorporated by reference to Exhibit 10.19 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.21	Warrant to purchase shares of Series B Preferred Stock issued on March 31, 2015 to Midcap Financial Trust (incorporated by reference to Exhibit 10.20 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.22	Warrant to purchase shares of Series B Preferred Stock issued on March 31, 2015 to Flexpoint MCLS Holdings, LLC (incorporated by reference to Exhibit 10.21 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the Securities and Exchange Commission on May 13, 2015)
10.23	Summary of Non-employee Director Compensation Program (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the Securities and Exchange Commission on May 12, 2016)
10.24	Sales Agreement, dated May 14, 2019, by and between the Registrant and Cowen and Company, LLC (Incorporated by reference to Exhibit 1.1 to the Registrant's Registration Statement on Form S-3 (File No. 333-231441) filed with the Securities and Exchange Commission on May 14, 2019).
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to the Registrant's Annual Report on Form 10-K (File No. 001-37467) filed with the Securities and Exchange Commission on March 15, 2016)
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm
24.1	Power of Attorney (see signature page of this Annual Report on Form 10-K)
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended

Exhibit Number	Description of Exhibit
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Calculation Linkbase
101.LAB	XBRL Taxonomy Labels Linkbase Document
101.PRE	XBRL Taxonomy Presentation Linkbase Document
101.DEF	Taxonomy Extension Definition Linkbase Document

* Management contract or compensatory plan arrangement.

Item 16. Form 10-K Summary

Not applicable.

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Catabasis Pharmaceuticals, Inc. (the "Company") as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles.

Adoption of ASU 2016-02

As discussed in Note 2 to the consolidated financial statements, the Company has changed its method of accounting for leases as of January 1, 2019 due to the adoption of ASU No. 2016-02, Leases (Topic 842), and the related amendments.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2010.

Boston, Massachusetts

March 10, 2020

Catabasis Pharmaceuticals, Inc.

Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 9,899	$ 15,294
Short-term investments	26,345	22,276
Prepaid expenses and other current assets	2,714	1,345
Total current assets	38,958	38,915
Right-of-use asset	2,349	—
Other assets	473	254
Total assets	$ 41,780	$ 39,169
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,197	$ 1,408
Accrued expenses	2,610	2,763
Current portion of operating lease liabilities	1,225	—
Total current liabilities	5,032	4,171
Other long-term liabilities	—	56
Long-term portion of operating lease liabilities	1,028	—
Total liabilities	6,060	4,227
Commitments (Note 6)		
Stockholders' equity:		
Preferred stock, $0.001 par value per share, 5,000,000 shares authorized and no shares issued and outstanding	—	—
Common stock, $0.001 par value per share, 150,000,000 shares authorized; 12,433,600 and 7,141,996 shares issued and outstanding at December 31, 2019 and December 31, 2018, respectively	12	7
Additional paid-in capital	259,305	232,243
Accumulated other comprehensive loss	—	(4)
Accumulated deficit	(223,597)	(197,304)
Total stockholders' equity	35,720	34,942
Total liabilities and stockholders' equity	$ 41,780	$ 39,169

The accompanying notes are an integral part of these consolidated financial statements.

Catabasis Pharmaceuticals, Inc.

Consolidated Statements of Operations

(in thousands, except share and per share data)

	Year Ended December 31,	
	2019	2018
Operating expenses:		
Research and development	18,317	17,042
General and administrative	8,771	9,329
Total operating expenses	27,088	26,371
Loss from operations	(27,088)	(26,371)
Other income (expense):		
Interest expense	—	(100)
Interest and investment income	845	425
Other (expense) income, net	(50)	176
Total other income, net	795	501
Net loss	$ (26,293)	$ (25,870)
Net loss per share—basic and diluted	$ (2.35)	$ (5.12)
Weighted-average common shares outstanding used in net loss per share—basic and diluted	11,199,057	5,054,823

The accompanying notes are an integral part of these consolidated financial statements

Catabasis Pharmaceuticals, Inc.

Consolidated Statements Comprehensive Loss

(in thousands)

	Year Ended December 31,	
	2019	2018
Net loss	$ (26,293)	$ (25,870)
Other comprehensive income:		
Gains (losses) on short-term investments	4	(4)
Total other comprehensive income (loss):	4	(4)
Comprehensive loss	$ (26,289)	$ (25,874)

The accompanying notes are an integral part of these consolidated financial statements

Catabasis Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity

(in thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive (Loss) Gain	Total Stockholders' Equity
	Number of Shares	Par Value				
Balance at December 31, 2017	2,364,526	$ 2	$ 183,224	$ (171,434)	$ —	$ 11,792
Issuance of common stock and warrants in public offering, net of $3.1 million in issuance costs	4,200,000	4	38,882	—	—	38,886
Issuance of common stock for at-the-market offerings, net of issuance costs of $0.4 million	577,195	1	8,362	—	—	8,363
Proceeds from exercises of common stock options	291	—	4	—	—	4
Stock-based compensation expense	—	—	1,771	—	—	1,771
Fractional shares eliminated pursuant to reverse stock split	(16)	—	—	—	—	—
Unrealized loss on short-term investments	—	—	—	—	(4)	(4)
Net loss	—	—	—	(25,870)	—	(25,870)
Balance at December 31, 2018	7,141,996	$ 7	$ 232,243	$ (197,304)	$ (4)	$ 34,942
Issuance of common stock and warrants in public offering, net of $1.5 million in issuance costs	4,000,000	4	18,501	—	—	18,505
Issuance of common stock for at-the-market offerings, net of issuance costs of $0.4 million	1,282,904	1	6,995	—	—	6,996
Proceeds from exercises of warrants	8,700	—	54	—	—	54
Stock-based compensation expense	—	—	1,512	—	—	1,512
Unrealized gain on short-term investments	—	—	—	—	4	4
Net loss	—	—	—	(26,293)	—	(26,293)
Balance at December 31, 2019	12,433,600	$ 12	$ 259,305	$ (223,597)	$ —	$ 35,720

The accompanying notes are an integral part of these consolidated financial statements

Catabasis Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows

(in thousands)

	Year Ended December 31,	
	2019	2018
Operating activities		
Net loss	$ (26,293)	$ (25,870)
Reconciliation of net loss to net cash used in operating activities:		
Depreciation and amortization	26	119
Stock-based compensation expense	1,512	1,771
Accretion of discount/premium on investment securities	5	(6)
Non-cash interest expense	—	37
Gain on disposal of property and equipment	18	(297)
Services received in non-monetary exchange	33	19
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(1,289)	(177)
Other assets	—	(85)
Right-of-use asset- operating	(96)	—
Accounts payable	(211)	662
Accrued expenses	(205)	396
Other liabilities	(69)	(34)
Net cash used in operating activities	(26,569)	(23,465)
Investing activities		
Purchases of short-term investments	(155,197)	(70,364)
Sales and maturities of short-term investments	151,127	48,090
Purchases of property and equipment	(12)	—
Proceeds from sale of property and equipment	—	369
Net cash used in investing activities	(4,082)	(21,905)
Financing activities		
Proceeds from public offerings, net of issuance costs	18,505	38,886
Proceeds from at-the-market offering, net of issuance costs	7,061	8,253
Proceeds from exercise of common stock options and warrants	54	4
Payments on borrowing	—	(2,848)
Net cash provided by financing activities	25,620	44,295
Net decrease in cash, cash equivalents and restricted cash	(5,031)	(1,075)
Cash, cash equivalents and restricted cash, beginning of period	15,407	16,482
Cash, cash equivalents and restricted cash, end of period	$ 10,376	$ 15,407
Supplemental disclosure of cash flow information		
Cash paid for interest	$ —	$ 79
Non-cash investing activities:		
Fixed asset purchases included in accounts payable	$ —	$ 18
Non-cash financing activities:		
At-the-market issuance costs included in current liabilities	$ 65	$ 110

The accompanying notes are an integral part of these consolidated financial statements.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

1. Organization and Operations

The Company

Catabasis Pharmaceuticals, Inc. (the "Company") is a clinical-stage biopharmaceutical company. The Company's lead program is edasalonexent, an oral small molecule designed to inhibit NF-kB, or nuclear factor kappa-light-chain-enhancer of activated B cells, in development for the treatment of Duchenne muscular dystrophy ("DMD"). The Company believes 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 has granted orphan drug, fast track and rare pediatric disease designations to edasalonexent for the treatment of DMD. The European Commission has granted orphan medicinal product designation to edasalonexent for the treatment of DMD. The Company was incorporated in the State of Delaware on June 26, 2008.

Liquidity

The Company has entered into various sales agreements with Cowen and Company LLC, ("Cowen"), pursuant to which the Company could issue and sell shares of common stock under at-the-market offering programs (the "ATM Programs"). Shares sold pursuant to these sales agreements were sold pursuant to shelf registration statements, one of which became effective on July 19, 2016 and which was replaced by a new shelf registration statement, which became effective May 22, 2019. The Company pays Cowen 3% of the gross proceeds from any common stock sold through these sales agreements. The Company currently has $43.6 million remaining available under its sales agreement.

During the year ended December 31, 2019, the Company sold an aggregate of 1,282,904 shares of common stock pursuant to the ATM Programs, at an average price of $5.81 per share, for gross proceeds of $7.5 million, resulting in net proceeds of $7.0 million after deducting sales commissions and offering expenses.

On February 6, 2019, the Company entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering (the "February 2019 Financing") of 4,000,000 shares of common stock and accompanying warrants to purchase up to 2,000,000 shares of common stock, at a combined price to the public of $5.00 per unit, for net proceeds of $18.5 million.

On June 19, 2018, the Company entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering (the "June 2018 Financing") of 4,200,000 shares of the Company's common stock, par value $0.001 per share, and accompanying warrants to purchase up to 4,200,000 shares of common stock, at a combined price to the public of $10.00 per unit, for gross proceeds of $42.0 million, and net proceeds of $38.9 million.

As of December 31, 2019, the Company had an accumulated deficit of $223.6 million. The Company has been primarily involved with research and development activities and has incurred operating losses and negative cash flows from operations since its inception.

The Company is subject to a number of risks similar to other life science companies, including, but not limited to, successful discovery and development of its drug candidates, raising additional capital, development by its competitors of new technological innovations, protection of proprietary technology and regulatory approval and market acceptance of the Company's products. The Company anticipates that it will continue to incur significant operating losses for the next several years as it continues to develop its product candidates.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

1. Organization and Operations (Continued)

As of December 31, 2019, the Company had available cash, cash equivalents and short-term investments of $36.2 million. Subsequent to December 31, 2019, the Company raised net proceeds of $25.6 million through 2020 equity financings. Based on the Company's current operating plan, the Company believes it has sufficient cash, cash equivalents and short-term investments to fund operations for at least 12 months following the issuance of these consolidated financial statements.

The Company will require substantial additional capital to fund operations. The Company has not generated any product revenues and has financed its operations primarily through public offerings and private placements of its equity securities. There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate product revenue or revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations, and financial condition.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary, Catabasis Securities Corporation. All intercompany balances and transactions have been eliminated in consolidation. These consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ from such estimates.

The Company utilizes certain estimates to record expenses relating to research and development contracts. These contract estimates, which are primarily related to the length of service of each contract and the amount of service provided as of each measurement date, are determined by the Company based on input from internal project management, as well as from third-party service providers.

Off-Balance Sheet Risk and Concentrations of Credit Risk

The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts or other foreign hedging arrangements. Financial instruments that subject the Company to credit risk primarily consist of cash, cash equivalents, short-term investments and restricted cash. The primary objectives for the Company's investment portfolio are the preservation of capital and the maintenance of liquidity. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Cash and Cash Equivalents and Restricted Cash

The Company considers highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents, which consist of money market funds, corporate debt securities and reverse repurchase agreements are stated at fair value. Cash and cash equivalents consist of the following (in thousands):

	December 31,	
	2019	2018
Cash	$ 2,530	$ 4,390
Money market fund	5,432	5,956
Corporate debt securities	1,937	1,948
Reverse repurchase agreements	—	3,000
Total	$ 9,899	$ 15,294

The reconciliation of cash, cash equivalents and restricted cash reported within the applicable balance sheet that sum to the total of the same such amount shown in the statement of cash flows is as follows:

	December 31,	
	2019	2018
Cash and cash equivalents	$ 9,899	$ 15,294
Restricted cash(1)	477	113
Total	$ 10,376	$ 15,407

(1) Included in prepaid expenses and other current assets and other assets as of December 31, 2019 and other assets as of December 31, 2018 in the consolidated balance sheets

Short-Term Investments

The Company classifies all corporate debt securities with a remaining maturity of greater than three months and reverse repurchase agreements with a remaining maturity of greater than one business day at the time of purchase as short-term investments. Short-term investments are recorded at fair value, with the unrealized gains and losses reported in other comprehensive loss. The amortized cost of debt securities is adjusted for the amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest and investment income. Realized gains and losses, interest, dividends and declines in value judged to be other-than-temporary are included in interest and investment income.

The cost of securities sold is based on the specific identification method for purposes of recording realized gains and losses. To determine whether an other-than-temporary impairment exists, the Company considers whether it has the ability and intent to hold the investment until a market price recovery, and whether evidence indicating the recoverability of the cost of the investment outweighs evidence to the contrary.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Fair Value of Financial Instruments

The fair value hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three broad levels as follows: Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities; Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; and Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

The carrying amounts reflected in the balance sheets for cash equivalents, restricted cash, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values at December 31, 2019 and 2018, due to their short-term nature. There have been no changes to the valuation methods during the years ended December 31, 2019 and 2018. The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between levels during the year ended December 31, 2019 and 2018.

The Company's investment portfolio may include fixed income securities that do not always trade on a daily basis. As a result, the pricing services used by the Company apply other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare valuations. The Company validates the prices provided by its third party pricing services by obtaining market values from other pricing sources and analyzing pricing data in certain instances. The Company also invests in certain reverse repurchase agreements which are collateralized by deposits in the form of U.S. Government Securities and Obligations for an amount no less than 102% of their value. The Company does not record an asset or liability for the collateral as the Company is not permitted to sell or re-pledge the collateral. The collateral has at least the prevailing credit rating of U.S. Government Treasuries and Agencies. The Company utilizes a third party custodian to manage the exchange of funds and ensure that collateral received is maintained at 102% of the value of the reverse repurchase agreements on a daily basis.

Impairment of Long-Lived Assets

The Company continually evaluates whether events or circumstances have occurred that indicate that the estimated remaining useful life of its long-lived assets may warrant revision or that the carrying value of these assets may be impaired. The Company has not recognized any significant impairment charges from inception through December 31, 2019.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs include salaries and personnel-related costs, stock-based compensation, consulting fees, fees paid for contract research services, the costs of laboratory equipment and facilities and other external costs. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred. The deferred amounts are expensed as the related goods are delivered or the services are performed.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with Accounting Standards Codification ("ASC") Topic 718, *Compensation—Stock Compensation (*"ASC 718"). ASC 718 requires all share-based payments to employees, including grants of employee stock options, to be recognized in the statements of operations based on their grant date fair values. For granted stock options, the Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model. The use of the Black-Scholes option-pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the Common Stock consistent with the expected term of the option, risk-free interest rates and expected dividend yields of the Common Stock.

For awards subject to service-based vesting conditions, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock options on a straight-line basis over the requisite service period.

The Company expenses restricted stock awards based on the fair value of the award on a straight-line basis over the associated service period of the award.

During the years ended December 31, 2019 and 2018, the Company recorded stock-based compensation expense for employee and non-employee stock options and restricted stock, which was allocated as follows in the statements of operations (in thousands):

	Year Ended December 31,	
	2019	2018
Research and development	$ 616	$ 673
General and administrative	896	1,098
Total	$ 1,512	$ 1,771

No related tax benefits were recognized for the years ended December 31, 2019 and 2018.

Net Loss Per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for Common Stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of Common Stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the Company's dilutive net loss per share calculation, stock options and warrants to purchase Common Stock were considered to be Common Stock equivalents but were excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share were the same for all periods presented.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

The following Common Stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2019	2018
Stock options	785,832	433,389
Common stock warrants	6,193,749	4,202,449
	6,979,581	4,635,838

Income Taxes

The Company provides deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax assets to the amount that will more likely than not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC Topic 740, *Expenses—Income Taxes*. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. The Company did not have any significant uncertain tax positions for any periods presented.

Segment Information

Operating segments are identified as components of an enterprise for which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision making group, in making decisions on how to allocate resources and assess performance. The Company views its operations and manages its business in one operating segment. The Company operates in one geographic segment.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. For the years ended December 31, 2019 and 2018 amounts in accumulated other comprehensive loss were comprised of unrealized gains and losses on short-term investments.

Leases

Effective January 1, 2019, the Company determines if an arrangement is a lease at inception. Operating leases are included in right-of-use ("ROU") lease assets, current portion of lease obligations, and long-term lease obligations on the Company's balance sheets. The Company does not currently hold any financing leases.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

ROU lease assets represent the Company's right to use an underlying asset for the lease term and lease obligations represent the Company's obligation to make lease payments arising from the lease. Operating ROU lease assets and obligations are recognized at the commencement date based on the present value of lease payments over the lease term. As the Company's facility leases do not provide an implicit rate, the Company uses its estimated incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The Company's ROU lease assets also include any lease payments made and excludes lease incentives. If the Company's facility lease includes options to terminate the lease which would affect the lease period when it is reasonably certain that the Company will exercise that option. Lease expense for lease payments under facility leases are recognized on a straight-line basis over the lease term.

Recent Accounting Pronouncements—Adopted

In February 2016, the Financial Accounting Standards Board, ("FASB") issued Accounting Standards Update ("ASU") 2016-02, *Leases*. This standard amends the existing guidance to require lessees to present most leases on their balance sheets and recognize corresponding expenses on their statements of operations. The FASB also provided practical expedients that give lessors an option to combine non-lease and associated lease components when certain criteria are met and requires a lessor to account for the combined component in accordance with the new revenue standard if the associated non-lease components are the predominant component. The Company adopted this standard effective January 1, 2019 by recording the cumulative effect on the date of the adoption. The Company has elected the package of practical expedients permitted under the transition guidance in ASC Topic 842, *Leases*, ("ASC Topic 842"). Accordingly, the Company accounted for its existing operating leases as operating leases under the new guidance, without reassessing (a) whether the contracts contain a lease under ASC Topic 842, (b) whether classification of the operating leases would be different in accordance with ASC Topic 842, or (c) whether the unamortized initial direct costs before transition adjustments would have met the definition of initial direct costs in ASC Topic 842 at lease commencement. As a result of the adoption of the new lease accounting guidance, the Company recognized on January 1, 2019 a lease liability and right-of-use asset of approximately $1.9 million. The lease liability represents the present value of the remaining lease payments, discounted using the Company's estimated incremental borrowing rate of 7.49%. The ROU asset represents the lease liability adjusted for any prepaid and accrued rent payments as well as any remaining liability associated with an active sublease. This standard did not have a material impact on the Company's cash flows from operations and had no impact on the Company's operating results. The most significant impact was the recognition of ROU assets and lease obligations for operating leases.

Recent Accounting Pronouncements—Not Yet Adopted

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

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments— Credit Losses (Topic 326).* This standard requires a financial asset to be presented at amortized cost basis at the net amount expected to be collected. It also requires that credit losses relating to available-for-sale debt securities should be recorded through an allowance for credit losses. In November 2019, the FASB issued an

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

amendment making this ASU effective for annual reporting periods beginning after December 15, 2022 for smaller reporting companies. The Company is currently evaluating the impact that this standard will have on its consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820)*. This standard includes amendments regarding changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and disclosure requirements of measurement uncertainty. This amendment is effective for annual reporting periods beginning after December 15, 2019. The Company is currently evaluating the impact that this standard will have on its consolidated financial statements.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

3. Financial Instruments

The following tables present information about the Company's financial assets and liabilities that have been measured at fair value, and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value. Below is a summary of assets and liabilities measured at fair value on a recurring basis (in thousands):

	As of December 31, 2019			
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Cash and cash equivalents:				
Money market funds	$ 5,432	$ —	$ —	$ 5,432
Corporate debt securities	—	1,937	—	1,937
Short-term investments:				
Commercial paper	—	1,993	—	1,993
Corporate debt securities	—	3,352	—	3,352
Reverse repurchase agreements	—	21,000	—	21,000
Total assets	$ 5,432	$ 28,282	$ —	$ 33,714

	As of December 31, 2018			
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Cash and cash equivalents:				
Money market funds	$ 5,956	$ —	$ —	$ 5,956
Corporate debt securities	—	1,948	—	1,948
Reverse repurchase agreements	—	3,000	—	3,000
Short-term investments:				
Corporate debt securities	—	7,276	—	7,276
Reverse repurchase agreements	—	15,000	—	15,000
Total assets	$ 5,956	$ 27,224	$ —	$ 33,180

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

4. Short-Term Investments

The following table summarizes the short-term investments held at December 31, 2019 and 2018 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2019				
Commercial paper	$ 1,993	$ —	$ —	$ 1,993
Corporate debt securities	3,352	—	—	3,352
Reverse repurchase agreements	21,000	—	—	21,000
Total	$ 26,345	$ —	$ —	$ 26,345

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2018				
Corporate debt securities	$ 7,280	$ —	$ (4)	$ 7,276
Reverse repurchase agreements	15,000	—	—	15,000
Total	$ 22,280	$ —	$ (4)	$ 22,276

The contractual maturities of all short-term investments held at December 31, 2019 and 2018 were one year or less. There were four short-term investments in an unrealized loss position at December 31, 2019, none of which had been in an unrealized loss position for more than 12 months. The aggregate fair value of these securities at December 31, 2019 was approximately $3.4 million. There were seven short-term investments in an unrealized loss position at December 31, 2018, none of which had been in an unrealized loss position for more than 12 months. The aggregate fair value of these securities at December 31, 2018 was approximately $7.3 million. The Company did not hold any securities with other-than-temporary impairments at December 31, 2019 and 2018.

Gross realized gains and losses on the sales of short-term investments are included in other income, net. Unrealized holding gains or losses for the period that have been included in accumulated other comprehensive income, as well as gains and losses reclassified out of accumulated other comprehensive income into other income, net were not material to the Company's consolidated results of operations. During the years ended December 31, 2019 and 2018 all proceeds related to maturities of underlying securities. The gains on proceeds of maturities of short-term investments were not material to the Company's consolidated results of operations for the years ended December 31, 2019 and 2018.

5. Restricted Cash

At December 31, 2019 the Company had two outstanding letters of credit for a total of approximately $0.5 million as security deposits for its operating lease agreements for office space (Note 7). The Company is required to maintain these deposits for the duration of the lease agreements.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

6. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2019	2018
Accrued compensation	$ 1,365	$ 1,241
Accrued contracted research costs	737	680
Accrued professional fees	370	393
Accrued other	98	109
Accrued franchise tax	40	168
Accrued severance	—	172
Total	$ 2,610	$ 2,763

7. Commitments

In November 2010, the Company entered into an operating lease for office and laboratory space, which has been amended multiple times. Based on the latest amendment, the lease agreement includes escalating rent payments and is effective through June 30, 2020.

On October 15, 2018, the Company entered into a short-term lease with Inzen Therapeutics ("Inzen"), to sublease a portion of the Company's facility (the "Sublease"). The sublease term is from October 15, 2018 through June 30, 2020. Inzen is obligated to pay the Company approximately $0.5 million in base rent during the year ended December 31, 2020, respectively. The Company is still obligated to all payment terms pursuant to the lease agreement, as amended. During the years ended December 31, 2019 and 2018, the Company received $1.0 million and $0.3 million in payments from Inzen which was recorded as a reduction to rent expense in the accompanying consolidated statement of operations.

In November 2019, the Company entered into a sublease for office space which was classified as an operating lease. At inception of the lease, the Company recognized a lease liability and right-of-use asset of approximately $1.7 million. The lease liability represents the present value of the remaining lease payments, discounted using the Company's estimated incremental borrowing rate of 7.49%. The ROU asset represents the lease liability adjusted for any prepaid and accrued rent payments.

Future minimum payments required under the non-cancelable operating leases as of December 31, 2019 are summarized as follows (in thousands):

Period Ending December 31,	Amount
2020	1,449
2021	740
2022	438
Total minimum lease payments	$ 2,627

Rent expense was $0.4 million and $1.1 million for the years ended December 31, 2019 and 2018, respectively. Lease payments were $1.4 million for each of the years ended December 31, 2019 and 2018, respectively.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

8. Stockholders' Equity

Preferred Stock

As of December 31, 2019, the Company had 5,000,000 shares of preferred stock authorized for issuance, $0.001 par value per share, with none issued or outstanding. Preferred stock may be issued from time to time in one or more series, each series to have such terms as stated or expressed in the resolutions providing for the issue of such series adopted by the board of directors of the Company. Preferred stock which may be redeemed, purchased or acquired by the Company may be reissued except as otherwise provided by law.

Common Stock Warrants

February 2019 Warrants

In the February 2019 Financing, the Company issued warrants to purchase 2,000,000 shares of common stock with an exercise price of $6.25 per share, which were immediately exercisable upon issuance and will expire five years from the date of issuance.

The terms of the warrants include certain provisions related to fundamental transactions, a cashless exercise provision in the event registered shares are not available, and do not include any mandatory redemption provisions. Therefore, the warrants have been classified in stockholders' equity. Any changes to the fair value of the warrants will not be recognized so long as the warrants continue to be equity classified.

As of December 31, 2019, warrants to purchase 1,991,300 shares that were issued in the February 2019 Financing were outstanding with a remaining contractual life of 4.11 years.

June 2018 Warrants

In the June 2018 Financing, the Company issued warrants to purchase 4,200,000 shares of common stock with an exercise price of $12.00 per share, which were immediately exercisable upon issuance and will expire five years from the date of issuance.

The terms of the warrants include certain provisions related to fundamental transactions, a cashless exercise provision in the event registered shares are not available and do not include any mandatory redemption provisions. Therefore, the warrants have been classified in stockholders' equity. Any changes to fair value of the warrants will not be recognized so long as the warrants continue to be equity classified.

As of December 31, 2019, all warrants related to this transaction were outstanding with a remaining contractual life of 3.47 years.

Common Stock

As of December 31, 2019, the Company had 150,000,000 shares of Common Stock authorized for issuance, $0.001 par value per share, with 12,433,600 shares issued and outstanding. The voting, dividend and liquidation rights of holders of Common Stock are subject to and qualified by the rights,

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

8. Stockholders' Equity (Continued)

powers and preferences of the holders of any outstanding Preferred Stock. The Company's Common Stock has the following characteristics:

Voting

The holders of Common Stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders and written actions in lieu of meetings.

Dividends

The holders of Common Stock are entitled to receive dividends, if and when declared by the board of directors. Cash dividends may not be declared or paid to holders of Common Stock until paid on each series of outstanding Preferred Stock in accordance with their respective terms. No dividends have been declared or paid from the Company's inception through December 31, 2019.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, the holders of Common Stock are entitled to share ratably in the Company's assets available for distribution to stockholders, subject to any preferential or other rights of any then-outstanding Preferred Stock.

Reserved for Future Issuance

The Company has reserved for future issuance the following shares of Common Stock:

	December 31,	
	2019	2018
Warrants for the purchase of Common Stock	6,193,749	4,202,449
Options outstanding to purchase Common Stock	785,832	433,389
Options available for future issuance to purchase Common Stock	525,484	877,917
Shares reserved for the employee stock purchase plan	112,481	76,011
Total	7,617,546	5,589,766

9. Stock Incentive Plans

Prior to the Company's initial public offering in June 2015 (the "IPO"), the Company granted awards to eligible participants under its 2008 Equity Incentive Plan. In May 2015, the Company's board of directors adopted and, in June 2015, the Company's stockholders approved the 2015 Stock Incentive Plan ("2015 Plan"), which became effective immediately prior to the effectiveness of the IPO. Subsequent to the IPO, option grants are awarded to eligible participants only under the 2015 Plan.

The 2015 Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2015 Plan.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

9. Stock Incentive Plans (Continued)

Terms of stock option agreements, including vesting requirements, are determined by the Company's board of directors, subject to the provisions of the applicable stock incentive plan. Options granted by the Company generally vest ratably over four years, with a one-year cliff, and options are exercisable from the date of grant for a period of ten years. For options granted through December 31, 2019, the exercise price or purchase price, as applicable, equaled the estimated fair value of the Common Stock as determined by the Company's board of directors on the date of grant.

A summary of the Company's stock option activity and related information for employees and non-employees follows:

	Shares	Weighted-Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2018	433,389	$ 29.05	7.97	$ —
Granted	454,420	$ 4.86		
Cancelled or forfeited	(101,977)	$ 18.12		
Outstanding at December 31, 2019	785,832	$ 16.48	8.13	$ 470
Vested and Exercisable at December 31, 2019	289,782	$ 33.91	6.59	$ 9

There were no options exercised in the year ended December 31, 2019. The total intrinsic value of options exercised in the year ended December 31, 2018 was $1 thousand. The total fair value of employee options vested for the years ended December 31, 2019 and 2018 was $1.5 million and $1.7 million, respectively. The weighted-average grant date fair value of options granted to employees and non-employees for the years ended December 31, 2019 and 2018 was $3.25 and $6.64, respectively.

At December 31, 2019, the total unrecognized compensation expense related to unvested stock option awards was $1.7 million. The Company expects to recognize that cost over a weighted-average period of approximately 2.2 years.

Stock-Based Compensation Expense

The fair value of stock options granted to employees and non-employees was estimated using the Black-Scholes option-pricing model based on the following assumptions:

	Year Ended December 31,	
	2019	2018
Weighted-average expected volatility	68.9 - 110.5%	73.7 - 76.9%
Expected term (in years)	5.50 - 10.00	5.75 - 6.25
Risk-free interest rate	1.39 - 2.69%	2.67 - 2.84%
Expected dividend yield	0%	0%

Volatility

Due to the lack of company-specific historical and implied volatility data of its Common Stock, the Company does not have relevant historical data to support its expected volatility. As such, the

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

9. Stock Incentive Plans (Continued)

Company has used a weighted average of expected volatility based on the volatilities of a representative group of publicly traded biopharmaceutical companies. For purposes of identifying representative companies, the Company considered characteristics such as number of product candidates in early stages of product development, area of therapeutic focus, and length of trading history. The expected volatility was determined using an average of the historical volatilities of the representative group of companies for a period equal to the expected term of the option grant. The Company intends to continue to consistently apply this process using the same representative companies until a sufficient amount of historical information regarding the volatility of the Company's own share price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation.

Expected Term

The Company uses the "simplified method" to estimate the expected term of stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of the Company's stock options, taking into consideration multiple vesting tranches. The Company utilizes this method due to lack of historical exercise data and the plain-vanilla nature of the Company's share-based awards.

Risk-Free Rate

The risk-free rate was based on the yield curve of U.S. Treasury securities with periods commensurate with the expected term of the options being valued.

10. Income Taxes

For the years ended December 31, 2019 and 2018, the Company did not record a provision for federal or state income taxes as it has incurred cumulative net operating losses since inception.

A reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows for the years ended December 31, 2019 and 2018:

	Year Ended December 31,	
	2019	2018
Federal income tax (benefit) at statutory rate	21.00%	21.00%
Permanent differences	(0.57)	(0.68)
Federal research and development credits and adjustments	2.42	4.25
State income tax, net of federal benefit	5.50	6.84
Other	0.49	(1.41)
Change in valuation allowance	(28.85)	(30.00)
Effective income tax rate	—%	—%

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

10. Income Taxes (Continued)

The Company's deferred tax assets consisted of the following (in thousands):

	Year Ended December 31,	
	2019	2018
Deferred tax assets		
Net operating loss carryforwards	$ 55,283	$ 48,107
Tax credit carryforwards	8,030	7,174
Capitalized research and development	922	1,394
Capitalized legal expenses	1,073	1,132
Lease liability	639	—
Other differences	1,453	1,370
Total deferred tax assets	67,400	59,177
Deferred tax liabilities		
ROU asset	(639)	—
Valuation allowance	(66,761)	(59,177)
Net deferred tax assets	$ —	$ —

The Company recorded an increase to the valuation allowance of $7.6 million during the year ended December 31, 2019 due primarily to the federal and state net operating losses and tax credits generated. The Company recorded an increase to the valuation allowance of $7.8 million during the year ended December 31, 2018 which was also primarily due to the federal and state net operating losses and tax credits generated.

In assessing the realizability of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible. Due to the Company's history of losses and expectation of future losses, the deferred tax assets were fully offset by a valuation allowance at December 31, 2019 and 2018.

As of December 31, 2019, the Company had approximately $203.0 million of federal and $200.2 million of state net operating loss respectively, which may be available to offset future taxable income. Federal net operating loss carryforwards of $150.5 million and state net operating loss carryforwards of $200.2 million will expire at various dates from 2023 through 2039. Federal net operating loss carryforwards of $52.5 million can be carried forward indefinitely. The Company had approximately $6.3 million of federal and $2.2 million of state tax credit carryforwards available to reduce future tax liabilities as of December 31, 2019, which will expire at varying times through the year 2039.

The Internal Revenue Code of 1986, as amended (the "Code"), provides for a limitation of the annual use of net operating losses and other tax attributes (such as research and development tax credit carryforwards) following certain ownership changes (as defined by the Code) that could limit the Company's ability to utilize these carryforwards. At this time, the Company has not completed a study to assess whether an ownership change under Section 382 of the Code has occurred, or whether there have been multiple ownership changes since the Company's formation, due to the costs and

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

10. Income Taxes (Continued)

complexities associated with such a study. The Company may have experienced various ownership changes, as defined by the Code, as a result of past financing transactions. Accordingly, the Company's ability to utilize the aforementioned carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be applied against future taxes. Therefore, the Company may not be able to take full advantage of these carryforwards for federal or state income tax purposes.

As of December 31, 2019 and 2018, the Company did not have any significant unrecognized tax benefits. The Company had not accrued interest or penalties related to uncertain tax positions.

The federal and state income tax returns are generally subject to tax examinations for the tax years ended December 31, 2016 through December 31, 2019. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state taxing authorities to the extent utilized in a future period.

11. Defined Contribution Benefit Plan

The Company sponsors a 401(k) retirement plan, in which substantially all of its employees are eligible to participate. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. The Company did not provide any contributions to this plan during the years ended December 31, 2019 or 2018.

12. Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence for certain estimates and to identify matters that require additional disclosure. Subsequent events have been evaluated as required.

ATM Agreement

Subsequent to December 31, 2019, the Company sold an aggregate of 173,572 shares of common stock pursuant to its current ATM program, at an average price of $6.29 per share, for gross and net proceeds of $1.1 million.

January 2020 Financing

On January 30, 2020, the Company entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering of an aggregate of 5,290,000 shares of common stock at a price to the public of $5.00 per share, including 690,000 shares issued upon the exercise in full by Oppenheimer & Co. Inc. of its over-allotment option. This resulted in gross proceeds of $26.5 million, and net proceeds of $24.5 million.

Catabasis Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

13. Quarterly Financial Information (unaudited, in thousands, except share and per share data)

	Three Months Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
Operating expenses	$ 6,334	$ 7,325	$ 6,682	$ 6,747
Net loss	(6,038)	(7,131)	(6,514)	(6,610)
Net loss per share:				
Basic and Diluted	$ (0.62)	$ (0.62)	$ (0.56)	$ (0.55)
Weighted-average common shares outstanding used in net loss per share:				
Basic and Diluted	9,686,224	11,505,542	11,624,232	11,950,674

	Three Months Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
Operating expenses	$ 7,639	$ 6,636	$ 6,008	$ 6,088
Net loss	(7,652)	(6,479)	(5,679)	(6,060)
Net loss per share:				
Basic and Diluted	$ (2.88)	$ (1.98)	$ (0.80)	$ 0.85
Weighted-average common shares outstanding used in net loss per share:				
Basic and Diluted	2,655,584	3,272,877	7,103,841	7,115,507

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Catabasis Pharmaceuticals, Inc.

Date: March 10, 2020

By: /s/ JILL C. MILNE

Jill C. Milne
President and Chief Executive Officer

We, the undersigned directors and officers of Catabasis Pharmaceuticals, Inc. (the "Company"), hereby severally constitute and appoint Jill C. Milne and Noah Clauser, and each of them singly, our true and lawful attorneys, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney.

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

Signature	Title	Date
/s/ JILL C. MILNE Jill C. Milne	President and Chief Executive Officer and Director (Principal Executive Officer)	March 10, 2020
/s/ NOAH CLAUSER Noah Clauser	Vice President of Finance and Treasurer (Principal Financial Officer, Principal Accounting Officer)	March 10, 2020
/s/ KENNETH BATE Kenneth Bate	Chairman	March 10, 2020
/s/ BURT ADELMAN Burt Adelman	Director	March 10, 2020
/s/ JOANNE BECK Joanne Beck	Director	March 10, 2020
/s/ HUGH COLE Hugh Cole	Director	March 10, 2020

Signature	Title	Date
/s/ MICHAEL KISHBAUCH Michael Kishbauch	Director	March 10, 2020
/s/ GREGG LAPOINTE Gregg Lapointe	Director	March 10, 2020

Exhibit 4.4

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

As of December 31, 2019, Catabasis Pharmaceuticals, Inc. ("we", "us" or the "Company") had one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"): our common stock, $0.001 par value per share.

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our certificate of incorporation, our by-laws and applicable provisions of Delaware corporate law. You should read our certificate of incorporation and by-laws, which are filed as exhibits to the Annual Report on Form 10-K of which this exhibit is a part, for the provisions that are important to you.

Our authorized capital stock consists of 150,000,000 shares of common stock, $0.001 par value per share, and 5,000,000 shares of preferred stock, $0.001 par value per share.

Common Stock

Voting Rights. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, except that unless otherwise required by law, holders of our common stock are not entitled to vote on any amendment to the certificate of incorporation that relates solely to the terms of one or more outstanding series of preferred stock, if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more such other series, to vote thereon pursuant to the certificate of incorporation. Holders of our common stock do not have cumulative voting rights.

An election of directors will be decided by a plurality of the votes cast by the stockholders entitled to vote on the election at a duly held stockholders' meeting at which a quorum is present. All other questions will be decided by a majority of the votes cast by stockholders entitled to vote thereon at a duly held meeting of stockholders at which a quorum is present, except when a different vote is required by law, our certificate of incorporation or by-laws.

Dividends. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend or other rights of any series of preferred stock that we may designate and issue in the future.

Liquidation and Dissolution. In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock.

Other Rights. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Effects of Authorized but Unissued Stock

Our authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing requirements of the Nasdaq Global Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make it more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise. In addition, if we issue preferred stock, the issuance could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation.

Provisions of Our Certificate of Incorporation and By-laws and Delaware Law That May Have Anti-Takeover Effects

Delaware law, our certificate of incorporation and our by-laws contain provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

Staggered Board; Removal of Directors. Our certificate of incorporation and by-laws divide our board of directors into three classes with staggered three-year terms. In addition, a director is only able to be removed for cause and only by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in an annual election of directors. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, is only able to be filled by vote of a majority of our directors then in office. The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action by Written Consent; Special Meetings. Our certificate of incorporation provides that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of our stockholders and may not be effected by any consent in writing by our stockholders. Our certificate of incorporation and by-laws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our chairman of the board, our chief executive officer or our board of directors.

Advance Notice Requirements for Stockholder Proposals. Our by-laws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of

persons for election to our board of directors. Stockholders at an annual meeting are only able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities.

Delaware Business Combination Statute. We are subject to Section 203 of the General Corporation Law of the State of Delaware. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Amendment of Certificate of Incorporation and By-laws. The General Corporation Law of the State of Delaware provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless a corporation's certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our by-laws may be amended or repealed by a majority vote of our board of affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above under "*—Staggered Board; Removal of Directors*" and "*—Stockholder Action by Written Consent; Special Meetings*."

Exclusive Forum Selection. Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on behalf of our company, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, (3) any action asserting a claim against our company arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or by-laws, or (4) any action asserting a claim against our company governed by the internal affairs doctrine. Although our certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

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Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

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

1) Registration Statement (Form S-1 Nos. 333-225410 and 333-225734) of Catabasis Pharmaceuticals, Inc., and

2) Registration Statement (Form S-3 No. 333-231441) of Catabasis Pharmaceuticals, Inc., and

3) Registration Statement (Form S-8 Nos. 333-206394, 333-210229, 333-216793, 333-223721, 333-229643) pertaining to the equity incentive plans of Catabasis Pharmaceuticals, Inc.;

of our report dated March 10, 2020, with respect to the consolidated financial statements of Catabasis Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Catabasis Pharmaceuticals, Inc. for the year ended December 31, 2019.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 10, 2020

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Exhibit 31.1

CERTIFICATION

I, Jill C. Milne, certify that:

1. I have reviewed this Annual Report on Form 10-K of Catabasis Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2020

/s/ JILL C. MILNE

Jill C. Milne
President and Chief Executive Officer
(Principal Executive Officer)

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Exhibit 31.2

CERTIFICATION

I, Noah C. Clauser, certify that:

1. I have reviewed this Annual Report on Form 10-K of Catabasis Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2020

/s/ NOAH C. CLAUSER

Noah C. Clauser
Vice President of Finance and Treasurer
(Principal Financial Officer)

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Exhibit 32.1

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

In connection with this Annual Report on Form 10-K of Catabasis Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Jill C. Milne, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to her knowledge on the date hereof:

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

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

Date: March 10, 2020

/s/ JILL C. MILNE

Jill C. Milne
President and Chief Executive Officer (Principal Executive Officer)

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Exhibit 32.2

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

In connection with this Annual Report on Form 10-K of Catabasis Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Noah C. Clauser Vice President of Finance and Treasurer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

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

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

Date: March 10, 2020

/s/ NOAH C. CLAUSER

Noah C. Clauser
Vice President of Finance and Treasurer
(Principal Financial Officer)

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