

CATABASIS PHARMACEUTICALS INC  
Form 10-K  
March 16, 2017

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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, DC 20549

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**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, 2016

or

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

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

**Catabasis Pharmaceuticals, Inc.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**26-3687168**  
(IRS Employer  
Identification No.)

**One Kendall Square  
Bldg. 1400E, Suite B14202  
Cambridge, Massachusetts**  
(Address of principal executive offices)

**02139**  
(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**  
**Common Stock, \$0.001 par value per share**

**Name of each exchange on which registered**  
**NASDAQ Global Market**

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

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Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.  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.  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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes  No

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

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

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

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

Aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last sale price for such stock on June 30, 2016: \$22,128,335.

As of March 8, 2017, there were 18,898,547 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 2017 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 plans to identify, develop and commercialize novel therapeutics based on our SMART linker drug discovery platform;

our plans to continue to evaluate data from Part C of our MoveDMD<sup>®</sup> clinical trial of edasalonexent for the treatment of Duchenne muscular dystrophy;

ongoing and planned clinical trials for edasalonexent and other product candidates, whether conducted by us or by any future collaborators, including the timing of initiation of these trials and of the anticipated results;

our plans to enter into collaborations for the development and commercialization of product candidates;

the potential benefits of any future collaboration;

our ability to receive research and development funding and achieve anticipated milestones under our collaborations;

the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;

the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;

our commercialization, marketing and manufacturing capabilities and strategy;

our intellectual property position and strategy;

our ability to identify additional products or product candidates with significant commercial potential;

our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;

developments relating to our competitors and our industry; and

the impact of government laws and regulations.

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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.

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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.

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**PART I**

**Item 1. Business**

**Overview**

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics based on our proprietary Safely Metabolized And Rationally Targeted, or SMART, linker drug discovery platform. Our SMART linker drug discovery platform enables us to engineer product candidates that can simultaneously modulate multiple targets in a disease. Our proprietary product candidates impact pathways that are central to diseases where efficacy may be optimized by a multiple target approach. We have applied our SMART linker drug discovery platform to build an internal pipeline of product candidates for rare diseases, our primary focus, and plan to pursue partnerships to develop additional product candidates.

Our lead product candidate is edasalonexent, formerly known as CAT-1004, an oral small molecule. Based on its mechanism of action, the inhibition of NF- $\kappa$ B, or nuclear factor kappa-light-chain-enhancer of activated B cells, we believe edasalonexent has the potential to be a disease-modifying therapy for all patients affected by Duchenne muscular dystrophy, or 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 are currently conducting the MoveDMD<sup>®</sup> Phase 1/2 trial of edasalonexent in ambulatory boys with DMD between ages four and seven. The MoveDMD trial is a three-part clinical trial investigating the safety and efficacy of edasalonexent in DMD. We previously reported positive safety, tolerability, pharmacokinetics and biomarker results from Part A of the MoveDMD trial. We reported top-line Part B results in January 2017, indicating that the primary efficacy endpoint of 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 was not met. There were, however, consistent numerical improvements versus placebo across all functional exploratory endpoint measures for the higher dose, as well as numerical improvement versus placebo across multiple functional exploratory endpoint measures for the lower dose, while the lower dose had mixed results versus the higher dose. Changes in these functional measures were not statistically significant in Part B of the MoveDMD trial, which was not powered for functional measures. We believe that the potential treatment-associated effects from these exploratory endpoints warrant further evaluation in Part C of the MoveDMD trial, which is the ongoing open-label extension portion of the trial. We intend to transition all patients participating in Part C of the trial to the 100 mg/kg/day dose, the higher of the two dosing levels administered in Part B, and extending Part C by an additional 24 weeks, subject to institutional review board approval. We intend to report the results from Part C in 2017. We anticipate providing an interim update on Part C of the MoveDMD trial in the second quarter of 2017. In addition to our work in DMD, we are evaluating other diseases where the inhibition of NF- $\kappa$ B may be beneficial for further therapeutic applications of edasalonexent. There are a number of other rare diseases where NF- $\kappa$ B is believed to play an important role, such as Becker muscular dystrophy, which is one of nine types of muscular dystrophy and is characterized by slowly progressive muscle weakness of the legs and pelvis, and IgA nephropathy, a kidney disease that is believed to result from activation of mucosal immunity leading to the synthesis of aberrantly glycosylated polymeric immunoglobulin A1, or IgA1, which enters the circulation and lodges in a patient's kidneys interfering with their proper function.

In addition to edasalonexent, we are developing a pipeline of product candidates using our SMART linker drug discovery platform as potential treatments for rare diseases including cystic

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fibrosis, or CF, amyotrophic lateral sclerosis, or ALS, and Friedreich's ataxia, or FA. Our pipeline includes CAT-5571 and CAT-4001, for which we are currently conducting preclinical activities. We are developing CAT-5571 initially as a potential oral treatment for CF, with potential beneficial effects on both trafficking and function of cystic fibrosis transmembrane conductance regulator, or CFTR, and the clearance of *Pseudomonas aeruginosa*. In CF, a malfunctioning CFTR 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 *Pseudomonas aeruginosa*, that are difficult to treat with standard antibiotics. CAT-5571 is a small molecule that activates autophagy, a process that maintains cellular homeostasis and host defense mechanisms, which are known to be impaired in CF. In addition, we are developing CAT-4001 as a potential treatment for neurodegenerative diseases such as FA and ALS, irrespective of mutation status. FA is a rare genetic disease that causes nervous system damage and compromises motor coordination. ALS, sometimes called Lou Gehrig's disease or classical motor neuron disease, is a rapidly progressive, fatal neurological disease that attacks the nerve cells responsible for controlling voluntary muscles. CAT-4001 is a small molecule that activates Nuclear factor (erythroid-derived 2)-like 2, or Nrf2, and inhibits NF- $\kappa$ B, two pathways that have been implicated in FA and ALS.

We have previously applied our SMART linker drug discovery platform to engineer our CAT-2000 series product candidates to inhibit the Sterol Regulatory Element Binding Protein, or SREBP, pathway. Inhibitors of SREBP have been proposed for the treatment of nonalcoholic steatohepatitis, or NASH, based on the role of SREBP in lipid metabolism and known human polymorphisms associated with NASH disease progression. NASH is characterized by the build-up of fat in the liver and chronic inflammation, which can trigger progression to fibrosis and ultimately cirrhosis and sometimes hepatocellular carcinoma. We have advanced two CAT-2000 molecules, CAT-2003 and CAT-2054, into clinical development and intend to pursue a partnership for further development of the CAT-2000 series in NASH, which, in addition to CAT-2003 and CAT-2054, includes other discovery-stage molecules with intermediate rates of hydrolysis.

As of December 31, 2016, we owned five issued U.S. patents with composition of matter and method of use claims directed to edasalonexent, four issued U.S. patents with composition of matter and method of use claims directed to the CAT-2000 series, two issued U.S. patents with composition of matter claims generically covering CAT-5571 and two issued U.S. patents with composition of matter and method of use claims directed to CAT-4001. These patents are expected to expire between 2029 and 2031, without taking into account potential patent term extensions. In addition, our patent portfolio includes over 50 issued foreign patents, over 10 pending U.S. patent applications and over 35 pending foreign patent applications.

**Our Scientific Approach**

Our SMART linker drug discovery platform enables us to engineer product candidates that can simultaneously modulate multiple biological targets in a disease. Our proprietary product candidates impact pathways that are central to diseases where efficacy may be optimized by a multiple target approach.

Multi-target therapies have in many cases been developed to provide treatment options where single-target therapies have been ineffective. These multi-target therapies have traditionally followed one of two approaches: either use of a single drug that binds to multiple biological targets or co-administration of two or more drugs that interact with different targets. While each of these approaches has well-established benefits in a variety of indications, each is also characterized by significant limitations. For example, use of a single broadly targeted drug can lead to off-target toxicities, side-effects and tolerability issues, and co-administration of two or more drugs can be confounded by differences in the pharmacokinetics and tissue distribution of the drugs, thereby



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reducing the likelihood of each agent being simultaneously active in the same cell. Our SMART linker drug discovery platform is designed to address these issues.

Our aim is to leverage the growing body of knowledge associated with disease pathways, and to rationally design orally bioavailable product candidates that simultaneously interact with multiple biological targets in a disease. While other technologies exist to conjugate or combine two bioactives, we believe that our SMART linker drug discovery platform provides substantial improvements over previous approaches to bioactive conjugation.

**SMART Linker Drug Discovery Platform**

We have leveraged our SMART linker drug discovery platform to engineer molecules that can simultaneously modulate multiple biological targets in a disease. Our drug discovery platform includes a broad array of linkers that we use to engineer molecular series. The linkers used in our drug discovery platform are small chemicals designed to join two separate bioactives into a single conjugate molecule, and some linkers are also bioactives. In systemic circulation, our SMART linker conjugates are typically stable and inactive, potentially reducing off-target toxicities and side-effects. Certain of our conjugates are designed to be cleaved by specific enzymes exclusively within cells in order to release the two bioactives inside the cells. By releasing the bioactive components of the conjugate molecule inside cells, the SMART linker allows the bioactives to reach their targets more efficiently and have greater efficacy than if the bioactives were dosed independently or in combination.

To create a conjugate using our SMART linker drug discovery platform, we begin by analyzing pathways that are disrupted in a disease. We then select two bioactive molecules known for their clinical safety and demonstrated effect along one or more of these biological pathways. We then design a SMART linker that will conjugate the two selected bioactives, allow the conjugate molecule to be carried to biological tissues and, following entry into cells, be cleaved by enzymes resident in the cells to release the bioactives.

We have SMART linker conjugates that are designed to be stable with oral dosing, as well as stable in both the lumen of the intestine and in systemic circulation, which we have now observed in clinical trials for two product candidate series. We can design the SMART linker to chemically link the two bioactive molecules through their pharmacophores, the regions of the bioactive molecules that are responsible for carrying out their biological activity, resulting in inactivation of the bioactives while conjugated. Once the conjugate enters a cell, the SMART linker may be cleaved by specific enzymes which reside only within cells, releasing the two bioactives to interact with their biological targets. Simultaneous delivery of the bioactives through the SMART linker conjugate into the cell results in the two bioactives having the same pharmacokinetics and tissue distribution. As a result, our SMART linker conjugates can simultaneously modulate two biological targets in diseases of interest within the same cell. In addition, release of the bioactives inside cells can potentially reduce or eliminate off-target, extracellular activity of the bioactives, which may improve safety and tolerability.

We have observed in multiple preclinical studies that our SMART linker conjugates achieved greater efficacy than administration of the two bioactives either independently or in combination. In clinical trials, SMART linker conjugates have demonstrated significant improvements in activity on disease pathways and tolerability relative to equivalent doses of the two bioactives delivered in combination. We also have observed statistically significant pharmacological effects with SMART linker conjugates at dose levels significantly lower than the prescribed doses of the two component bioactives, as further described below under " Our Product Candidates Edasalonexent Edasalonexent Clinical Development Completed Clinical Trials". We are developing a pipeline of preclinical assets using our SMART linker drug discovery platform to potentially treat rare diseases including CF, ALS, FA, and others.

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We believe that our SMART linker drug discovery platform has the potential to:

enhance activity on diseases through modulation of multiple biological targets;

improve efficacy by matching the pharmacokinetics and tissue distribution of the component bioactives; and

improve safety and tolerability by releasing the component bioactives within cells.

**Our Product Candidates**

The following chart summarizes key information regarding our product candidates. We hold rights to all of our product candidates throughout the world.

***Edasalonexent***

Edasalonexent is a SMART linker conjugate of salicylic acid and the omega-3 fatty acid docosahexaenoic acid, or DHA, a naturally occurring unsaturated fatty acid with anti-inflammatory properties. We designed edasalonexent to inhibit NF- $\kappa$ B, a protein that is activated in DMD and that drives inflammation, fibrosis and muscle degeneration, and suppresses muscle regeneration. We reported results from Part A of the MoveDMD trial in January 2016 and reported top-line safety and efficacy results for Part B of the trial in January 2017. Results from both Part A and Part B of the MoveDMD trial are described further below under " Edasalonexent Clinical Development". In July 2016, we initiated an open-label extension, Part C of the MoveDMD trial, which is expected to provide safety and efficacy data on edasalonexent when administered for up to 48 weeks. 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.

In September 2016, we announced a pre-clinical joint research collaboration with Sarepta Therapeutics, Inc., or Sarepta, a commercial stage developer of RNA targeted therapeutics, established to explore a combination drug treatment approach for DMD. In the Catabasis and Sarepta



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collaboration, increased dystrophin protein expression was seen with an exon-skip modality in combination with edasalonexent in the designated mouse model 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, including diaphragm, and cardiac muscle. When muscles contract or stretch during normal use, the absence of normally functioning dystrophin results in activation of the NF- $\kappa$ B pathway, triggering inflammation in the muscles, resulting in muscle damage 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 the European Union.

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 their mid-twenties.

*The Role of NF- $\kappa$ B in Duchenne Muscular Dystrophy*

NF- $\kappa$ B 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. Activated NF- $\kappa$ B 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- $\alpha$ , interleukin 6, or IL-6, and interleukin-1 beta, or IL-1 $\beta$ ; chemokines; cell adhesion molecules; and tissue degrading enzymes, such as matrix metalloproteinase 9, or MMP-9. In addition, activated NF- $\kappa$ B 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- $\kappa$ B is observed in muscle tissues of patients with DMD prior to the onset of other clinical manifestations, and activated NF- $\kappa$ B is persistently elevated in the immune cells and degenerating muscle fibers of patients with DMD. Moreover, evidence exists that mechanical stress activates NF- $\kappa$ B in muscles and increases levels of activated NF- $\kappa$ B by a factor of three to four times and drives NF- $\kappa$ B mediated inflammation. Muscles with increased mechanical stress and inflammation, such as quadriceps and hamstrings, show the greatest progression of disease.

*Unaddressed Market Opportunity*

There are currently only two therapies approved in the United States for the treatment of DMD: Sarepta's drug Exondys 51, also known as eteplirsen, an exon skipping therapy targeting the skipping of exon 51, that was granted accelerated approval by the FDA, and Marathon Pharmaceuticals' EMFLAZA, also known as deflazacort, a corticosteroid, which is indicated for the treatment of DMD

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in patients five years of age and older. Corticosteroid therapy, including treatment with prednisone, is often prescribed to treat the inflammation underlying DMD and to delay loss of ambulation. Corticosteroids have demonstrated efficacy in DMD patients, which is believed to be driven by reductions in activated NF- $\kappa$ B. However, corticosteroids primarily act through another pathway called the glucocorticoid receptor-mediated pathway, and also can cause significant complications including growth suppression, excessive weight gain, behavioral changes, reduction in bone strength and compromise of the immune system. Over time, corticosteroids induce chronic myopathy in many diseases through induction of muscle protein breakdown, which ultimately leads to muscle damage. DMD patients treated with corticosteroids typically show an initial improvement in measures of muscle function but then resume a progressive decline. Approximately half of DMD patients treated with steroids lose the ability to walk by age thirteen and the vast majority are in wheelchairs by age sixteen. DMD patients typically live until their mid-twenties, despite the availability of corticosteroids.

Additionally, there are several treatments for DMD that are approved or under review in the European Union or are expected to be under review by regulatory agencies in the near future. Santhera Pharmaceuticals, or Santhera, has filed a marketing authorization application with the European Medicines Agency, or EMA, for Raxone<sup>®</sup>, also known as idebenone, for the treatment of DMD in patients with respiratory function decline and not taking concomitant glucocorticoids. Sarepta's Exondys 51 is under review by the EMA, and PTC Therapeutics' ataluren is conditionally approved in the European Union and several other countries for treatment of nonsense mutation DMD under the trade name Translarna. PTC Therapeutics also re-filed a new drug application, or NDA, with the FDA in March 2017. Exondys 51 and ataluren target mechanisms to increase levels of dystrophin in muscles. Each of these agents addresses a specific type of genetic mutation in order to produce a partially functional dystrophin protein. The therapeutic goal of these product candidates is to reduce disease severity and extend survival in those DMD patients who are candidates for therapy with these agents. Based on the prevalence of the specific mutations that Exondys 51 and ataluren are designed to address, they would be expected to be effective in an aggregate of approximately 26% of DMD patients. We believe that DMD patients, including those treated with these dystrophin therapies, will continue to require treatments to reduce muscle inflammation and degeneration and enhance muscle regeneration.

*Edasalonexent for the Treatment of Duchenne Muscular Dystrophy*

Based on the mechanism of action by which edasalonexent suppresses NF- $\kappa$ B 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 and agents targeting utrophin. We intend to commercialize edasalonexent in North America ourselves and commercialize edasalonexent outside of North America either ourselves or with a collaborator.

*Edasalonexent Clinical Development*

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

Our MoveDMD Phase 1/2 trial enrolled ambulatory boys between ages four and seven 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 are not limited to any specific dystrophin mutations. The MoveDMD trial is designed to be conducted in three sequential parts, Part A and Part B, both of which have been completed, and Part C, an open-label extension initiated in July 2016, which is on-going.

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In Part A of the MoveDMD trial, which was conducted at three sites in the United States, we assessed the safety, tolerability and pharmacokinetics of edasalonexent in 17 patients, following seven days of dosing, across three dosing levels: 33 mg/kg/day, taken in a single daily dose, 67 mg/kg/day, taken in two daily doses, and 100 mg/kg/day, taken in three daily doses. We also compared edasalonexent exposure levels to exposure levels achieved in previous edasalonexent clinical trials in adults where inhibition of NF- $\kappa$ B was observed. In January 2016, we reported that all three doses of edasalonexent tested were generally well tolerated with no safety signals observed. The majority of adverse events were mild, and the most common adverse events were gastrointestinal, primarily diarrhea. There were no serious adverse events and no drug discontinuations. For the 67 mg/kg/day and 100 mg/kg/day dosing levels, pharmacokinetic results demonstrated edasalonexent plasma exposure levels consistent with those previously observed in adults at which inhibition of NF- $\kappa$ B was observed, and edasalonexent significantly reduced the expression of a set of genes that are controlled by NF- $\kappa$ B. We subsequently reported results with positive NF- $\kappa$ B biomarker data that supported NF- $\kappa$ B target engagement via statistically significant reduction in NF- $\kappa$ B controlled gene expression for the 67 mg/kg/day and 100 mg/kg/day dosing levels. These two dosing levels were advanced to Part B of the trial.

Thirty-one boys enrolled in Part B of the MoveDMD trial and all completed Part B of the trial. Both dose levels of edasalonexent evaluated were well tolerated with no safety signals observed. The majority of adverse events were mild in nature and the most common treatment-related adverse events were gastrointestinal, primarily mild diarrhea and vomiting. There were no treatment-related serious adverse events, no drug discontinuations and no dose reductions. Edasalonexent plasma exposure in Part B of the MoveDMD trial was consistent with that observed in Part A.

In Part B of the MoveDMD trial, we assessed the effects of edasalonexent using MRI T2 as an early biomarker at 12 weeks in a randomized, double-blind, placebo-controlled trial. Part B of the MoveDMD trial was conducted at five sites in the United States, and we believe that it was the first Phase 2 trial in DMD to use MRI as a primary endpoint. MRI is a non-invasive imaging technique that allows investigators to view muscle structure and composition and measure disease status in children with DMD. Changes in MRI measures, particularly fat fraction, have been correlated in natural history studies with longer-term changes in clinically meaningful measures of functional activity. We used MRI T2 as the primary endpoint to serve as an early biomarker for demonstrating a benefit on muscle composition that potentially would allow us to see an effect of edasalonexent at 12 weeks of treatment, as has been seen by others with corticosteroids. We 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 (0.37 milliseconds for the pooled edasalonexent treatment groups versus 0.47 milliseconds for placebo; a smaller increase in MRI T2 is believed to correlate with less muscle inflammation). Although we did not see a similar treatment effect as corticosteroids on the MRI T2 composite measure at 12 weeks, we observed potential treatment-associated functional effects at both dose levels of edasalonexent on the exploratory endpoints described below, as well as continued to observe acceptable safety, tolerability and plasma exposure data in Part B of the MoveDMD trial. Therefore, as planned, we are measuring the effects of edasalonexent on patients with DMD in the MoveDMD trial in Part C to see if signals strengthen in the longer-term data from the ongoing open-label extension.

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Exploratory endpoints also included the following functional tests in Parts B and C of the MoveDMD trial: timed function tests best suited for the age group of the trial subjects, including the 10-meter walk/run, 4-stair climb and time-to-stand tests; the North Star Ambulatory Assessment; assessments of muscle strength; and the Pediatrics Outcomes Data Collection Instrument, a parent-proxy measure of functional ability. The trial is not powered to detect statistically significant changes in any of the exploratory endpoints during Part B or Part C, and no significant changes were detected in these measures for those dosed with edasalonexent versus placebo at 12 weeks. Top-line results from Part B demonstrated that the edasalonexent 100 mg/kg/day treatment group, whose patients took 33mg/kg capsules three times a day, consistently showed numerical improvement versus placebo across all measures of the functional test exploratory endpoints, although the changes were not statistically significant. Similarly, the 67 mg/kg/day treatment group, whose patients took 33mg/kg capsules twice a day, consistently showed numerical improvement versus placebo across multiple measures of the functional test exploratory endpoints, although the changes were not statistically significant and were mixed compared to the 100 mg/kg/day treatment group. Compared to the placebo group, patients in the edasalonexent 100 mg/kg/day group had characteristics of more advanced disease at baseline. This was indicated by the age at onset, age at diagnosis and the baseline values for time to complete the 4-stair climb and time-to-stand. In addition, baseline assessments were performed at the beginning of Part A and Part B of the MoveDMD trial to compare changes in functional measures in this control period to those observed in Part B and Part C. There were twelve boys who participated in Part A and received active treatment in Part B, and the rate of decline in functional measures for these boys generally showed numerical improvement over the active treatment period compared to the control period. We believe that the top-line results from the functional exploratory endpoints and additional functional assessments warrant further evaluation as planned in Part C of the MoveDMD trial. We intend to transition all patients participating in Part C of the trial to the 100 mg/kg/day dose and extending Part C by an additional 24 weeks, subject to institutional review board approval, so that we have the opportunity to assess the higher dose in all of the boys in Part C and so that the boys that started the open-label extension since July last year are able to continue to receive edasalonexent treatment. We intend to report the results from Part C in 2017. We anticipate providing an interim update on Part C of the MoveDMD trial in the second quarter of 2017.

Following additional assessment of the effects in patients of edasalonexent in Part C of the MoveDMD trial, we will determine next steps for the edasalonexent program in DMD.

*Completed Clinical Trials*

To date, we have studied edasalonexent in three completed Phase 1 clinical trials, in addition to Part A of the MoveDMD trial, which is described above. The design for each of these other clinical trials are discussed below.

Table of Contents*Edasalonexent Completed Phase 1 Clinical Trials*

<b>Trial</b>	<b>Description</b>	<b>Duration Of Dosing</b>	<b>Total</b>	<b>Subjects Treated with edasalonexent</b>
CAT-1004-101	Randomized, double-blind, placebo-controlled, single ascending dose clinical trial to evaluate safety, tolerability and pharmacokinetics of edasalonexent in healthy subjects	1 day	52	39
CAT-1004-102	Randomized, double-blind, placebo-controlled multiple ascending dose clinical trial to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of edasalonexent in adults with Type 2 diabetes	14 days	44	32
CAT-1004-103	Single-blind biomarker trial in healthy adults to compare activity of edasalonexent, a combination of salicylate and DHA, or placebo on activated NF-κB	1 day	9	8

*Phase 1 Single Ascending Dose Trial (CAT-1004-101):* We conducted a randomized, double-blind, placebo-controlled, single ascending dose Phase 1 clinical trial in 52 healthy volunteers at a single site in the United States to assess the safety, tolerability and pharmacokinetics of edasalonexent in both fasted and fed states. The participants were randomized to receive edasalonexent or placebo. Edasalonexent was administered orally in soft gelatin capsules at doses ranging from 300 mg to 6000 mg.

Single doses of edasalonexent, administered to subjects in both fed and fasted conditions, appeared to be well tolerated. Subjects in the fasted state reported few adverse events, with the most commonly reported adverse events being headache, diarrhea and dizziness. Of the 44 subjects in the fasted state, five reported headache, three reported diarrhea and two reported dizziness. The majority of the adverse events in the fasted state were mild in severity. Of the 35 subjects in the fed state, six reported diarrhea, six reported headache and four reported abdominal pain. The most common adverse events in the fed state were diarrhea, headache and abdominal pain, and all of the adverse events in the fed state were mild in severity. Subjects in the fed state receiving single doses of edasalonexent of 4000 mg or more reported gastrointestinal adverse events more frequently than subjects receiving lower doses. No treatment-related severe adverse events were reported. There were no observed trends in laboratory, vital signs or electrocardiogram results following edasalonexent administration in either the fasted or fed state.

Edasalonexent was rapidly absorbed in plasma, with mean maximum and overall plasma exposure generally increasing with edasalonexent dose levels. Neither component bioactive, salicylate or DHA, was detected in plasma at levels above background, consistent with intracellular cleavage of edasalonexent and intracellular delivery of the component bioactives. Administration of a high-fat meal increased edasalonexent mean maximum and overall exposure by approximately three- to eight-fold.

*Phase 1 Multiple Ascending Dose Trial (CAT-1004-102):* We conducted a randomized, double-blind, placebo-controlled, multiple ascending dose Phase 1 clinical trial in 44 subjects at a single center in the United States to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of edasalonexent. These subjects had Type 2 diabetes and mild background inflammation, which enabled us to assess the activity of edasalonexent on activated NF-κB. Subjects were randomized to receive



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edasalonexent or placebo. edasalonexent was administered orally in soft gelatin capsules at total daily doses ranging from 300 mg to 4000 mg.

Edasalonexent administered for two weeks appeared to be well tolerated. The adverse events reported in more than one subject were each reported by two subjects. These adverse events were diarrhea (both instances reported by subjects receiving 4000 mg daily doses of edasalonexent), gastroenteritis (one instance reported by a subject in the placebo group and the other by a subject receiving 1000 mg daily doses of edasalonexent) and upper respiratory tract infection (both instances reported by subjects receiving 4000 mg daily doses of edasalonexent). The majority of the adverse events were mild in severity. No treatment-related severe adverse events were reported.

Edasalonexent was rapidly absorbed in plasma, with mean maximum and overall plasma exposure generally increasing with escalating single or multiple doses of edasalonexent. Neither component bioactive, salicylate or DHA, was detected in plasma at levels above background, again consistent with intracellular cleavage of edasalonexent and intracellular delivery of the component bioactives.

In the Phase 1 multiple ascending dose trial, we observed by two methods that edasalonexent inhibited activated NF- $\kappa$ B. For the first method, we stimulated NF- $\kappa$ B activity *ex vivo* in whole blood from subjects treated with edasalonexent or placebo, and then observed NF- $\kappa$ B activity in monocytes, or immune cells, that we isolated from the whole blood. NF- $\kappa$ B activity was reduced in a majority of subjects following two weeks of edasalonexent treatment but not following treatment with placebo. For the second method, we performed gene expression analyses on whole blood taken from subjects prior to treatment and after two weeks of treatment with edasalonexent or placebo. Edasalonexent significantly reduced the expression of a set of genes that are controlled by NF- $\kappa$ B. In contrast, treatment with placebo for two weeks did not significantly reduce expression of NF- $\kappa$ B regulated genes.

*Phase 1 NF- $\kappa$ B Biomarker Trial (CAT-1004-103):* We conducted a single-blind, crossover Phase 1 clinical trial with edasalonexent in nine healthy adult volunteers at a single center in the United States to compare activity of a single dose of 2000 mg of edasalonexent on activated NF- $\kappa$ B to a combination of salicylate and DHA or placebo. No adverse events were reported in this clinical trial. The salicylate and DHA were dosed at approximately equivalent amounts to those contained in the edasalonexent conjugate. We assessed NF- $\kappa$ B activity in peripheral blood mononuclear cells, or PBMCs, isolated from subjects before dosing and two hours after dosing. PBMCs are circulating immune cells that can mount an NF- $\kappa$ B response and migrate into tissue such as muscle and drive inflammation. Prior to the determination of NF- $\kappa$ B activity, we stimulated whole blood with lipopolysaccharide, or LPS, to activate the NF- $\kappa$ B pathway. Treatment of subjects with edasalonexent significantly reduced the level of activated NF- $\kappa$ B, as measured by nuclear p65, a surrogate marker for activated NF- $\kappa$ B. In contrast, no change in the level of activated NF- $\kappa$ B was observed upon treatment with the combination of salicylate and DHA, or upon treatment with placebo. In this trial, edasalonexent, which is a SMART linker conjugate of salicylate and DHA, exhibited greater activity on the NF- $\kappa$ B pathway than the combination of its component bioactives.

*Edasalonexent Preclinical Development*

In preclinical studies, we have observed that edasalonexent inhibited NF- $\kappa$ B activity *in vitro* and *in vivo*, and produced disease-modifying effects in two established animal models of DMD, the *mdx* mouse model and the Golden Retriever muscular dystrophy, or GRMD, dog model.

*In Vivo Studies in Animal Models of DMD*

We have created several SMART linker conjugates that inhibit activated NF- $\kappa$ B. Two of these conjugates, edasalonexent and CAT-1041, exhibit very similar effects on NF- $\kappa$ B activity in cell based assays, in animal studies and on functional activity in animal models. CAT-1041 is a closely related analog of edasalonexent in which the DHA component of the salicylate-DHA conjugate has been

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replaced with the omega-3 fatty acid eicosapentaenoic acid, or EPA. In some preclinical studies, we used CAT-1041 as a surrogate for edasalonexent. Both edasalonexent and CAT-1041 produced disease-modifying efficacy in established animal models of DMD. We decided to advance edasalonexent into clinical trials rather than CAT-1041 based on scientific literature suggesting that DHA has superior anti-inflammatory activity compared to EPA.

*mdx Mouse Model.* We examined the potential therapeutic effects of edasalonexent using the *mdx* mouse model of DMD. We observed that four weeks of treatment with edasalonexent or prednisolone, a steroid, reduced muscle inflammation and the number of degenerating muscle fibers in *mdx* mice. However, only edasalonexent-treated animals showed preservation of muscle mass and an increase in the number of regenerating fibers, suggesting that chronic treatment with edasalonexent can protect muscle from the damage expected to occur over time in *mdx* mice.

In a long-term *mdx* mouse study, we observed that, compared to the control group of *mdx* mice, six months of treatment with CAT-1041 significantly improved muscle endurance as measured by mean weekly and total running distance determined based upon cumulative revolutions on a running wheel. Improvements in muscle endurance following CAT-1041 treatment versus control were also observed in post-mortem assessments of twitch force, tetanic force and specific force generation, each of which is an established measurement of muscle endurance, in excised diaphragm muscle.

We also observed in this same study that *mdx* mice treated with CAT-1041 showed significantly increased mass of two major leg muscles, the gastrocnemius and quadriceps. These increases were independent of changes in total body weight. CAT-1041 treated mice also had a statistically significant reduction in cardiac mass and fibrosis, suggesting that chronic treatment with CAT-1041 may have reduced the dilated cardiomyopathy typically observed in *mdx* mice.

In this study, we also observed that edasalonexent and CAT-1041 exhibited similar activity on muscle contractions of the extensor digitorum longus muscle in *mdx* mice with significant preservation of muscle function compared to control. Finally, in this study we observed a reduction in diaphragm and quadricep muscle fibrosis in *mdx* mice treated with CAT-1041 in comparison to control.

*Golden Retriever Dog Model.* We also evaluated the effects of edasalonexent in the GRMD dog model. A single oral dose of edasalonexent inhibited basal, or unstimulated, NF- $\kappa$ B activity by 48% in GRMD dogs. Edasalonexent also inhibited LPS-stimulated NF- $\kappa$ B activity by 75% and LPS-stimulated plasma levels of TNF $\alpha$  protein, a key marker of inflammatory response, by 77%. Together, these data suggest that a single oral dose of edasalonexent achieves sufficient exposure levels to inhibit activated NF- $\kappa$ B in a dog model of DMD.

*In Vitro Studies*

In an *in vitro* study in a mouse macrophage cell line, we observed that edasalonexent inhibited LPS-stimulated NF- $\kappa$ B activity to a greater extent than either of its components, salicylate and DHA, alone or in combination. We also observed that edasalonexent inhibited LPS-stimulated NF- $\kappa$ B activity in human PBMCs, which are a potential target tissue for edasalonexent. In studies performed with a mouse macrophage cell line, edasalonexent reduced the LPS-stimulated expression of a set of genes that encode pro-inflammatory mediators and whose expression is controlled by NF- $\kappa$ B.

*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

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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 benefiting from more frequent communication with the FDA to discuss all aspects of clinical development. In addition, drugs that receive fast track designation are eligible for accelerated approval and priority review if certain criteria are met. The FDA's rare pediatric disease designation gives us the potential to receive a priority review voucher if edasalonexent is approved. However, the rare pediatric disease program is set to expire in September 2020.

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

**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. We are developing CAT-5571 initially as a potential oral treatment for CF with potential effects on both the CFTR and on the clearance of *Pseudomonas aeruginosa*. CAT-5571 is a small molecule that activates autophagy, a process that maintains cellular homeostasis and host defense mechanisms, which are known to be impaired in CF.

We have shown in preclinical studies that CAT-5571 synergistically activates autophagy in cultured primary human bronchial epithelial cells isolated from patients with CF. In addition, we have shown in *ex vivo* preclinical studies that CAT-5571, in combination with lumacaftor/ivacaftor, a combination drug that consists of lumacaftor, which increases CFTR proteins that are trafficked to the cell surface, and ivacaftor, which increases the activity of the CFTR protein at the surface of epithelial cell, enhances cell-surface trafficking and function of CFTR with the F508del mutation, which is the most frequent CFTR mutation and is present in 86% of patients included in the Cystic Fibrosis Foundation United States Patient Registry. We have also shown that CAT-5571 enhances the clearance of *Pseudomonas aeruginosa* infection in preclinical models of CF, irrespective of CFTR mutation status. We are conducting additional preclinical activities with CAT-5571.

In 2017, we plan to continue preclinical evaluation of CAT-5571 in animal models of CF, and to conduct investigational new drug, or IND, application-enabling activities for CAT-5571. If we are successful in these activities, we intend to advance CAT-5571 into a Phase 1 clinical trial in 2018.

*Cystic Fibrosis*

Cystic fibrosis 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 CFTR 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 *Pseudomonas 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.

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**CAT-4001**

CAT-4001 is a SMART linker conjugate that we designed to combine the potentially beneficial activities of monomethyl fumarate and DHA on the Nrf2 and NF- $\kappa$ B pathways. CAT-4001 is a small molecule designed to activate the Nrf2 pathway and inhibit the NF- $\kappa$ B pathway. We are developing CAT-4001 initially for the treatment of severe, rare neurodegenerative diseases, such as FA and ALS, two diseases of the central nervous system in which the Nrf2 and NF- $\kappa$ B pathways have been implicated, irrespective of mutation status. Nrf2 is a gene transcription factor, a protein that works inside of cells to control the expression of genes, that control the body's response to cellular stress and oxidative damage. We are conducting preclinical activities with CAT-4001.

We have shown that CAT-4001 modulates the Nrf2 and NF- $\kappa$ B pathways in both cellular assays and animal models. In these studies, we have also observed that the activity produced by CAT-4001 was greater than that produced by the individual bioactives, monomethyl fumarate and DHA, either alone or in combination at approximately equivalent amounts to those contained in the CAT-4001 conjugate. Oxidative stress and neuroinflammation are believed to play a central role in a number of neurodegenerative diseases, including FA and ALS. In addition, monomethyl fumarate is the circulating form of the active ingredient of Biogen's Tecfidera (dimethyl fumarate), an FDA-approved treatment for multiple sclerosis, another neurodegenerative disease. We believe that this known therapeutic effectiveness of monomethyl fumarate offers further support for the potential for CAT-4001 to be developed for the treatment of neurodegenerative diseases.

Based on its mechanism of action, we believe that CAT-4001 has the potential to be a disease modifying agent in certain neurodegenerative diseases. In 2017, we plan to continue preclinical evaluation of CAT-4001 in animal models of FA as well as ALS.

*Friedreich's Ataxia*

Friedreich's ataxia is a rare genetic disease that causes nervous system damage and compromises motor coordination. FA is caused by a defect in the frataxin gene, which regulates iron levels in the mitochondria. In the majority of cases, the genetic defect in FA causes a reduction in the production of the frataxin protein and iron levels in mitochondria become poorly regulated. In FA, iron overload in mitochondria affects metabolism, causing oxidative stress and ultimately damaging mitochondrial DNA. Progressive degeneration of central and peripheral nervous systems in FA patients causes impaired gait and coordination, muscle loss and fatigue. Disease progression varies, but generally, the patient is confined to a wheelchair within 10 to 20 years after the appearance of the first symptoms. Patients may become completely incapacitated in later stages of the disease.

FA occurs in both males and females and is estimated to affect 1 in 50,000 individuals. Based on this prevalence rate, we believe there are up to 6,000 patients with FA in the US and up to 15,000 FA patients in the European Union.

The Friedreich's Ataxia Research Alliance announced in January 2016 that we were the recipient of the Kyle Bryant Translational Research Award. The Kyle Bryant Translational Research Award specifically focuses on pre-clinical and clinical investigations that target treatments for FA.

*Amyotrophic Lateral Sclerosis*

ALS, sometimes called Lou Gehrig's disease or classical motor neuron disease, is a rapidly progressive, fatal neurological disease that attacks the nerve cells responsible for controlling voluntary muscles. Eventually, muscle weakness and atrophy occur. People with ALS lose the ability to stand and walk, and use their hands and arms. In later stages of the disease, individuals have difficulty breathing as the muscles of the respiratory system weaken. Although ventilation support can enable breathing and

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prolong survival, it does not affect the progression of ALS. Most people with ALS die from respiratory failure, usually within three to five years of diagnosis.

According to the ALS Association, approximately 5,600 people in the United States are diagnosed with ALS each year. The incidence of ALS is two per 100,000 people, and it is estimated that as many as 30,000 Americans may have the disease at any given time. ALS occurs throughout the world and affects all racial, ethnic and socioeconomic groups.

***CAT-2000 Series***

Our CAT-2000 compounds are SMART linker conjugates of nicotinic acid and EPA. The linkers for our CAT-2000 series compounds are cleaved through intracellular enzymatic hydrolysis, to release the component bioactives to inhibit SREBP. By using different linkers, we have produced product candidates within the CAT-2000 series that possess different hydrolysis rates, resulting in distinct pharmacokinetics, biodistribution and pharmacology. We have been able to demonstrate enzymatic hydrolysis and inhibition of SREBP in *in vitro* studies with CAT-2000 molecules. In addition, *in vivo*, CAT-2000 molecules have demonstrated efficacy in multiple preclinical models of hyperlipidemias and NASH. We believe that our portfolio of CAT-2000 molecules, which includes the clinical-stage molecules CAT-2003 and CAT-2054 and other discovery-stage molecules with intermediate rates of hydrolysis, provides an opportunity to develop a therapy for NASH. We intend to pursue a partnership for further development of the CAT-2000 series in NASH.

**Sales and Marketing**

Given our stage of development, we have not yet established a commercial organization or distribution capabilities, nor have we entered into any collaboration or co-promotion arrangements. If we are able to progress our edasalonexent program, we intend to commercialize edasalonexent in North America ourselves and commercialize edasalonexent outside of North America either ourselves or with a collaborator. In addition, we intend to expand the drug development applications of our SMART linker drug discovery platform through selective collaborations with leading biotechnology and pharmaceutical companies.

**Manufacturing and Supply**

Each of our SMART linker conjugate product candidates is a small molecule compound 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.

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

***Edasalonexent for Duchenne Muscular Dystrophy***

There are currently only two therapies approved in the United States for the treatment of DMD. Sarepta's drug Exondys 51, also known as eteplirsen, was approved by the FDA for the treatment of DMD under the accelerated approval pathway in September 2016 for patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. In addition, in February 2017, Marathon Pharmaceuticals, LLC announced that the FDA granted approval of EMFLAZA, also known as deflazacort, a corticosteroid, for the treatment of DMD in patients five years and older. Outside of the United States, PTC Therapeutics' drug ataluren, also known as Translarna, has been conditionally approved within the European Union Member States, Iceland, Liechtenstein, Norway, Israel and South Korea for the treatment of nonsense mutation DMD. Although not previously approved for the treatment of DMD, corticosteroid therapy, including prednisone, is considered standard of care and is often prescribed to treat the inflammation underlying DMD and to delay loss of ambulation.

A number of companies are developing therapies to treat DMD in patients with specific mutations in the dystrophin gene. In addition to eteplirsen, Sarepta has two additional exon-skipping therapies for DMD in Phase 3 clinical development. These agents, SRP-4053 and SRP-4045, target skipping of exons 53 and 45, respectively. 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. NS Pharma has a compound, NS-065/NCNP-01, in Phase 2 clinical development in the United States and Japan for patients with mutations amenable to exon 53 skipping. Based on the prevalence of the specific mutations that these product candidates being developed by Sarepta, Daiichi-Sankyo and NS-Pharma are designed to address, they would be expected to have the potential to be effective in an aggregate of approximately 16% of DMD patients. In addition to these clinical stage programs, BioMarin has announced its intent to continue to explore the development of next generation oligonucleotides for the treatment of DMD, and Wave Life Sciences is developing an exon 51 skipping candidate, WVE-210201, for which it has announced plans to enter the clinic in the second half of 2017.

In addition to exon-skipping therapies, other companies have alternative therapeutic approaches to the treatment of DMD in late stage clinical development. Santhera announced in September 2016 that it enrolled its first patient in its Phase 3 trial (SIDEROS) that will assess the efficacy of its drug Raxone®, also known as idebenone, in slowing the rate of respiratory function decline in DMD patients receiving concomitant glucocorticoids. Santhera has stated that successful completion of the SIDEROS trial will provide the necessary data to support an NDA filing with FDA for Raxone. Santhera has filed a marketing authorization application with the EMA for Raxone for the treatment of DMD in patients with respiratory function decline and not taking concomitant glucocorticoids. PTC Therapeutics' ataluren provides another alternative therapeutic approach to treating DMD, already approved outside of the United States as mentioned above. Ataluren is designed to enable the formation of a functioning dystrophin protein in patients with DMD caused by a nonsense mutation. In February 2016, PTC Therapeutics received a Refuse to File letter for ataluren from the FDA and appealed this decision, and this appeal was subsequently denied by the FDA in October 2016. PTC Therapeutics filed a new ataluren NDA for nonsense mutation DMD over protest with the FDA in March 2017. A number of companies also have products candidates in clinical development for DMD, including Akashi Therapeutics, Bristol-Myers Squibb, Capricor Therapeutics, Cardero Therapeutics, Italfarmaco SpA, Pfizer, Phrixus Pharmaceuticals, Reveragen, Summit Plc and Taiho Pharmaceuticals. If successfully

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

As of December 31, 2016, our patent estate included over 20 issued U.S. patents, over 50 issued foreign patents, over 10 pending U.S. patent applications and over 35 pending foreign patent applications.

With regard to edasalonexent, we have five issued U.S. patents with composition of matter and method of use claims directed to 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 including Australia, China, Europe, Japan, Mexico and New Zealand, which are expected to expire in 2029, without taking potential patent term extensions into account, and at least five pending patent applications in various other countries and regions in North America, South America, and Asia, which, if issued, are expected to expire in 2029, without taking potential patent term extensions into account.

With regard to CAT-5571, we have two granted U.S. patents with composition of matter claims generically covering CAT-5571, which are scheduled to expire in 2030, without taking potential patent term extensions into account. We also have a pending international patent application with claims covering CAT-5571 and related compounds and their use, including their use in the treatment of cystic fibrosis.

With regard to CAT-4001, we have two granted U.S. patents with composition of matter and method of use claims directed to CAT-4001 and its use. These U.S. patent are scheduled to expire in 2031, without taking a potential patent term extension into account. In addition, we have patents that have been granted in various countries including Australia, China, Japan, Mexico, New Zealand and Taiwan, which are expected to expire in 2031, without taking potential patent term extensions into account, and at least 5 pending patent applications in various other countries and regions in North

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America, South America, Europe and Asia, which, if issued, are expected to expire in 2031, without taking potential patent term extensions into account.

With regard to CAT-2003 and CAT-2054, we have four issued U.S. patents with composition of matter and method of use claims directed to CAT-2003 and CAT-2054 and their use. These U.S. patents are scheduled to expire in 2030 and 2031, without taking potential patent term extensions into account. In addition, we have patents that have been granted in several different countries including Australia, Mexico, China, Japan and New Zealand, which are expected to expire in 2030, without taking potential patent term extensions into account and at least 20 pending applications in various other countries and regions including North and South America, Europe, and Asia, which, if issued, are expected to expire in 2030, without taking patent term extensions into account. In addition, we have a pending U.S. patent application covering CAT-2054, which, if issued, is expected to expire in 2033, without taking a potential patent term extension into account. We have at least 10 counterpart patent applications pending in various countries and regions in North America, South America, Europe and Asia, which, if issued, are expected to expire in 2033, without taking potential patent term extensions into account.

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, CAT-5571, CAT-4001, CAT-2003 and CAT-2054 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 European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, 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



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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.

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*

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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

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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 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. 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 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,

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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 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.

*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.

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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.

*Submission of an NDA to the FDA*

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, which for federal fiscal year 2017 is \$2,038,100. The sponsor of an approved NDA is also subject to annual product and establishment user fees, which for fiscal year 2017 are \$97,750 per product and \$512,200 per establishment.

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

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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.

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

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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

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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



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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 marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

*Abbreviated New Drug Applications for Generic Drugs*

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

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the 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

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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.

*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).

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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.

*Pediatric Studies and Exclusivity*

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.

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

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot 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 drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

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If a product with orphan status 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 be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances, such as if the later product is shown to be clinically superior to our product or due to an inability to assure a sufficient quantity of the orphan drug. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

*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.

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*The 21st Century Cures Act*

On December 13, 2016, President Obama signed the Cures Act into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the National Institutes of Health. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Health Service Act, or PHSA, Title III of the Cures Act seeks to accelerate the discovery, development and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

***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.

***Procedures Governing Approval of Drug Products in the European Union***

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a product under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing

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authorization by the EC that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a 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 European Union, 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 European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 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.

*Clinical Trial Approval*

Requirements for the conduct of clinical trials in the European Union, including GCP, are set forth in the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the European Union member states. Under this system, approval must be obtained from the competent national authority of each European Union member state in which a study is planned to be conducted. To this end, a Clinical Trial Application is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

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In April 2014, the European Union passed the new Clinical Trials Regulation, (EU) No 536/2014, which will replace the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the European Union, the new European Union clinical trials legislation was passed as a regulation that is directly applicable in all European Union member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable. According to the current plans of the EMA, the new Clinical Trials Regulation will become applicable in October 2018. The Clinical Trials Directive 2001/20/EC will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the European Union portal; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states; a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed jointly by all member states concerned. Part II is assessed separately by each member state concerned; strictly defined deadlines for the assessment of clinical trial applications; and the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

*Data and Market Exclusivity in the European Union*

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

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*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 European Union 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 European Union. 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.

*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, which is commonly referred to as "Brexit". The withdrawal of the U.K. from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the U.K. provides a notice of withdrawal pursuant to the European Union Treaty. The U.K. Prime Minister has stated that notice of withdrawal will be given by the end of March 2017. Since the regulatory framework for pharmaceutical products in the U.K. 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,



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Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the U.K. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the U.K.

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

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***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;

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

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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 2024 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.

With the new Presidential Administration and Congress, there will likely be additional legislative changes, including repeal and replacement of certain provisions of the Affordable Care Act. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the Affordable Care Act. The Budget Resolution is not a law, however, it is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the Affordable Care Act. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices.

The President and Congressional leaders have expressed interest in repealing certain Affordable Care Act provisions and replacing them with alternatives that may be less costly and provide state Medicaid programs and private health plans more flexibility. It is possible that these repeal and replacement 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. The scope of potential future legislation to repeal and replace Affordable Care Act provisions is highly uncertain in many respects, and it is possible that some of the Affordable Care Act provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with

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Affordable Care Act coverage expansion provisions. However, at this time the coverage expansion provisions of the Affordable Care Act appear most likely to be repealed and replaced.

**Employees**

As of December 31, 2016, we had 38 employees, 29 of whom were primarily engaged in research and development activities. A total of 19 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 One Kendall Square, Bldg. 1400E, Suite B14202, Cambridge, Massachusetts 02139, and our telephone number is (617) 349-1971. Our website address is [www.catabasis.com](http://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](http://www.catabasis.com) as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission (the "SEC"). These reports are also available at the SEC's Internet website at [www.sec.gov](http://www.sec.gov). The public may also read and copy any materials filed with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330.

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](http://www.catabasis.com), under "Corporate Governance" and are available in print to any person who requests copies by contacting us by calling (617) 349-1971 or by writing to Catabasis Pharmaceuticals, Inc., One Kendall Square, Bldg. 1400E, Suite B14202, Cambridge, Massachusetts 02139.

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**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 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 \$36.1 million, \$32.6 million and \$21.9 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of \$144.1 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, as well as 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 develop and conduct clinical trials with respect to our lead product candidate edasalonexent, including an ongoing Phase 1/2 clinical trial of edasalonexent for the treatment of Duchenne muscular dystrophy, or DMD;

initiate and continue research and preclinical and clinical development efforts for 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;

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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.

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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 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 collaborators does, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations. A decline in the value of our company could cause you to lose all or part of your investment.

***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 early-stage 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.

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

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase, if and to the extent of certain ongoing activities, particularly if we initiate new clinical trials of, initiate new research and preclinical development efforts for and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a future collaborator. 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 substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We will be required to expend significant funds in order to advance the development of edasalonexent, as well as our other product candidates. In addition, while we may seek one or more collaborators for future development of our product candidates or programs, such as our CAT-2000

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program in nonalcoholic steatohepatitis, or NASH, 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 and cash equivalents will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds.

Adequate additional financing may not be available to us on acceptable terms, on a timely basis or at all. Further, our ability to obtain additional debt financing may be limited by covenants we have made under our loan and security agreement with MidCap Financial Trust, or MidCap, Flexpoint MCLS SPV LLC, or Flexpoint, and Square 1 Bank, or Square 1, including our negative pledge with respect to intellectual property in favor of Flexpoint and Square 1, as well as our pledge to MidCap, Flexpoint and Square 1 of substantially all of our assets, other than our intellectual property, as collateral. Our failure to raise capital on acceptable terms as and when needed would have a material adverse effect on our business, results of operations, and our financial condition and our ability to pursue our business strategy.

We believe that our existing cash and cash equivalents and available-for-sale securities as of December 31, 2016 will enable us to fund our operating expenses, and debt service and capital expenditure requirements based on our current operating plan through March 31, 2018, assuming that we are not required to make unscheduled payments of indebtedness prior to such date. As our current lenders have the ability to call our existing debt prior to the maturity date, that condition could affect our ability to continue as a going concern for a period of one year from the date of this Annual Report on Form 10-K. We believe that the condition is mitigated by our management's plans, which include the ability to reduce or delay expenditures including expenditures for employee incentive compensation and direct program expenses. However, such actions to reduce or delay expenditures, if taken, could require us to delay, limit, reduce or terminate our product development efforts or other activities or undertake a restructuring of our workforce. Our estimate as to how long we expect our cash and cash equivalents 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, both short-term and long-term, will depend on many factors, including:

the progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, our product candidates and potential product candidates, including current and future clinical trials;

our ability to 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;



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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.***

We expect that 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. 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. For example, our credit facility with MidCap, Flexpoint and Square 1 contains restrictive covenants that, among other things and subject to certain exceptions, prohibit us from transferring any of our material assets, exclusively licensing our intellectual property (subject to certain exceptions), merging with or acquiring another entity, entering into a transaction that would result in a change of control, incurring additional indebtedness, creating any lien on our property, making investments in third parties or redeeming stock or paying dividends. Future debt securities or other financing arrangements could contain similar or more restrictive negative covenants. In addition, securing additional financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

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

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

As of December 31, 2016, we had \$5.8 million of outstanding principal payments under our credit facility with MidCap, Flexpoint and Square 1. We are required to repay principal and interest on these borrowings in monthly installments through October 2018. Subject to the restrictions in this existing credit facility, we could in the future incur additional indebtedness beyond our borrowings from MidCap, Flexpoint and Square 1.

Our outstanding indebtedness, including any additional indebtedness beyond our borrowings from MidCap, Flexpoint and Square 1, 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;

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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.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents. However, we may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under our existing debt instruments. Failure to make payments or comply with other covenants under our existing debt instruments could result in an event of default and acceleration of amounts due. Under our loan and security agreement with MidCap, Flexpoint and Square 1, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets or condition is an event of default. If an event of default occurs and the lenders accelerate the amounts due, we may not be able to make accelerated payments, and the lenders could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all of our assets other than our intellectual property. In addition, the covenants under our credit facility, the pledge of our assets as collateral and the negative pledge with respect to our intellectual property could limit our ability to obtain additional debt financing.

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

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

We are focused on discovering and developing novel small molecule drugs by applying our Safely Metabolized And Rationally Targeted, or 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 later stage clinical trials or in obtaining marketing approval thereafter. For example, although we have discovered and evaluated numerous compounds using our SMART linker drug discovery platform, we have not yet advanced a compound into Phase 3 clinical development and 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 could be substantially harmed.*

We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources in the development of 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.

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

completion of the ongoing open-label extension of our MoveDMD clinical trial;

initiation and successful enrollment and completion of additional clinical trials;

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;



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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, utrophin, 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 could 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 are conducting involves the development of new compounds using our SMART linker drug discovery platform. The 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.

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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, our ability to develop product candidates and obtain product revenues in future periods

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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 new drug applications, or NDAs, that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. If the FDA does not accept or approve our NDAs for either of our most advanced product candidates, 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- $\kappa$ B biomarker data in Part A of our MoveDMD Phase 1/2 clinical trial of edasalonexent for the treatment of DMD that demonstrated NF- $\kappa$ B target engagement via statistically significant reduction in NF- $\kappa$ B controlled gene expression for the 67 mg/kg/day and 100 mg/kg/day dosing levels, the primary efficacy endpoint in Part B of the trial 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.

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***Because we are developing edasalonexent for the treatment of DMD, a disease for which regulatory authorities have not issued definitive guidance as to how to measure and demonstrate efficacy, there is increased risk that the outcome of our clinical trials will not be satisfactory for marketing approval.***

There are currently only two therapies approved in the United States for the treatment of DMD. In addition, there has been limited historical clinical trial experience for the development of drugs to treat the underlying cause of DMD. As a result, the design and conduct of clinical trials for this disease, particularly for drugs to address the underlying cause of this disease, is subject to increased risk. In particular, while a general FDA Guidance for Industry on developing drugs for the treatment of DMD has been issued, regulatory authorities in the United States have not issued definitive direction as to how to measure and demonstrate efficacy. For example, we chose the primary endpoint in our MoveDMD Phase 1/2 clinical trial of edasalonexent for the treatment of DMD as change in muscle inflammation as measured by magnetic resonance imaging, or MRI, of leg muscles, which we believe had not previously been used as a primary endpoint for a Phase 2 or Phase 3 trial in DMD. We also included as exploratory endpoints the timed function tests best suited for this age group, specifically the 10-meter walk/run, 4-stair climb and time-to-stand tests, as well as other strength and functional measures, including the North Star ambulatory assessment questionnaire and the pediatric outcome data collection instrument. However, there is no definitive guidance from regulatory authorities that any of these endpoints, if met in a Phase 3 trial for DMD, would be satisfactory for marketing approval. In addition, since we believe we were the first company to use MRI T2 at 12 weeks as a primary endpoint in a DMD clinical trial, it is unclear whether the failure of edasalonexent to meet this efficacy endpoint is indicative of edasalonexent not having a treatment effect over the 12-week period, or if MRI T2 is an appropriate measure of treatment effect over a 12-week period.

***The regulatory approval processes for product candidates that target rare diseases, including DMD, cystic fibrosis, Friedreich's ataxia and ALS, 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, cystic fibrosis, Friedreich's Ataxia and ALS, 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.

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***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 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,



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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. For example, in 2014, in our clinical trials of CAT-2003 we observed gastrointestinal tolerability issues, including nausea, diarrhea and vomiting, and in some cases these adverse events led to dose reductions or discontinuations. 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;



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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, such as the delay we experienced in 2014 in one of our Phase 2 clinical trials of CAT-2003 while we reformulated CAT-2003 in a coated capsule and evaluated its tolerability;

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.

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



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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.

In particular, the successful completion of our clinical development program for edasalonexent for the treatment of DMD is 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. 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 may make it difficult for us to enroll enough patients to complete our clinical trials for edasalonexent in a timely and cost-effective manner.

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 co-medications. These inclusion criteria 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.



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***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;



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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.***

## Edgar Filing: CATABASIS PHARMACEUTICALS INC - Form 10-K

We do not have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We plan to use a combination of 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

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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 two therapies approved for the treatment of DMD in the United States, Sarepta Therapeutics' drug Exondys 51, also known as eteplirsen, and Marathon Pharmaceuticals' EMFLAZA, also known as deflazacort, a corticosteroid. Additionally, corticosteroid therapy, including prednisone, is often prescribed to treat the inflammation underlying DMD and to delay loss of ambulation. In addition, a number of companies are developing therapies to treat DMD, one of which is already on the market in Europe and others are in the process of registration or late stage clinical development, including, 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

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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.

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*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.

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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.

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**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, our loan and security agreement with MidCap, Flexpoint and Square 1 contains, and any 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.

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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,

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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;

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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.

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

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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, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Moreover, 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,

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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

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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

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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. Recent 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 includes 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. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a "first to file" system. The first-to-file provisions, however, only became effective in March 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. 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.

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***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 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.



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***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

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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.

***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

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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.

***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.

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*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.

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***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 will 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



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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 2024 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 the ACA, 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.

In addition, with the new Presidential Administration and Congress, there will likely be additional legislative changes, including repeal and replacement of certain provisions of the ACA. It remains to be seen, however, precisely what the new legislation will provide, when it will be enacted and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare. Such reforms 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 or commercialize product candidates. For example, the President and Congressional leaders have expressed interest in repealing certain ACA provisions and replacing them with alternatives that may be less costly and provide state Medicaid programs and private health plans more flexibility. It is possible that these repeal and replacement 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. The scope of potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, and it is 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.

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



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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.

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***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.

***A rare pediatric disease designation may not lead to the receipt of a Priority Review Voucher, even if edasalonexent is approved, due to the potential expiration of the FDA's Rare Pediatric Disease program.***

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

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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. 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 and Managing Growth**

***Our future success depends on our ability to retain our Chief Executive Officer and to attract, retain and motivate qualified personnel.***

We are highly dependent on the pharmaceutical research and development and business development expertise of Jill C. Milne, our President and Chief Executive Officer. Although we have entered into an employment agreement with Dr. Milne, this agreement does not prevent her from

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terminating her employment with us at any time. In the future, we may be dependent on other members of our management, scientific and development team.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. If we lose one or more of our executive officers or other key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers or other key employees 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, 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. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. 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.

**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 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.

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***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 Stock Market, including maintaining a minimum bid price of \$1.00 per share. The closing price of our common stock from February 1, 2017 to March 8, 2017 ranged from a high of \$1.25 per share and a low of \$1.13 per share. If in the future our common stock fails to meet the minimum bid price requirement to remain listed on The NASDAQ Stock Market, we could be subject to delisting from The NASDAQ Stock Market. If we were to be delisted, it could make trading in our stock more difficult.

If the minimum bid price of our common stock were to close below \$1.00 for 30 consecutive business days, we would likely receive notification from The NASDAQ Stock Market that we were not in compliance with the \$1.00 minimum bid price rule. If we do not regain compliance within the allotted compliance period, including any extensions that may be granted by The NASDAQ Stock Market, The NASDAQ Stock Market would notify us that our common stock would be delisted from The NASDAQ Stock Market, eliminating the only established trading market for our shares. We would then be entitled to appeal this determination to a NASDAQ Hearings Panel, which we may request review the matter in a written or an oral hearing.

In the event we are delisted from The NASDAQ Stock Market, we would be forced to list our shares on the OTC Electronic Bulletin Board or another quotation medium, such as the pink sheets, depending on our ability to meet the specific listing requirements of those quotation systems. As a result, an investor might find it more difficult to trade, or to obtain accurate price quotations for, such shares. Delisting might also reduce the visibility, liquidity, and price of our common stock.

***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, you may lose some or all of your investment. 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;

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the results of our efforts to develop additional product candidates or products;

actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

announcement or expectation of additional financing efforts;

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

variations in our financial results or those of companies that are perceived to be similar to us;

changes in estimates or recommendations by securities analysts, if any, that cover our stock;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors;

general economic, industry and market conditions; and

the other factors described in this "Risk Factors" section.

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 the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.***

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. 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," 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

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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. However, while we remain an emerging growth company, we will not 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 significant 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 December 31, 2016, we had outstanding 18,817,572 shares of common stock. The holders of an aggregate of 6,474,446 of these outstanding shares of common stock, along with the holders of warrants to purchase 24,556 shares of common stock, have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Following registration, such shares could be freely sold in the public market, subject to volume limitations applicable to affiliates.

We have filed registration statements registering a significant portion of the shares of common stock that we may issue under our equity compensation plans. As of December 31, 2016, we had outstanding options to purchase an aggregate of approximately 2,270,169 shares of our common stock, of which options to purchase approximately 851,769 shares were vested. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates.

***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. Furthermore, the terms of our credit facility with MidCap, Flexpoint and Square 1 preclude us from paying dividends, and any future debt agreements may also preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.



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***Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control all matters submitted to stockholders for approval.***

Our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding common stock and their affiliates, in the aggregate, beneficially owned shares representing approximately 63.8% of our capital stock as of December 31, 2016. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

delay, defer or prevent a change in control;

entrench our management or the board of directors; or

impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

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

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your 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.

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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

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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 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 Cambridge, Massachusetts and consist of approximately 19,000 square feet of leased office and laboratory space. The lease expires in June 2018. 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.

Table of Contents**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. The following table shows the high and low intraday sale prices per share of common stock as reported on the NASDAQ Global Market for the periods indicated:

	Common Stock			
	2016		2015	
	High	Low	High	Low
First Quarter	\$ 8.15	\$ 3.90	N/A	N/A
Second Quarter	\$ 7.23	\$ 3.53	\$ 14.00	\$ 11.51
Third Quarter	\$ 7.89	\$ 3.31	\$ 16.96	\$ 7.31
Fourth Quarter	\$ 6.25	\$ 3.22	\$ 10.83	\$ 6.32

On March 8, 2017, the last reported sale price for our common stock on the NASDAQ Global Market was \$1.16 per share.

**Holdings**

As of March 8, 2017, there were approximately 31 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. In addition, our ability to pay cash dividends on our common stock is prohibited by the covenants of our credit facility with MidCap Financial Trust, Flexpoint MCLS SPV LLC and Square 1 Bank.

**Comparative Stock Performance Graph**

*The performance graph in this Item 5 is not deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, or otherwise subject to the liabilities under that Section, and shall not be deemed incorporated by reference into any filing of Catabasis Pharmaceuticals, Inc. under the Securities Act of 1933 or the Securities Exchange Act of 1934, except to the extent we specifically incorporate it by reference into such a filing.*

The following graph shows a comparison from June 25, 2015, the date on which our common stock first began trading on the NASDAQ Global Market, of the cumulative total return on an assumed investment of \$100.00 in cash on June 25, 2015, in our common stock as compared to the same investment in the NASDAQ Composite Index, the NASDAQ Biotechnology Index, and the BioShares Biotechnology Clinical Trials Index, all through December 31, 2016. These returns are based on historical results and are not intended to suggest future performance. Data assumes the reinvestment of dividends. The graph assumes our closing sales price on June 25, 2015 of \$13.00 per share as the initial value of our common stock and not the initial offering price to the public of \$12.00 per share.

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The comparisons shown in the graph below are based upon historical data. We caution that the stock price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our common stock.

**COMPARISON OF CUMULATIVE TOTAL RETURN\***

Catabasis Pharmaceuticals, Inc., NASDAQ Composite Index,  
NASDAQ Biotechnology Index, and BioShares Biotechnology Clinical Trials Index

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\*  
\$100 invested on June 25, 2015

**Securities Authorized for Issuance under Equity Compensation Plans**

The following table contains information about our equity compensation plans as of December 31, 2016:

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	2,270,169(1)	\$ 6.11	669,799(2)
Equity compensation plans not approved by security holders			
<b>Total</b>	<b>2,270,169</b>	<b>\$ 6.11</b>	<b>669,799</b>

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- (1) Consists of stock options outstanding as of December 31, 2016 under our Amended and Restated 2008 Equity Incentive Plan, as amended, and our 2015 Stock Incentive Plan.
- (2) Consists of shares issuable under our 2015 Stock Incentive Plan and our 2015 Employee Stock Purchase Plan, but does not reflect automatic increases that were effective as of January 1, 2017 of 752,700 shares and 188,175 shares under the respective plans. Our 2015 Stock Incentive Plan provides for further annual increases, to be added as of the first day of each fiscal year, from January 1, 2018 until, and including, January 1, 2025, equal to the lowest of 1,297,334 shares of our

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common stock, 4% of the number of shares of our common stock outstanding on such first day of the fiscal year in question and an amount determined by our board of directors. 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, 2018 until, and including, January 1, 2026, in an amount equal to the least of 364,705 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.

**Recent Sales of Unregistered Securities**

Set forth below is information regarding securities issued by us during the year ended December 31, 2016 that were not registered under the Securities Act of 1933, as amended, or the Securities Act. Included is the consideration, if any, we received for such securities and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, or the SEC, under which exemption from registration was claimed. No underwriters were involved in any such issuances.

***Warrant exercises***

In February 2016, we issued 2,917 shares of our common stock upon the exercise of warrants at an exercise price of \$1.67 per share.

In March 2016, we issued 11,668 shares of our common stock upon the exercise of warrants at an exercise price of \$1.67 per share, and 5,987 shares of our common stock upon the cashless exercise of warrants to purchase 8,753 shares of our common stock.

In April 2016, we issued 10,669 shares of our common stock upon the exercise of warrants at an exercise price of \$1.67 per share.

All recipients either received adequate information about us or had access, through employment or other relationships, to such information. These issuances of shares of our common stock were exempt from registration under the Securities Act, pursuant to Section 4(a)(2) of the Securities Act.

**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.

**Use of Proceeds from IPO**

In June 2015, we completed our initial public offering, or the IPO, in which we issued and sold 5,750,000 shares of our common stock at a public offering price of \$12.00 per share, including 750,000 shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares of common stock, for aggregate gross proceeds of \$69.0 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-204144), which was declared effective by the SEC on June 24, 2015.

The net offering proceeds to us, after deducting underwriting discounts of \$4.8 million and offering expenses payable by us totaling \$2.5 million, were approximately \$61.7 million.

As of December 31, 2016, we had used approximately \$49.5 million of the net offering proceeds primarily to fund the costs of the clinical development of edasalonexent and CAT-2054, to fund research and development to advance other product candidates and for working capital and general corporate purposes. None of the offering proceeds were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates, other than payments in the ordinary course of business to officers for salaries and to non-employee directors as compensation for board or board committee service. There has been no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on June 25, 2015.

Table of Contents**Item 6. Selected Financial Data**

The selected consolidated statements of operations data for each of the three years in the period ended December 31, 2016 and the selected consolidated balance sheet data at December 31, 2016 and 2015 have been derived from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. We derived the consolidated financial data for the years ended December 31, 2013 and 2012 and as of December 31, 2014, 2013 and 2012 from our audited consolidated financial statements that are not included elsewhere in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our interim period results are not necessarily indicative of results to be expected in any future period.

The information set forth below should be read in conjunction with the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this Annual Report on Form 10-K and with our consolidated financial statements and notes thereto included elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data in this section are not intended to replace the consolidated financial statements and are qualified in their entirety by the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

Consolidated Statement of Operations Data	Catabasis Pharmaceuticals, Inc. Year Ended December 31,				
	2016	2015	2014	2013	2012
	(in thousands, except share and per share data)				
Operating expenses	\$ 35,558	\$ 31,659	\$ 21,681	\$ 18,119	\$ 15,673
Loss from operations	(35,558)	(31,659)	(21,681)	(18,119)	(15,673)
Other income (expense)	\$ (502)	\$ (971)	\$ (203)	\$ 1	\$ 4
Net loss	(36,060)	(32,630)	(21,884)	(18,118)	(15,669)
Net loss per share:					
Basic and Diluted	\$ (2.22)	\$ (4.06)	\$ (51.56)	\$ (47.80)	\$ (42.26)
Weighted-average common shares outstanding used in net loss per share:					
Basic and Diluted	16,230,190	8,041,948	424,477	379,025	370,772
<b>Balance Sheet Data:</b>					
Cash and cash equivalents	\$ 23,596	\$ 62,780	\$ 14,668	\$ 30,474	\$ 5,434
Working capital	31,203	55,773	10,788	27,651	3,728
Total assets	40,209	64,169	15,876	31,002	6,314
Notes payable, net of current portion and discount	2,479	5,720	4,390		
Preferred stock			80,146	80,146	38,724
Common stock and additional paid-in-capital	173,160	158,503	2,327	1,312	942
Total stockholders' equity (deficit)	29,086	50,493	(73,053)	(52,184)	(34,436)



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

*You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes 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 based on our proprietary Safely Metabolized And Rationally Targeted, or SMART, linker drug discovery platform. Our SMART linker drug discovery platform enables us to engineer product candidates that can simultaneously modulate multiple targets in a disease. Our proprietary product candidates impact pathways that are central to diseases where efficacy may be optimized by a multiple target approach. We have applied our SMART linker drug discovery platform to build an internal pipeline of product candidates for rare diseases, our primary focus, and plan to pursue partnerships to develop additional product candidates.

Our lead product candidate is edasalonexent, formerly known as CAT-1004, an oral small molecule. Based on its mechanism of action, the inhibition of NF- $\kappa$ B, or nuclear factor kappa-light-chain-enhancer of activated B cells, we believe edasalonexent has the potential to be a disease-modifying therapy for all patients affected by Duchenne muscular dystrophy, or 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 are currently conducting the MoveDMD<sup>®</sup> Phase 1/2 trial of edasalonexent in ambulatory boys with DMD between ages four and seven. The MoveDMD trial is a three-part clinical trial investigating the safety and efficacy of edasalonexent in DMD. We previously reported positive safety, tolerability, pharmacokinetics and biomarker results from Part A of the MoveDMD trial. We reported top-line Part B results in January 2017 indicating that the primary efficacy endpoint of 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 was not met. There were, however, consistent numerical improvements versus placebo across all functional exploratory endpoint measures for the higher dose, as well as numerical improvement versus placebo across multiple functional exploratory endpoint measures for the lower dose, while the lower dose had mixed results versus the higher dose. Changes in these functional measures were not statistically significant in Part B of the MoveDMD trial, which was not powered for functional measures. We believe that the potential treatment-associated effects from these exploratory endpoints warrant further evaluation in Part C of the MoveDMD trial, which is the ongoing open-label extension portion of the trial. We intend to transition all patients participating in Part C of the trial to the 100 mg/kg/day dose, the higher of the two dosing levels administered in Part B, and extending Part C by an additional 24 weeks, subject to institutional review board approval. We intend to report the results from Part C in 2017. We anticipate providing an interim update on Part C of the MoveDMD trial in the second quarter of 2017. In addition to our work in DMD, we are evaluating other diseases where the inhibition of NF- $\kappa$ B may be beneficial for further therapeutic applications of edasalonexent. There are a number of other rare

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diseases where NF- $\kappa$ B is believed to play an important role, such as Becker muscular dystrophy, which is one of nine types of muscular dystrophy and is characterized by slowly progressive muscle weakness of the legs and pelvis, and IgA nephropathy, a kidney disease that is believed to result from activation of mucosal immunity, leading to the synthesis of aberrantly glycosylated polymeric immunoglobulin A1, or IgA1, which enters the circulation and lodges in a patient's kidneys interfering with their proper function.

In addition to edasalonexent, we are developing a pipeline of product candidates using our SMART linker drug discovery platform as potential treatments for rare diseases including cystic fibrosis, or CF, amyotrophic lateral sclerosis, or ALS, and Friedreich's ataxia, or FA. Our pipeline includes CAT-5571 and CAT-4001, for which we are currently conducting preclinical activities. We are developing CAT-5571 initially as a potential oral treatment for CF, with potential beneficial effects on both trafficking and function of cystic fibrosis transmembrane conductance regulator, or CFTR, and the clearance of *Pseudomonas aeruginosa*. In CF, a malfunctioning CFTR 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 *Pseudomonas aeruginosa*, that are difficult to treat with standard antibiotics. CAT-5571 is a small molecule that activates autophagy, a process that maintains cellular homeostasis and host defense mechanisms, which are known to be impaired in CF. In addition, we are developing CAT-4001 as a potential treatment for neurodegenerative diseases such as FA and ALS, irrespective of mutation status. FA is a rare genetic disease that causes nervous system damage and compromises motor coordination. ALS, sometimes called Lou Gehrig's disease or classical motor neuron disease, is a rapidly progressive, fatal neurological disease that attacks the nerve cells responsible for controlling voluntary muscles. CAT-4001 is a small molecule that activates Nuclear factor (erythroid-derived 2)-like 2, or Nrf2, and inhibits NF- $\kappa$ B, two pathways that have been implicated in FA and ALS.

We have previously applied our SMART linker drug discovery platform to engineer our CAT-2000 series product candidates to inhibit the Sterol Regulatory Element Binding Protein, or SREBP, pathway. Inhibitors of SREBP have been proposed for the treatment of nonalcoholic steatohepatitis, or NASH, based on the role of SREBP in lipid metabolism and known human polymorphisms associated with NASH disease progression. NASH is characterized by the build-up of fat in the liver and chronic inflammation, which can trigger progression to fibrosis and ultimately cirrhosis and sometimes hepatocellular carcinoma. We have advanced two CAT-2000 molecules, CAT-2003 and CAT-2054, into clinical development and intend to pursue a partnership for further development of the CAT-2000 series in NASH, which, in addition to CAT-2003 and CAT-2054, includes other discovery-stage molecules with intermediate rates of hydrolysis.

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, 2016, we have raised an aggregate of \$185.8 million, of which \$92.9 million was from private placements of preferred stock, \$69.0 million represented gross proceeds from our IPO, \$11.5 million represented gross proceeds from our September 2016 registered direct offering, \$10.0 million was from a secured debt financing, \$1.6 million represented gross proceeds from our at-the-market, or ATM, offering program, and \$0.8 million was from common stock option and warrant exercises.

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**Financial Overview**

***Revenue***

To date, we have not generated any revenue from product sales or any other source and do not expect to generate any revenue from the sale of products in the near future. In the future, we will seek to generate revenue primarily from a combination of product sales and collaborations with strategic partners.

***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, or CROs, 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 preclinical 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*** Edasalonexent is a SMART linker conjugate of salicylic acid and the omega-3 fatty acid docosahexaenoic acid, or DHA, a naturally occurring unsaturated fatty acid with anti-inflammatory properties. We designed edasalonexent to inhibit NF- $\kappa$ B, a protein that is activated in DMD and that drives inflammation, fibrosis and muscle degeneration, and suppresses muscle regeneration. We reported results from Part A of the MoveDMD trial in January 2016 and reported top-line safety and efficacy results for Part B of the trial in January 2017. Results from both Part A and Part B of the MoveDMD trial are described further under "Business Our Product Candidates Edasalonexent Edasalonexent Clinical Development" above. In July 2016, we initiated an open-label extension, Part C of the MoveDMD trial, which is on-going and is expected to provide additional safety and efficacy data on edasalonexent. Following continued assessment of the effects in patients on edasalonexent in Part C of the MoveDMD trial, we will determine next steps for the edasalonexent program in DMD.

***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. We are developing CAT-5571 initially as a potential oral treatment for CF with potential effects on both the CFTR and on the clearance of *Pseudomonas aeruginosa*. CAT-5571 is a small molecule that activates autophagy, a process that maintains cellular homeostasis and host defense mechanisms, which are known to be impaired in CF. In 2017, we plan to continue preclinical evaluation of CAT-5571 in animal models of CF, and to conduct investigational new drug, or IND, application-enabling activities for CAT-5571. If we are successful in these activities, we intend to advance CAT-5571 into a Phase 1 clinical trial in 2018.



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**CAT-4001** CAT-4001 is a SMART linker conjugate that we designed to combine the potentially beneficial activities of monomethyl fumarate and DHA on the Nrf2 and NF-κB pathways. We are developing CAT-4001 initially for the treatment of severe, rare neurodegenerative diseases, such as FA and ALS, two diseases of the central nervous system in which the Nrf2 and NF-κB pathways have been implicated, irrespective of mutation status. Nrf2 is a gene transcription factor, a protein that works inside of cells to control the expression of genes, that control the body's response to cellular stress and oxidative damage. In 2017, we plan to continue preclinical evaluation of CAT-4001 in animal models of FA as well as ALS.

### **Other Programs**

Other research and development programs include activities related to pathway biology validation and SMART linker conjugate design and optimization. Our focus in these efforts is on rare diseases.

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,		
	2016	2015	2014
Edasalonexent	\$ 9,012	\$ 6,036	\$ 879
CAT-2054	3,474	5,365	3,208
CAT-2003	195	1,028	3,807
Other research and platform programs	3,450	2,395	1,276
Costs not directly allocated to programs:			
Employee expenses including cash compensation, benefits and stock-based compensation	6,593	5,879	4,575
Facilities	1,019	828	733
Consultants and professional expenses, including stock-based compensation	931	987	736
Other	776	512	472
Total costs not directly allocated to programs	9,319	8,206	6,516
Total research and development expenses	\$ 25,450	\$ 23,030	\$ 15,686

Since inception, the total direct expenses to support the edasalonexent program have been \$23.5 million. Since we began separately tracking CAT-2054 in 2013, the direct expenses to support that program have totaled \$12.7 million. Since inception, the total direct expenses to support the CAT-2003 program have been \$15.6 million.

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 the numerous risks and uncertainties associated with developing medicines, including the uncertainties of:

establishing an appropriate safety profile with IND-enabling toxicology studies;

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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, if and to the extent that our product candidate development programs progress. We expect that our research and development expenses in the year ending December 31, 2017 will be lower than in the year ending December 31, 2016 as a result of our plans to conduct clinical trials supporting one program in 2017 as compared to two programs in 2016. 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, business development 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 our general and administrative expenses will increase in the future, if and to the extent necessary to support our continued operations, potential commercialization of our product candidates and costs of operating as a public company. These increases, if necessary, will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. Additionally, we anticipate increased costs associated with being a public company including expenses related to services associated with maintaining compliance with exchange listing and Securities and Exchange Commission requirements, insurance costs and investor relations costs.

***Other Expense, Net***

Other expense, net consists of interest expense incurred on debt instruments, amortized deferred financing costs and amortized debt discount, net amortization expense on available-for-sale securities and changes in the fair value of warrant liability, as offset by any interest income earned on our cash and cash equivalents as well as any gains from insurance settlements. Upon completion of our IPO in

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June 2015, warrants to purchase preferred stock were converted to warrants to purchase common stock and as a result, we no longer record a fair value adjustment for warrants.

**Critical Accounting Policies and Significant 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 policies are 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 quotations and 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 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 quotes and 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.

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***Stock-Based Compensation***

We issue stock-based awards to employees and non-employees, generally in the form of stock options. We account for our stock-based awards in accordance with the Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, *Compensation - Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and modifications to existing stock options, to be recognized in the consolidated statements of operations and comprehensive loss based on their fair values. We account for stock-based awards to non-employees in accordance with FASB ASC Topic 505-50, *Equity-Based Payments to Non-Employees*, which requires the fair value of the award to be re-measured at fair value as the award vests.

Our stock-based awards are subject to either service or performance-based vesting conditions. Compensation expense related to awards to employees and directors with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Compensation expense related to awards to non-employees with service-based vesting conditions is recognized on the then-current fair value at each financial reporting date prior to the measurement date over the associated service period of the award, which is generally the vesting term, using the accelerated attribution method. Compensation expense related to awards to employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable. Compensation expense related to awards to non-employees with performance-based vesting conditions is recognized based on the then-current fair value at each financial reporting date prior to the measurement date over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

Described below is the methodology we have utilized in measuring stock-based compensation expense. Following the consummation of our IPO, stock option values have been determined based on the quoted market price of our common stock.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (i) the expected volatility of our stock, (ii) the expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. Due to the lack of company-specific historical and implied volatility data, we base our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. For these analyses, we select companies with comparable characteristics to ours including enterprise value, risk profiles and position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We estimate the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option were based on the U.S. Treasury yield curve in effect during the period the options were granted.

We are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from our estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based



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compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

We have computed the fair value of employee, director, consultant and advisor stock options at date of grant using the following weighted-average assumptions:

	Year Ended December 31,		
	2016	2015	2014
Weighted average expected volatility	72.0 - 73.9%	73.6 - 86.8%	75.2 - 83.4%
Expected term (in years)	6.25	6.17 - 10.00	6.25 - 10.00
Risk free interest rate	1.24 - 2.00%	0.92 - 2.45%	1.71 - 3.01%
Expected dividend yield	0%	0%	0%

Prior to our IPO, the estimated fair value of our common stock was determined contemporaneously by our board of directors based on valuation estimates provided by management and prepared in accordance with the framework of the American Institute of Certified Public Accountants' *Technical Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Certain of these valuation estimates were prepared with the assistance of a third-party specialist. Our contemporaneous valuations of our common stock were based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector and the prices at which we sold shares of preferred stock, the superior rights and preferences of securities senior to our common stock at the time of each grant and the likelihood of achieving a liquidity event such as an IPO.

The following table summarizes the classification of our stock-based compensation expense recognized in our statements of operations (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Research and development	\$ 723	\$ 681	\$ 434
General and administrative	1,437	977	463
<b>Total</b>	<b>\$ 2,160</b>	<b>\$ 1,658</b>	<b>\$ 897</b>

### Results of Operations

#### *Comparison of the Years Ended December 31, 2016 and 2015*

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015, together with the dollar change in those items (in thousands):

	Year Ended December 31,		Period-to- Period Change
	2016	2015	
<b>Operating expenses:</b>			
Research and development	\$ 25,450	\$ 23,030	\$ 2,420
General and administrative	10,108	8,629	1,479
Total operating expenses	35,558	31,659	3,899
Loss from operations	(35,558)	(31,659)	(3,899)
Other expense, net	(502)	(971)	469
<b>Net loss</b>	<b>\$ (36,060)</b>	<b>\$ (32,630)</b>	<b>\$ (3,430)</b>



Table of Contents*Research and Development Expenses*

Research and development expenses increased by \$2.4 million to \$25.5 million for the year ended December 31, 2016 from \$23.0 million for the year ended December 31, 2015, an increase of 10%. The increase in research and development expenses was primarily attributable to a net increase of \$1.3 million in direct program costs, comprised of an increase of \$3.0 million in costs related to edasalonexent, primarily related to the MoveDMD clinical trial, and an increase of \$1.0 million in direct costs related to pre-clinical programs, partially offset by a decrease of \$2.7 million across the CAT-2054 and CAT-2003 programs. In addition, costs related to internal research and development operations increased by \$1.1 million, \$0.7 million of which was associated with salaries, benefits and stock-based compensation expenses for new hires, \$0.2 million of which was attributable to increased facilities expense, and \$0.2 million of which was spread across other categories, including depreciation and professional services.

*General and Administrative Expenses*

General and administrative expenses increased by \$1.5 million to \$10.1 million for the year ended December 31, 2016 from \$8.6 million for the year ended December 31, 2015, an increase of 17%. The increase in general and administrative expenses was attributable to increased employee costs of \$0.7 million associated with salaries, benefits, and stock-based compensation expenses for new hires; increased consulting and professional fees of \$0.5 million, driven by the costs of operating as a public company; and increased insurance expense of \$0.3 million due to our public company directors and officers insurance policy.

*Other Expense, Net*

Other expense, net decreased by \$0.5 million to \$0.5 million for the year ended December 31, 2016 from \$1.0 million for the year ended December 31, 2015. The decrease in other expense, net consisted of \$0.2 million in lower interest expense as a result of amortization of debt principal, \$0.2 million in increased interest and investment income as a result of our investments in available-for-sale securities, and \$0.1 million from property insurance claim gains.

*Comparison of the Years Ended December 31, 2015 and 2014*

The following table summarizes our results of operations for the years ended December 31, 2015 and 2014, together with the dollar change in those items (in thousands):

	Year Ended December 31,		Period-to- Period Change
	2015	2014	
Operating expenses:			
Research and development	\$ 23,030	\$ 15,686	\$ 7,344
General and administrative	8,629	5,995	5,995
Total operating expenses	31,659	21,681	13,339
Loss from operations	(31,659)	(21,681)	(9,978)
Other expense, net	(971)	(203)	(768)
Net loss	\$ (32,630)	\$ (21,884)	\$ (10,746)

*Research and Development Expenses*

Research and development expenses increased by \$7.3 million to \$23.0 million for the year ended December 31, 2015 from \$15.7 million for the year ended December 31, 2014, an increase of 46%. The

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increase in research and development expenses was primarily attributable to a net increase of \$5.7 million in direct program costs, reflecting an increase of \$5.2 million in costs related to edasalonexent primarily related to the MoveDMD Phase 1/2 clinical trial, and a net increase of \$0.5 million in costs related to our other programs. In addition, the costs related to internal research and development increased by \$1.6 million, \$0.8 million of which was attributable to compensation increases for new hires, \$0.4 million of which was attributable to obligations under a letter agreement with a former employee, pursuant to which we agreed to make severance payments, \$0.3 million of which was attributable to increases in consulting and professional services, and \$0.1 million of which was attributable to increased facilities expense.

*General and Administrative Expenses*

General and administrative expenses increased by \$2.6 million to \$8.6 million for the year ended December 31, 2015 from \$6.0 million for the year ended December 31, 2014, an increase of 43%. The increase in general and administrative expenses was primarily attributable to increased employee costs of \$1.4 million associated with salaries, benefits, and stock-based compensation expenses for new hires; increased consulting and professional fees and franchise taxes of \$0.8 million, driven by the costs of becoming and operating as a public company; increased insurance expense of \$0.3 million due to our public company directors and officers insurance policy; and increased facilities expense of \$0.1 million.

*Other Expense, Net*

Other expense, net increased by \$0.8 million to \$1.0 million for the year ended December 31, 2015 from \$0.2 million for the year ended December 31, 2014. Other expense primarily consists of interest expense, which increased by \$0.8 million for the year ended December 31, 2015 due to the interest expense on our credit facility, which we entered into in August 2014.

**Liquidity and Capital Resources**

From our inception through December 31, 2016, we have raised an aggregate of \$185.8 million, of which \$92.9 million was from private placements of preferred stock, \$69.0 million represented gross proceeds from our IPO, \$11.5 million represented gross proceeds from our September 2016 registered direct offering, \$10.0 million was from a secured debt financing, \$1.6 million represented gross proceeds from our ATM offering program and \$0.8 million was from common stock option and warrant exercises. As of December 31, 2016, we had \$38.5 million in cash, cash equivalents and available-for-sale securities.

We have not generated any revenue to date. We have incurred significant annual net operating losses in every year since our inception and expect to incur a net operating loss in 2017 and continue to incur net operating losses for the foreseeable future. As of December 31, 2016, we had an accumulated deficit of \$144.1 million. We expect to continue to incur significant expenses and operating losses for the next several years. 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.

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***Initial Public Offering***

In June 2015, we completed the sale of an aggregate of 5,750,000 shares of our common stock, including 750,000 shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares of common stock, in our IPO, at a price to the public of \$12.00 per share. Net proceeds from the IPO were \$61.7 million, after deducting underwriting discounts, commissions and offering-related expenses of approximately \$7.3 million.

In connection with our IPO, all shares of our preferred stock were automatically converted into an aggregate of 9,029,549 shares of our common stock and our outstanding warrants to purchase 315,688 shares of preferred stock were automatically converted into warrants to purchase 24,566 shares of common stock with an exercise price of \$12.2114 per share.

***At-the-Market Offering***

In August 2016, we entered into a sales agreement with Cowen and Company LLC, or Cowen, pursuant to which we may issue and sell shares of our common stock for an aggregate maximum offering amount of \$10.0 million under an ATM offering program. Cowen is not required to sell any specific amount, but acts as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. Shares sold pursuant to the sales agreement have been sold pursuant to a shelf registration statement, which became effective on July 19, 2016, or the Shelf Registration Statement. We pay Cowen 3% of the gross proceeds from any common stock sold through the sales agreement.

During the year ended December 31, 2016, we sold an aggregate of 368,015 shares of common stock pursuant to the ATM offering program, at an average price of \$4.35 per share, for gross proceeds of \$1.6 million, resulting in net proceeds of \$1.4 million after deducting sales commissions and offering expenses of approximately \$0.2 million in the aggregate. As of December 31, 2016, \$8.4 million of common stock remained available for sale under the ATM offering program.

***Registered Direct Offering***

In September 2016, we closed an underwritten registered direct offering, in which we sold 2,875,000 shares of our common stock (including 375,000 shares of common stock sold pursuant to the exercise of an option by the underwriter to purchase additional shares) at an offering price of \$4.00 per share. The shares sold in the offering were sold pursuant to the Shelf Registration Statement. We received aggregate gross proceeds from the offering of \$11.5 million, resulting in net proceeds of \$10.6 million after deducting underwriting discounts and commissions and offering expenses of approximately \$0.9 million in the aggregate.

***Preferred Stock Financing***

In March 2015, we raised \$12.4 million in gross proceeds from the sale of 13,062,965 shares of our series B preferred stock at a price per share of \$0.9503.

***Credit Facility***

On August 27, 2014, we entered into a loan and security agreement with MidCap Financial Trust, Flexpoint MCLS Holdings, LLC and Square 1 Bank, or the Credit Facility. In March and December 2015, we entered into amendments to the Credit Facility, or the March 2015 Amendment and the December 2015 Amendment, respectively. As amended, the Credit Facility provided for initial borrowings of \$5.0 million and additional borrowings of up to \$20.0 million. Concurrently with entering into the Credit Facility in August 2014, we borrowed \$5.0 million under a term loan under the Credit Facility and we issued to the lenders warrants to purchase an aggregate of 157,844 shares of our

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series B preferred stock at an exercise price of \$0.9503 per share. Concurrently with the March 2015 Amendment, we drew down an additional \$5.0 million under our term loan under the Credit Facility and we issued to the lenders warrants to purchase an aggregate of 157,844 shares of our series B preferred stock at an exercise price of \$0.9503 per share. The remaining amounts available for borrowing under this arrangement expired unused as of July 31, 2015. All borrowings under the Credit Facility are due on October 1, 2018 and are collateralized by substantially all of our personal property, other than our intellectual property. The December 2015 Amendment revised terms to allow for the creation of a wholly owned subsidiary entity.

There are no financial covenants associated with the Credit Facility; however, there are negative covenants that prohibit us from transferring any of our material assets except to our subsidiary, exclusively licensing our intellectual property (subject to certain exceptions), merging with or acquiring another entity, entering into a transaction that would result in a change of control, incurring additional indebtedness, creating any lien on our property, making investments in third parties or redeeming stock or paying dividends.

The Credit Facility also includes events of default, the occurrence and continuation of any of which provides the lenders the right to exercise remedies against us and the collateral securing the loans under the Credit Facility, including cash. These events of default include, among other things, failure to pay amounts due under the Credit Facility, insolvency, the occurrence of a material adverse event, which includes a material adverse change in our business, operations or conditions (financial or otherwise) or a material impairment of the prospect of repayment of any portion of the obligations, the occurrence of any default under certain other indebtedness and a final judgment against us in an amount greater than \$250,000. The occurrence of a material adverse event could result in acceleration of payment of the debt. At December 31, 2016 and December 31, 2015, we concluded that the likelihood of the acceleration of the debt was remote, as a material adverse event had not occurred and was unlikely to occur and therefore the debt was classified in current and long-term liabilities based on scheduled principal payments.

We were obligated to make monthly interest-only payments on any term loans borrowed under the Credit Facility until September 1, 2015 and we are obligated to pay 36 consecutive, equal monthly installments of principal and interest from October 1, 2015 through September 1, 2018. Term loans under the Credit Facility bear interest at an annual rate of 7.49%. Following the occurrence and during the continuance of an event of default, borrowings under the Credit Facility will bear interest at an annual rate that is 5.00% above the rate that is otherwise applicable. In addition, a final payment equal to 3.48% of any amounts drawn under the Credit Facility is due upon the earlier of the maturity date, acceleration of the term loans or prepayment of all or part of the term loans.

***Funding Requirements***

If, and to the extent that, we continue the research and development of, and conduct clinical trials and seek marketing approval for, our product candidates, we expect our expenses to increase in connection with such activities. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We believe that our existing cash and cash equivalents and available-for-sale securities as of December 31, 2016 will enable us to fund our operating expenses and debt service and capital expenditure requirements based on our current operating plan through March 31, 2018, assuming no

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unscheduled repayment of indebtedness prior to such date. As our current lenders have the ability to call our existing debt prior to the maturity date, that condition could affect our ability to continue as a going concern for a period of one year from the date of this Annual Report on Form 10-K. We believe that the condition is mitigated by management's plans, which include the ability to reduce or delay expenditures including expenditures for employee incentive compensation and direct program expenses.

Our estimate that we will be able to fund our operating expenses and debt service and capital expenditure requirements through March 31, 2018 is based on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of edasalonexent and our other current and potential product candidates, and because the extent to which we may enter into collaborations with third parties for the development of these product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;

the success of any future collaborations;

the extent to which we acquire or in-license other medicines and technologies;

the costs, timing and outcome of regulatory review of our product candidates;

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

our ability to establish and maintain collaborations on favorable terms, if at all.

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 many 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. 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 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.

Table of Contents**Cash Flows****Comparison of the Years Ended December 31, 2016 and 2015**

The following table provides information regarding our cash flows for the years ended December 31, 2016 and 2015 (in thousands):

	Year Ended December 31,	
	2016	2015
Net cash used in operating activities	\$ (32,858)	\$ (29,793)
Net cash used in investing activities	(15,490)	(421)
Net cash provided by financing activities	9,164	78,326
Net (decrease) increase in cash and cash equivalents	\$ (39,184)	\$ 48,112

*Net Cash Used in Operating Activities*

Net cash used in operating activities was \$32.9 million for the year ended December 31, 2016 and consisted primarily of a net loss of \$36.1 million adjusted for non-cash items, including stock-based compensation expense of \$2.2 million, depreciation and amortization expense of \$0.4 million, non-cash interest expense of \$0.3 million and accretion of discount/premium on investment securities of \$0.1 million, and a net decrease in operating assets of \$0.2 million, which resulted primarily from an increase in accrued expenses of \$0.4 million, partially offset by an increase in prepaid expenses and other current assets of \$0.2 million.

Net cash used in operating activities was \$29.8 million for the year ended December 31, 2015 and consisted primarily of a net loss of \$32.6 million adjusted for non-cash items, including stock-based compensation expense of \$1.7 million, non-cash interest expense of \$0.3 million and depreciation and amortization expense of \$0.2 million, and a net decrease in operating assets of \$0.6 million, which resulted primarily from an increase in accrued expenses of \$0.9 million and an increase in accounts payable of \$0.2 million, partially offset by an increase in prepaid expenses and other current assets of \$0.5 million.

*Net Cash Used in Investing Activities*

Net cash used in investing activities was \$15.5 million for the year ended December 31, 2016 compared to \$0.4 million for the year ended December 31, 2015, an increase of \$15.1 million, which primarily resulted from net purchases of available-for-sale securities.

*Net Cash Provided by Financing Activities*

Net cash provided by financing activities was \$9.2 million for the year ended December 31, 2016 compared to \$78.3 million for the year ended December 31, 2015. The cash provided by financing activities for the year ended December 31, 2016 primarily consisted of net proceeds from our registered direct offering of \$10.6 million, net proceeds from our ATM offering program of \$1.4 million, and \$0.5 million in proceeds from exercises of common stock options and warrants, partially offset by \$3.3 million in payments made on borrowings under the Credit Facility. The cash provided by financing activities for the year ended December 31, 2015 primarily consisted of net proceeds received from our IPO of \$61.7 million, net proceeds of \$12.3 million from the issuance of 13,062,965 shares of our series B preferred stock in March 2015, net borrowings of \$4.2 million from our Credit Facility, and \$0.1 million from stock option exercises.



Table of Contents**Comparison of the Years Ended December 31, 2015 and 2014**

The following table provides information regarding our cash flows for the years ended December 31, 2015 and 2014 (in thousands):

	<b>Year Ended December 31,</b>	
	<b>2015</b>	<b>2014</b>
Net cash used in operating activities	\$ (29,793)	\$ (20,412)
Net cash used in investing activities	(421)	(228)
Net cash provided by financing activities	78,326	4,834
Net increase (decrease) in cash and cash equivalents	\$ 48,112	\$ (15,806)

*Net Cash Used in Operating Activities*

Net cash used in operating activities was \$29.8 million for the year ended December 31, 2015 and consisted primarily of a net loss of \$32.6 million adjusted for non-cash items, including stock-based compensation expense of \$1.7 million, non-cash interest expense of \$0.3 million and depreciation and amortization expense of \$0.2 million, and a net decrease in operating assets of \$0.6 million, which resulted primarily from an increase in accrued expenses of \$0.9 million and an increase in accounts payable of \$0.2 million, partially offset by an increase in prepaid expenses and other current assets of \$0.5 million.

Net cash used in operating activities was \$20.4 million for the year ended December 31, 2014 and consisted primarily of a net loss of \$21.9 million adjusted for non-cash items, including stock-based compensation expense of \$0.9 million and depreciation and amortization expense of \$0.3 million, and a net decrease in operating assets of \$0.3 million, which resulted primarily from a net increase in accounts payable and accrued expenses of \$0.5 million, partially offset by an increase in prepaid expenses and other current assets of \$0.2 million.

*Net Cash Used in Investing Activities*

Net cash used in investing activities was \$0.4 million during the year ended December 31, 2015 compared to \$0.2 million during the year ended December 31, 2014, an increase of \$0.2 million, which primarily resulted from leasehold improvements pursuant to expanding our leased office space.

*Net Cash Provided by Financing Activities*

Net cash provided by financing activities was \$78.3 million during the year ended December 31, 2015 compared to \$4.8 million during the year ended December 31, 2014. The cash provided by financing activities for the year ended December 31, 2015 primarily consisted of net proceeds received from our IPO of \$61.7 million, net proceeds of \$12.3 million from the issuance of 13,062,965 shares of our series B preferred stock in March 2015, net borrowings of \$4.2 million from our Credit Facility, and \$0.1 million from stock option exercises. The cash provided by financing activities for the year ended December 31, 2014 primarily consisted of net borrowings of \$4.7 million from our Credit Facility, and \$0.1 million in proceeds from the exercise of common stock options.

**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 Securities and Exchange Commission, or SEC, rules.

Table of Contents**Contractual Obligations**

The following table summarizes our significant contractual obligations as of payment due date by period at December 31, 2016:

(In thousands)	Total	Payments due by period			More than 5 Years
		Less than 1 Year	1 - 3 Years	3 - 5 Years	
Term loan(1)	\$ 6,587	\$ 3,660	\$ 2,927	\$	\$
Operating lease obligations(2)	1,968	1,288	680		
<b>Total contractual cash obligations</b>	<b>\$ 8,555</b>	<b>\$ 4,948</b>	<b>\$ 3,607</b>	<b>\$</b>	<b>\$</b>

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(1) Consists of repayment obligations under the Credit Facility, including interest and exit fee.

(2) Represents future minimum lease payments under our non-cancelable operating lease. 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 30 days' prior written notice to the CRO, and therefore we believe that our non-cancelable obligations under these agreements are not material.

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**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, 2016, we had cash, cash equivalents and available-for-sale securities of \$38.5 million and, as of December 31, 2015, we had cash and cash equivalents of \$62.8 million. In each case, our cash equivalents consisted primarily of money market funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Our available-for-sale securities are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to hold our available-for-sale securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

As of December 31, 2016 and December 31, 2015, 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, 2016, 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, 2016, our disclosure controls and procedures were effective at the reasonable assurance level.

We continue to review and document our disclosure controls and procedures, including our internal controls and procedures for financial reporting, and may from time to time make changes aimed at enhancing their effectiveness and to ensure that our systems evolve with our business.

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**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, 2016. 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, 2016, 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, 2016, 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.

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**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 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2016, 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. This information will be set forth under the caption "Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive proxy statement for the 2017 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.

**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 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2016, 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**

See "Securities Authorized for Issuance under Equity Compensation Plans" in Item 5 of this Annual Report on Form 10-K.

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 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2016, 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 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2016, 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 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days of December 31, 2016, and is incorporated into this Annual Report on Form 10-K by reference.

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**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.

<u>Report of Independent Registered Public Accounting Firm</u>	<u>F-1</u>
<u>Consolidated Balance Sheets at December 31, 2016 and 2015</u>	<u>F-2</u>
<u>Consolidated Statements of Operations for the years ended December 31, 2016, 2015 and 2014</u>	<u>F-3</u>
<u>Consolidated Statements of Comprehensive Loss for the years ended December 31, 2016, 2015 and 2014</u>	<u>F-4</u>
<u>Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit) for the years ended December 31, 2016, 2015 and 2014</u>	<u>F-5</u>
<u>Consolidated Statements of Cash Flows for the years ended December 31, 2016, 2015 and 2014</u>	<u>F-6</u>
<u>Notes to Consolidated Financial Statements</u>	<u>F-7</u>

**(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 Exhibit Index immediately preceding the exhibits and are incorporated herein by reference.

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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Stockholders of  
Catabasis Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Catabasis Pharmaceuticals, Inc. (the "Company") as of December 31, 2016 and 2015, and the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Catabasis Pharmaceuticals, Inc. at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts  
March 16, 2017

Table of Contents**Catabasis Pharmaceuticals, Inc.****Consolidated Balance Sheets****(in thousands, except share and per share data)**

	<b>As of December 31,</b>	
	<b>2016</b>	<b>2015</b>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 23,596	\$ 62,780
Available-for-sale securities	14,931	
Prepaid expenses and other current assets	1,001	772
Total current assets	39,528	63,552
Property and equipment, net	568	504
Restricted cash	113	113
Total assets	\$ 40,209	\$ 64,169
<b>Liabilities and stockholders' equity</b>		
Current liabilities:		
Accounts payable	\$ 1,405	\$ 1,328
Accrued expenses	3,677	3,278
Current portion of notes payable, net of discount	3,243	3,173
Total current liabilities	8,325	7,779
Deferred rent, net of current portion	53	26
Notes payable, net of current portion and discount	2,479	5,720
Other liability	266	151
Total liabilities	11,123	13,676
Commitments (Note 9)		
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; 18,817,572 and 15,313,297 shares issued and outstanding at December 31, 2016 and December 31, 2015, respectively	19	15
Additional paid-in capital	173,141	158,488
Accumulated other comprehensive loss	(4)	
Accumulated deficit	(144,070)	(108,010)
Total stockholders' equity	29,086	50,493
Total liabilities and stockholders' equity	\$ 40,209	\$ 64,169



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

Table of Contents**Catabasis Pharmaceuticals, Inc.****Consolidated Statements of Operations****(in thousands, except share and per share data)**

	Year Ended December 31,		
	2016	2015	2014
Operating expenses:			
Research and development	\$ 25,450	\$ 23,030	\$ 15,686
General and administrative	10,108	8,629	5,995
Total operating expenses	35,558	31,659	21,681
Loss from operations	(35,558)	(31,659)	(21,681)
Other (expense) income:			
Interest expense	(837)	(978)	(206)
Interest and investment income	242		
Other income, net	93	7	3
Total other expense, net	(502)	(971)	(203)
Net loss	\$ (36,060)	\$ (32,630)	\$ (21,884)
Net loss per share basic and diluted	\$ (2.22)	\$ (4.06)	\$ (51.56)
Weighted-average common shares outstanding used in net loss per share basic and diluted	16,230,190	8,041,948	424,477

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

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**Catabasis Pharmaceuticals, Inc.**

**Consolidated Statements Comprehensive Loss**

(in thousands)

Year Ended December 31,

	2016	2015	2014
Net Loss	\$ (36,060)	\$ (32,630)	\$ (21,884)
Other comprehensive loss:			
Unrealized loss on available-for-sale securities	(4)		
Total other comprehensive loss:	(4)		
Comprehensive loss	\$ (36,064)	\$ (32,630)	\$ (21,884)

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

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## Catabasis Pharmaceuticals, Inc.

## Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(in thousands, except share data)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock			Accumulated Comprehensive Loss	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Number of Shares	Par Value	Additional Paid-in Capital		
<b>Balance at December 31, 2013</b>	68,837,703	\$ 47,898	34,129,571	\$ 32,248	393,346	\$	1,312	\$ (53,496)	\$ (52,184)
Proceeds from exercises of common stock options					99,854	1	117		118
Stock-based compensation expense							897		897
Net loss								(21,884)	(21,884)
<b>Balance at December 31, 2014</b>	68,837,703	47,898	34,129,571	32,248	493,200	1	2,326	(75,380)	(73,053)
Issuance of common stock from initial public offering, net of issuance costs of \$7.3 million					5,750,000	5	61,739		61,744
Issuance of series B convertible preferred stock, net of issuance cost of \$0.1 million			13,062,965	12,331					
Conversion of convertible preferred stock into common stock	(68,837,703)	(47,898)	(47,192,536)	(44,579)	9,029,549	9	92,468		92,477
Conversion of series B preferred stock warrants into warrants for the purchase of common stock							206		206
Proceeds from exercises of common stock options					40,548		91		91
Stock-based compensation expense							1,658		1,658
Net loss								(32,630)	(32,630)
<b>Balance at December 31, 2015</b>					15,313,297	15	158,488	(108,010)	50,493
Issuance of common stock for registered direct and at-the-market offerings, net of issuance costs of \$1.1 million					3,243,015	3	11,991		11,994
Proceeds from exercises of common stock options and warrants					261,260	1	502		503
Stock-based compensation expense							2,160		2,160
Unrealized losses on short-term investments									(4)
Net loss								(36,060)	(36,060)
<b>Balance at December 31, 2016</b>		\$		\$	18,817,572	19	\$ 173,141	\$ (144,070)	(4) \$ 29,086

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

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Table of Contents**Catabasis Pharmaceuticals, Inc.****Consolidated Statements of Cash Flows**

(in thousands)

	Year Ended December 31,		
	2016	2015	2014
<b>Operating activities</b>			
Net loss	\$ (36,060)	\$ (32,630)	\$ (21,884)
Reconciliation of net loss to net cash used in operating activities:			
Depreciation and amortization	395	202	248
Stock-based compensation expense	2,160	1,658	897
Accretion of discount/premium on investment securities	148		
Non-cash interest expense	277	293	74
Gain on the sale of fixed assets	(52)		
Changes in assets and liabilities:			
Prepaid expenses and other current assets	(229)	(450)	(208)
Other assets		2	
Accounts payable	77	196	481
Accrued expenses	418	954	8
Deferred rent	8	(18)	(28)
<b>Net cash used in operating activities</b>	<b>(32,858)</b>	<b>(29,793)</b>	<b>(20,412)</b>
<b>Investing activities</b>			
Purchases of available-for-sale securities	(45,539)		(4,976)
Sales and maturities of available-for-sale securities	30,456		4,976
Purchases of property and equipment	(459)	(421)	(228)
Sale of property and equipment	52		
<b>Net cash used in investing activities</b>	<b>(15,490)</b>	<b>(421)</b>	<b>(228)</b>
<b>Financing activities</b>			
Proceeds from initial public offering, net of issuance costs		61,744	
Proceeds from issuance of preferred stock, net of issuance costs		12,331	
Proceeds from registered direct offering, net of issuance costs	10,603		
Proceeds from at-the-market offering, net of issuance costs	1,391		
Proceeds from exercise of common stock options and warrants	503	91	118
Proceeds from borrowing		5,000	5,000
Payments on borrowing	(3,333)	(833)	
Debt issuance costs		(7)	(284)
<b>Net cash provided by financing activities</b>	<b>9,164</b>	<b>78,326</b>	<b>4,834</b>
Net (decrease) increase in cash and cash equivalents	(39,184)	48,112	(15,806)
Cash and cash equivalents, beginning of period	62,780	14,668	30,474
Cash and cash equivalents, end of period	\$ 23,596	\$ 62,780	\$ 14,668
<b>Supplemental disclosure of cash flow information</b>			
Cash paid for interest	\$ 582	\$ 684	\$ 100

**Non-cash financing activities**

Warrants for the purchase of series B preferred stock issued in conjunction with credit facility	\$	\$	107	\$	110
Initial public offering costs in accounts payable and accrued liabilities	\$	\$	(492)	\$	492
Reclassification of deferred IPO costs from non-current assets to additional paid-in capital	\$	\$	1,787	\$	
Reclassification of warrant liability to additional paid-in capital	\$	\$	206	\$	

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

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**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 focused on the discovery, development and commercialization of novel therapeutics based on the Company's proprietary Safely Metabolized And Rationally Targeted, or SMART, linker drug discovery platform. The Company's SMART linker technology platform enables the Company to engineer product candidates that can simultaneously modulate multiple targets in a disease. The Company's proprietary product candidates impact pathways that are central to diseases where efficacy may be optimized by a multiple target approach. The Company's primary focus is on treatments for rare diseases. The Company has applied its SMART linker drug discovery platform to build an internal pipeline of product candidates for rare diseases and plans to pursue partnerships to develop additional product candidates. The Company was incorporated in the State of Delaware on June 26, 2008.

*Liquidity*

In June 2015, the Company completed its initial public offering (the "IPO"). All of the shares issued and sold in the IPO were registered pursuant to a registration statement on Form S-1, as amended. An aggregate of 5,750,000 shares of common stock ("Common Stock") registered pursuant to the registration statement were sold at a price to the public of \$12.00 per share (including 750,000 shares of Common Stock sold pursuant to the exercise of an overallotment option granted to the Company's underwriters in connection with the IPO). Net proceeds of the IPO were \$61.7 million, after deducting underwriting discounts, commissions and offering-related expenses payable by the Company of approximately \$7.3 million. In connection with the IPO, all shares of the Company's convertible Preferred Stock ("Preferred Stock") were automatically converted into an aggregate of 9,029,549 shares of its Common Stock and its outstanding warrants to purchase 315,688 shares of Preferred Stock were automatically converted into warrants to purchase 24,566 shares of Common Stock.

In August 2016, the Company entered into a sales agreement with Cowen and Company LLC ("Cowen"), pursuant to which the Company could issue and sell shares of Common Stock for an aggregate maximum offering amount of \$10.0 million under an at-the-market ("ATM") offering program. Cowen is not required to sell any specific amount, but acts as the Company's sales agent using commercially reasonable efforts that are consistent with Cowen's normal trading and sales practices. Shares sold pursuant to the sales agreement have been sold pursuant to a shelf registration statement, which became effective on July 19, 2016 (the "Shelf Registration Statement"). The Company pays Cowen 3% of the gross proceeds from any Common Stock sold through the sales agreement.

During the year ended December 31, 2016, the Company sold an aggregate of 368,015 shares of Common Stock pursuant to the ATM offering program, at an average price of \$4.35 per share, for gross proceeds of \$1.6 million, resulting in net proceeds of \$1.4 million after deducting sales commissions and offering expenses. As of December 31, 2016, \$8.4 million of common stock remained available under the ATM offering program.

In September 2016, the Company closed an underwritten registered direct offering, in which it sold 2,875,000 shares of Common Stock (including 375,000 shares of Common Stock sold pursuant to the exercise of an option by the underwriter to purchase additional shares) at an offering price of \$4.00 per share. The shares sold in the offering were sold pursuant to the Shelf Registration Statement. The Company received aggregate gross proceeds from the offering of \$11.5 million, resulting in net



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**Catabasis Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**1. Organization and Operations (Continued)**

proceeds of \$10.6 million after deducting underwriting discounts and commissions and offering expenses.

As of December 31, 2016, the Company had an accumulated deficit of \$144.1 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. The Company adopted Accounting Standards Update ("ASU") No. 2014-15, *Presentation of Financial Statements - Going Concern: Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern* ("ASU 2014-15") in connection with the issuance of its consolidated financial statements for the year ended December 31, 2016. The Company's current operating plan provides for cash to fund operations through March 31, 2018, assuming no unscheduled repayment of indebtedness prior to such date. As the lender has the ability to call the debt prior to the maturity date, that could affect the Company's ability to continue as a going concern for a period of one year from the date of issuance of the financial statements. The Company believes that the condition is mitigated by management's plans which include the ability to reduce or delay expenditures including expenditures for employee incentive compensation and direct program expenses.

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.

Table of Contents**Catabasis Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)**

Prior to completion of its IPO, the Company utilized significant estimates and assumptions in determining the fair value of its Common Stock. The board of directors determined the estimated fair value of the Common Stock based on a number of objective and subjective factors. Such factors included the external market conditions affecting the biotechnology industry sector, the prices at which the Company sold shares of Preferred Stock, the achievement of research and development milestones, the superior rights and preferences of securities senior to the Common Stock at the time and the likelihood of achieving a liquidity event, such as an initial public offering or sale of the Company.

The Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants ("AICPA"), Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation ("AICPA Practice Aid"), to estimate the fair value of its Common Stock. The methodologies included the Option Pricing Method utilizing the Back-solve Method (a form of the market approach defined in the AICPA Practice Aid) and the Probability-Weighted Expected Return Method based upon the probability of occurrence of certain future liquidity events such as an initial public offering or sale of the Company. Each valuation methodology included estimates and assumptions that required the Company's judgment. Significant changes to the key assumptions used in the valuations could result in different fair values of Common Stock at each valuation date.

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, 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 and cash equivalents 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.

***Cash and Cash Equivalents***

The Company considers highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents, which consist primarily of money market funds backed by U.S. government securities, are stated at fair value. Cash and cash equivalents consist of the following (in thousands):

	<b>December 31,</b>	
	<b>2016</b>	<b>2015</b>
Cash	\$ 1,173	\$ 776
Money market fund	22,423	62,004
<b>Total</b>	<b>\$ 23,596</b>	<b>\$ 62,780</b>

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**Catabasis Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**2. Summary of Significant Accounting Policies (Continued)**

***Available-for-Sale Investments***

The Company classifies all short-term investments with a remaining maturity of greater than three months at the time of purchase as available-for-sale. Available-for-sale securities 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.

***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, 2016 and 2015, due to their short-term nature. There have been no changes to the valuation methods during the years ended December 31, 2016 and 2015. 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, 2016 and 2015. At December 31, 2016, the carrying value of the Company's debt approximated fair value, which was determined using Level 3 inputs, including a quoted interest rate.

The Company's investment portfolio includes 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. In addition, model processes are used to assess interest rate impact and develop prepayment scenarios. These models take into consideration relevant credit information, perceived market movements, sector news and economic events. The inputs into these models may include benchmark yields, reported trades, broker-dealer quotes, issuer spreads and other relevant data. 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 determines the fair value of available-for-sale securities (Note 3) using Level 2 inputs.

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**Catabasis Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**2. Summary of Significant Accounting Policies (Continued)**

***Deferred Financing Costs***

Deferred financing costs include costs directly attributable to the Company's offerings of its equity securities and its debt financings. Costs attributable to equity offerings are charged against the proceeds of the offering once the offering is completed. Costs attributable to debt financings are deferred and amortized over the term of the debt using the effective interest rate method.

On April 7, 2015, the Financial Accounting Standards Board issued ASU No. 2015-03, *Simplifying the Presentation of Debt Issuance Costs* ("ASU 2015-03"). ASU 2015-03 requires debt issuance costs to be presented in an entity's balance sheet as a direct deduction from the associated debt liability. The standard is retrospectively effective for annual reporting periods beginning after December 15, 2015.

The Company adopted the standard in the three months ended March 31, 2016, which resulted in a balance sheet reclassification of issuance costs in connection with its notes payable of approximately \$32 thousand recorded in prepaid expenses and other current assets and approximately \$22 thousand recorded in other assets to a reduction in current portion of notes payable, net of discount and in notes payable, net of current portion and discount, respectively. The Company's adoption of this standard did not have any impact on its results of operations or cash flows for the twelve months ended December 31, 2016.

***Property and Equipment***

Property and equipment consist of laboratory equipment, computer equipment, leasehold improvements and furniture and fixtures. Property and equipment is stated at cost and depreciated using the straight-line method over the estimated useful lives of the respective assets. Costs of major additions and betterments are capitalized; maintenance and repairs, which do not improve or extend the life of the respective assets, are charged to expense as incurred. Upon retirement or sale, the cost of the disposed asset and the related accumulated depreciation are removed from the accounts and the resulting gain or loss is recognized.

***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, 2016.

***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.

Table of Contents**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 stock options granted to employees and to members of the board of directors for their services on the board of directors, 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, net of estimated forfeitures, 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.

Share-based payments issued to non-employees are recorded at their fair values, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period in accordance with the provisions of ASC Topic 505, *Equity*. For equity instruments granted to non-employees, the Company recognizes stock-based compensation expense on a straight-line basis.

During the years ended December 31, 2016, 2015 and 2014, 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):

	<b>Year Ended December 31,</b>		
	<b>2016</b>	<b>2015</b>	<b>2014</b>
Research and development	\$ 723	\$ 681	\$ 434
General and administrative	1,437	977	463
<b>Total</b>	<b>\$ 2,160</b>	<b>\$ 1,658</b>	<b>\$ 897</b>

No related tax benefits were recognized for the years ended December 31, 2016, 2015 and 2014.

***Grant Awards***

In the years ended December 31, 2016, 2015 and 2014, the Company received \$376,000, \$100,000 and \$0, respectively, in grants from the Muscular Dystrophy Association, Friedreich's Ataxia Research Alliance and Parent Project for Muscular Dystrophy. The awards were recorded as a reduction to research and development expenses as the related expenses were incurred in the Company's statements of operations.

Table of Contents**Catabasis Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)*****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 dilutive net loss per share calculation, Preferred Stock, stock options, warrants to purchase Common Stock and warrants to purchase Preferred Stock are considered to be Common Stock equivalents but are 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.

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:

	<b>Year Ended December 31,</b>		
	<b>2016</b>	<b>2015</b>	<b>2014</b>
Convertible preferred stock			8,012,988
Stock options	2,270,169	1,723,554	1,226,140
Common stock warrants	24,566	59,405	34,839
Preferred stock warrants			12,283
	2,294,735	1,782,959	9,286,250

***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. As of December 31, 2016, 2015 and 2014, the Company did not have any significant uncertain tax positions.

***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.

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**Catabasis Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**2. Summary of Significant Accounting Policies (Continued)**

***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 year ended December 31, 2016, amounts in accumulated other comprehensive loss were comprised of unrealized gains and losses on available-for-sale securities. For the years ended December 31, 2015 and 2014, comprehensive loss was equal to net loss.

***Recent Accounting Pronouncements***

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("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 August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements Going Concern: Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 is intended to define management's responsibility to evaluate whether there is substantial doubt about an organization's ability to continue as a going concern and to provide related footnote disclosures, if required. ASU 2014-15 is effective for annual reporting periods ending after December 15, 2016, and applies to annual and interim periods thereafter. The Company adopted this standard on December 31, 2016 (Note 1).

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers* (Topic 606), ("ASU 2014-09"). The standard will replace existing revenue recognition standards and significantly expand the disclosure requirements for revenue arrangements. It may be adopted either retrospectively or on a modified retrospective basis to new contracts and existing contracts with remaining performance obligations as of the effective date. The standard will become effective for us on January 1, 2018. At this time, the Company has not decided on which method it will use to adopt the new standard, nor has it determined the effects of the new guidelines on its results of operations and financial position as the Company does not currently have any arrangements that would be impacted by the new standard. As a result, the Company is continuing to evaluate the method of adoption and the impact of this standard on its consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, *Leases*. This standard amends the existing guidance to require lessees to present most leases on their balance sheets but recognize corresponding expenses on their statements of operations. It is effective for annual reporting periods beginning after December 15, 2018, but early adoption is permitted. The Company is currently evaluating the impact that this standard will have on its consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting*. This standard amends the existing guidance in an attempt to simplify several aspects of accounting for employee share-based payment transactions. It is effective for annual reporting periods beginning after December 15, 2016, but early adoption is permitted. The Company adopted the ASU on January 1, 2017 and adopted an accounting policy to record forfeitures as they occur. The Company does not expect this standard will have a material effect on its consolidated financial statements.

Table of Contents**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):

	Quoted Prices in Active Markets (Level 1)	As of December 31, 2016 Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Cash and cash equivalents:				
Money market funds	\$ 22,423	\$	\$	\$ 22,423
Available-for-sale securities:				
Corporate debt securities		13,930		13,930
U.S. government-sponsored securities		1,001		1,001
Total assets	\$ 22,423	\$ 14,931	\$	\$ 37,354

	Quoted Prices in Active Markets (Level 1)	As of December 31, 2015 Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Money market funds	\$ 62,004	\$	\$	\$ 62,004
Total assets	\$ 62,004	\$	\$	\$ 62,004

As of December 31, 2016 and December 31, 2015, the Company's cash equivalents consisted principally of money market funds, which approximated their fair value due to their short-term nature.

**4. Available-for-Sale Securities**

As of December 31, 2015, the Company held no available-for-sale securities. The following table summarizes the available-for-sale securities held at December 31, 2016 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
<b>December 31, 2016</b>				
Corporate debt securities	\$ 13,934	\$	\$ (4)	\$ 13,930
U.S. government-sponsored securities	1,001			1,001
Total	\$ 14,935	\$	\$ (4)	\$ 14,931



The contractual maturities of all available-for-sale securities held at December 31, 2016 were one year or less. There were fifteen available-for-sale securities in an unrealized loss position at December 31, 2016, 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, 2016 was approximately \$13.0 million. The

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Table of Contents**Catabasis Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****4. Available-for-Sale Securities (Continued)**

Company reviews its investments for other-than-temporary impairment whenever the fair value of an investment is less than amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. To determine whether an impairment is other-than-temporary, the Company considers whether it has the ability and intent to hold the investment until a market price recovery and considers whether evidence indicating the cost of the investment is recoverable outweighs evidence to the contrary. The Company does not intend to sell the investments that were in unrealized loss positions at December 31, 2016, and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost bases, which may be at maturity. The Company did not hold any securities with other-than-temporary impairment at December 31, 2016.

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, 2016 and 2015 the Company received \$7.8 million and \$0 million in proceeds from sales of available-for-sale securities, respectively, the gains on which were not material to the Company's consolidated results of operations.

**5. Restricted Cash**

At December 31, 2016 and 2015, the Company had an outstanding letter of credit for \$0.1 million as a security deposit for its operating lease agreement for office space (Note 9). The Company is required to maintain this deposit for the duration of the lease agreement.

**6. Property and Equipment**

Property and equipment and related accumulated depreciation were as follows (in thousands):

		December 31,	
	Estimated Useful Life (Years)	2016	2015
Lab equipment	3	\$ 1,565	\$ 1,350
Computer equipment	3	166	166
Furniture and fixtures	5	77	77
	Lesser of useful life or remaining lease term		
Leasehold improvements		259	261
		2,067	1,854
Less accumulated depreciation and amortization		(1,499)	(1,350)
<b>Total property and equipment, net</b>		<b>\$ 568</b>	<b>\$ 504</b>

Depreciation and amortization expense was \$0.4 million, \$0.2 million and \$0.2 million for the years ended December 31, 2016, 2015 and 2014, respectively.

Table of Contents**Catabasis Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****7. Accrued Expenses**

Accrued expenses consisted of the following (in thousands):

	<b>December 31,</b>	
	<b>2016</b>	<b>2015</b>
Accrued compensation	\$ 1,252	\$ 1,181
Accrued contracted research costs	1,850	1,261
Accrued professional fees	215	181
Accrued other	360	655
<b>Total</b>	<b>\$ 3,677</b>	<b>\$ 3,278</b>

**8. Notes Payable**

On August 27, 2014, the Company entered into a credit facility with MidCap Financial Trust, Flexpoint MCLS Holdings, LLC and Square 1 Bank, which was subsequently amended in March and December 2015 (as amended, the "Credit Facility"). The Credit Facility provided for initial borrowings of \$5.0 million under a term loan ("Term Loan A") and additional borrowings of up to \$20.0 million under other term loans, for a maximum of \$25.0 million. On August 27, 2014, the Company received proceeds of \$5.0 million from the issuance of promissory notes under Term Loan A. On March 31, 2015, the Company received proceeds of \$5.0 million from the issuance of promissory notes under another term loan ("Term Loan B"). The remaining amounts available for borrowing under this arrangement expired unused as of July 31, 2015, leaving total borrowings under the Credit Facility at \$10.0 million. All amounts outstanding under the Credit Facility are due on October 1, 2018 and are collateralized by substantially all of the Company's personal property, other than its intellectual property.

Interest-only payments were due monthly on amounts outstanding under the Credit Facility until September 1, 2015 and, thereafter, interest and principal payments are due in 36 equal monthly installments from October 1, 2015 through September 1, 2018. Amounts due under the Credit Facility bear interest at an annual rate of 7.49%. In addition, a final payment equal to 3.48% of any amounts drawn under the Credit Facility is due upon the earlier of the maturity date, acceleration of the term loans or prepayment of all or part of the term loans. The final payment is being accrued as additional interest expense using the effective-interest method from the date of issuance through the maturity date, and is recorded within other long-term liabilities. In the event of prepayment, the Company is obligated to pay 1% to 3% of the amount of the outstanding principal depending upon the timing of the prepayment. The effective interest rate as of December 31, 2016 was 11.2%.

In conjunction with Term Loan A, the Company issued warrants (the "2014 Warrants") to purchase 157,844 shares of Series B Convertible Preferred Stock at an exercise price of \$0.9503 per share to the lenders. In conjunction with Term Loan B, the Company issued warrants (the "2015 Warrants") to purchase an additional 157,844 shares of Series B Convertible Preferred Stock at an exercise price of \$0.9503 per share to the lenders. Upon the closing of the Company's IPO on June 30, 2015, the 2014 Warrants and 2015 Warrants were automatically converted into warrants to purchase an aggregate of 24,566 shares of Common Stock at an exercise price of \$12.2114 per share. The 2014 Warrants and 2015 Warrants were exercisable immediately and have seven-year lives. The 2014 Warrants and 2015 Warrants were initially valued at \$0.1 million and \$0.1 million, respectively, using the Black-Scholes option-pricing model. The Company recorded debt discounts of \$0.1 million and \$0.1

Table of Contents**Catabasis Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****8. Notes Payable (Continued)**

million upon issuance of the 2014 Warrants and 2015 Warrants, respectively, which are being accreted as interest expense using the effective-interest method over the remaining term of the loan.

There are no financial covenants associated with the Credit Facility; however, there are negative covenants restricting the Company's activities, including limitations on asset dispositions, mergers or acquisitions; encumbering or granting a security interest in its intellectual property; incurring indebtedness or liens; paying dividends; making certain investments; and entering into certain other business transactions.

Upon the occurrence and continuation of an event of default, the lenders have the right to exercise certain remedies against the Company and the collateral securing the loans under the Credit Facility, including cash. Events of default include, among other things, failure to pay amounts due under the Credit Facility, insolvency, the occurrence of a material adverse event, which includes a material adverse change in the business, operations or conditions (financial or otherwise) of the Company or a material impairment of the prospect of repayment of any portion of the obligations, the occurrence of any default under certain other indebtedness and a final judgment against the Company in an amount greater than \$250,000. The occurrence of a material adverse event could result in acceleration of the payment of the debt. At December 31, 2016 and 2015, the Company concluded that the likelihood of the acceleration of the debt was remote, as a material adverse event had not occurred and was unlikely to occur and therefore the debt was classified in current and long-term liabilities based on scheduled principal payments. Following the occurrence and during the continuance of an event of default, borrowings under the Credit Facility shall bear interest at a rate per annum, which is five hundred basis points, or 5.00%, above the rate that is otherwise applicable.

The Company assessed all terms and features of the Credit Facility in order to identify any potential embedded features that would require bifurcation or any beneficial conversion features. As part of this analysis, the Company assessed the economic characteristics and risks of the Credit Facility, including put and call features. The Company determined that all features of the Credit Facility were clearly and closely associated with a debt host and did not require bifurcation as a derivative liability, or the fair value of the feature was immaterial to the Company's financial statements. The Company reassesses the features on a quarterly basis to determine if they require separate accounting.

Estimated future principal payments at December 31, 2016 are as follows (in thousands):

<b>Year Ending December 31,</b>	<b>Amount</b>
2017	3,333
2018	2,500
<b>Total</b>	<b>\$ 5,833</b>
Less: discount for warrants and costs paid to lender	(111)
Less: current portion	(3,243)
Note payable, net of current portion and discount	\$ 2,479

During the years ended December 31, 2016, 2015 and 2014, the Company recognized \$0.8 million, \$1.0 million and \$0.2 million, respectively, of interest expense related to the Credit Facility.

Table of Contents**Catabasis Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****9. Commitments**

In November 2010, the Company entered into a five-year, non-cancelable operating lease for office and laboratory space that provided for a five-year extension upon the completion of the lease term. In December 2011, the Company signed a lease amendment (the "2011 Lease Amendment") that expanded the leased premises beginning in the second quarter of 2012. The 2011 Lease Amendment also extended the term of the existing lease through June 30, 2017. The 2011 Lease Amendment includes a free rent period for the expansion premises and escalating rent payments. In July 2015, the Company signed another lease amendment (the "2015 Lease Amendment") that expanded the leased premises beginning in the third quarter of 2015. The 2015 Lease Amendment includes escalating rent payments and is effective through June 30, 2017. In November 2016, the Company signed a third lease amendment (the "2016 Lease Amendment"). The 2016 Lease Amendment includes escalating rent payments and is effective through June 30, 2018. The Company is recognizing rent expense on a straight-line basis over the lease term.

Future minimum payments required under the non-cancelable operating lease as of December 31, 2016 are summarized as follows (in thousands):

<b>Period Ending December 31,</b>	<b>Amount</b>
2017	\$ 1,288
2018	680
<b>Total minimum lease payments</b>	<b>\$ 1,968</b>

Rent expense for the years ended December 31, 2016, 2015 and 2014 was \$0.9 million, \$0.8 million and \$0.7 million, respectively.

**10. Convertible Preferred Stock**

On March 13, 2015, the Company's board of directors authorized the Company to increase the authorized number of shares of Series B Preferred Stock to 56,026,590 in connection with an anticipated Series B Preferred Stock financing. The Company subsequently issued 13,062,965 shares of Series B Preferred Stock at \$0.9503 per share, and received net proceeds of \$12.3 million.

Prior to the IPO, the holders of the Company's convertible Preferred Stock had certain voting, dividend rights, as well as liquidation preferences and conversion privileges. All rights, preferences, and privileges associated with the convertible Preferred Stock were terminated at the time of the Company's IPO in conjunction with the conversion of all outstanding shares of convertible Preferred Stock into shares of Common Stock.

Upon the closing of the Company's IPO on June 30, 2015, all outstanding shares of the Company's Preferred Stock were automatically converted into 9,029,549 shares of Common Stock. As of December 31, 2016, 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.

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**Catabasis Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**11. Common Stock**

As of December 31, 2016, the Company had 150,000,000 shares of Common Stock authorized for issuance, \$0.001 par value per share, with 18,817,572 shares issued and outstanding. The voting, dividend and liquidation rights of holders of Common Stock are subject to and qualified by the rights, 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, 2016.

***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: