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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended: December 31, 2013

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

Commission file number: 001-35969

PTC THERAPEUTICS, INC.
(Exact Name of Registrant as Specified in its Charter)

Delaware (State or other jurisdiction of incorporation or organization)	**04-3416587** (I.R.S. Employer Identification No.)
100 Corporate Court **South Plainfield, New Jersey** (Address of Principal Executive Offices)	**07080** (Zip Code)

(908) 222-7000
(Registrant's telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Common Stock, $0.001 par value	NASDAQ Global Select Market

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

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

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

Indicate by check mark 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. o

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 o

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

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

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

The aggregate market value of the Common Stock held by non-affiliates of the registrant, based upon the last sale price of the Common Stock reported on the NASDAQ Global Select Market on June 28, 2013, the last business day of the registrant's most recently completed second fiscal quarter, was $260,280,900. For purposes of this calculation, shares of Common Stock held by directors, officers and 10% stockholders known to the registrant have been treated as shares held by affiliates.

As of March 4, 2014, the registrant had 30,076,773 shares of Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2014 Annual Meeting of Shareholders which is expected to be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2013.

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PTC Therapeutics, Inc.

FORWARD-LOOKING STATEMENTS

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 revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the timing and conduct of our clinical trials of ataluren for the treatment of Duchenne muscular dystrophy and cystic fibrosis caused by nonsense mutations, including statements regarding the timing of initiation and completion of the trials and the period during which the results of the trials will become available;
- the timing of and our ability to obtain marketing approval, including conditional approval in the European Union, of ataluren and our other product candidates, and the ability of ataluren and our other product candidates to meet existing or future regulatory standards;
- our expectations with respect to development and regulatory status of our program directed against spinal muscular atrophy in collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or the SMA Foundation, and our estimates regarding future revenues from achievement of milestones in that program;
- the potential receipt of revenues from future sales of ataluren;
- our plans to pursue development of ataluren for additional indications other than Duchenne muscular dystrophy and cystic fibrosis caused by nonsense mutations;
- our plans to pursue research and development of other product candidates;
- the potential advantages of ataluren;
- the rate and degree of market acceptance and clinical utility of ataluren;
- our estimates regarding the potential market opportunity for ataluren;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for manufacture of ataluren and our other product candidates;
- our intellectual property position;
- the impact of government laws and regulations;
- our competitive position; and
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing.

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 Part I, Item 1A. Risk Factors, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to the Annual Report on Form 10-K and 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 statements whether as a result of new information, future events or otherwise, except as required by applicable law.

In this Annual Report on Form 10-K, unless otherwise stated or the context otherwise requires, references to "PTC," "PTC Therapeutics," "we," "us," "our" and similar references refer to PTC Therapeutics, Inc. and, where appropriate, its subsidiary. The trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

All website addresses given in this prospectus are for information only and are not intended to be an active link or to incorporate any website information into this document.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the discovery and development of orally administered, proprietary small-molecule drugs that target post-transcriptional control processes. While our discovery programs are directed at targets in multiple therapeutic areas, we are focusing particularly on the development and commercialization of treatments for orphan and ultra-orphan disorders. Our lead product candidate is ataluren for the treatment of patients with genetic disorders that arise from a type of genetic mutation known as a nonsense mutation. We hold worldwide commercialization rights to ataluren for all indications in all territories.

We have initiated a confirmatory Phase 3 clinical trial of ataluren for the treatment of Duchenne muscular dystrophy caused by nonsense mutations, or nmDMD. We refer to this trial as the Ataluren Confirmatory Trial in DMD, or ACT DMD. We dosed the first patient in this trial in 2013 and expect to complete enrollment in mid-2014. In October 2012, we submitted a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for conditional approval of ataluren for the treatment of nmDMD. In January 2014, EMA's Committee for Medicinal Products for Human Use, or CHMP, adopted a negative opinion recommending the refusal of the granting of the conditional marketing authorization for ataluren for the treatment of nmDMD. We have requested a re-examination of the CHMP opinion and currently expect a final outcome in the second quarter of 2014. We are also planning a Phase 3 clinical trial of ataluren for the treatment of cystic fibrosis caused by nonsense mutations, or nmCF. We plan to begin dosing patients in this trial in the first half of 2014. In addition, we are pursuing early access programs for ataluren for nmDMD patients in selected territories that support reimbursement for such programs. There are currently no marketed therapies approved to treat the underlying cause of nmDMD or nmCF. The EMA has designated ataluren as an orphan medicinal product and the U.S. Food and Drug Administration, or FDA, has granted orphan drug designation to ataluren for the treatment of both nmDMD and nmCF. We also plan to pursue additional indications for ataluren beyond nmDMD and nmCF and expect to initiate a proof-of-concept study for a third indication in 2014.

We continue to advance the development of our spinal muscular atrophy collaboration with F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or SMA Foundation. A development candidate for the program was selected in August 2013, and a Phase 1 clinical program was initiated in healthy volunteers in January 2014. Each of these events triggered a milestone payment to us from Roche.

The letters "PTC" in our corporate name are an acronym for post-transcriptional control processes, which are the regulatory events that occur in cells after a messenger RNA, or mRNA, molecule is copied, or transcribed, from DNA. The mRNA molecules are key intermediates in protein production. Post-transcriptional control processes regulate the rate and timing of protein production and are essential to proper cellular function. The absence or overproduction of specific proteins can cause disease. The small-molecule compounds that we are developing are designed to alter post-transcriptional control processes to correct or compensate for a genetic defect. We apply proprietary technologies and our extensive knowledge of post-transcriptional control processes in our drug discovery and development activities. We believe that systematically targeting post-transcriptional control processes represents an unexploited approach to drug discovery and development.

We discovered ataluren by applying our technologies to identify molecules that promote or enhance the suppression of nonsense mutations. Nonsense mutations are implicated in a variety of genetic disorders. Nonsense mutations create a premature stop signal in the translation of the genetic code contained in mRNA and prevent the production of full-length, functional proteins. We believe

that ataluren interacts with the ribosome, which is the component of the cell that decodes the mRNA molecule and manufactures proteins, to enable the ribosome to read through premature nonsense stop signals on mRNA and allow the cell to produce a full-length, functional protein. As a result, we believe that ataluren has the potential to be an important therapy for muscular dystrophy, cystic fibrosis and other genetic disorders for which a nonsense mutation is the cause of the disease. Genetic tests are available for many genetic disorders, including Duchenne muscular dystrophy and cystic fibrosis, to determine if the underlying cause is a nonsense mutation.

Muscular dystrophies involve progressive muscle wasting and weakness and are caused by a mutation in the DNA that results in either the absence or very low levels of the dystrophin protein. Duchenne muscular dystrophy is the most common and one of the most severe types of muscular dystrophy. Patients with Duchenne muscular dystrophy typically lose walking ability by their early teens, require ventilation support in their late teens and, eventually, die due to heart and lung failure. The average age of death for Duchenne muscular dystrophy patients is in their mid-twenties.

Cystic fibrosis is caused by a mutation in the DNA that results in either the absence or very low levels of the cystic fibrosis transmembrane conductance regulator, or CFTR, protein. Cystic fibrosis results in the body producing abnormally thick and sticky mucus that clogs multiple organs, including the lungs, pancreas and liver. Cystic fibrosis leads to progressive loss of lung function, potentially life-threatening lung infections, permanent pancreatic damage and malnutrition. The average age of death for cystic fibrosis patients is approximately 27 years. A nonsense mutation is a type of mutation in the DNA that can cause both Duchenne muscular dystrophy and cystic fibrosis.

We have completed a Phase 2b clinical trial of ataluren for the treatment of nmDMD and a Phase 3 clinical trial of ataluren for the treatment of nmCF. We did not achieve the primary efficacy endpoint in either trial with the pre-specified level of statistical significance. However, we believe that the collective data from these trials, including retrospective and subgroup analyses that we have performed, provide strong support for concluding that ataluren was active and showed clinically meaningful improvements over placebo in these trials. In addition, we believe that our experience in these completed clinical trials has allowed us to enhance the designs of our confirmatory Phase 3 clinical trials and improve our likelihood of success in these trials. Accordingly, we initiated our confirmatory Phase 3 ACT DMD clinical trial and are planning a confirmatory Phase 3 clinical trial of ataluren for the treatment of nmCF. Ataluren has been generally well tolerated in all of our clinical trials to date.

In October 2012, we submitted an MAA to the EMA for conditional approval of ataluren for the treatment of nmDMD. During the review process, the EMA informed us of major objections that would preclude a recommendation for marketing authorization unless adequately addressed. These major objections related to, among other things, the EMA's views regarding insufficient evidence of efficacy based on our single Phase 2b clinical trial, resulting in a negative risk-benefit balance for purposes of conditional approval, and uncertainties about the effective dose. The EMA also questioned whether our confirmatory Phase 3 ACT DMD clinical trial could be completed if the EMA granted conditional approval. In December 2013, the EMA convened a scientific advisory group, or SAG, meeting as part of the regulatory review process followed by the oral explanation meeting with the CHMP. We believe that both the SAG and oral explanation meetings allowed us and independent experts in the DMD field to provide information to the SAG and CHMP members about important aspects of our clinical data and trial design.

In January 2014, the CHMP adopted a negative opinion recommending the refusal of the granting of the conditional marketing authorization for ataluren for the treatment of nmDMD. The CHMP stated that a principal reason for the negative opinion was that our prior Phase 2b clinical trial had failed to demonstrate in the primary analysis that patients taking ataluren could walk a greater distance than patients taking placebo in six minutes, the primary endpoint. Additionally, the CHMP noted that

other measures of efficacy provided only limited supportive evidence of the beneficial effects of ataluren. The CHMP acknowledged to us that the retrospective analyses that we presented to the CHMP were performed in line with the most current knowledge about the natural history of the disease and that our definition of the subgroups in the analyses were both clinically and scientifically justified. However, the CHMP concluded that we did not provide sufficiently compelling evidence of efficacy to justify conditional approval. In addition, the CHMP considered that we had not provided sufficient data to determine how ataluren works in the body and how its effects change with dose. Finally, the CHMP expressed concern that the conduct of the confirmatory Phase 3 ACT DMD clinical trial might be affected by the availability of an authorized product and therefore potentially jeopardize the feasibility of completing the trial. As a result, despite divergent minority positions, the CHMP concluded a favorable risk-benefit balance could not be established at that time and adopted a negative opinion. We have requested a re-examination of the CHMP opinion and currently expect a final outcome in the second quarter of 2014. Based upon the timelines for a re-examination process, we believe that our confirmatory Phase 3 ACT DMD clinical trial will be substantially enrolled at the time the CHMP would consider a revision of their initial opinion as part of the re-examination process.

We continue to believe that completion of our confirmatory Phase 3 ACT DMD clinical trial and submission of data to the regulatory authorities is the more likely path to obtain marketing approval of ataluren. There is substantial risk that the EMA will not grant us conditional approval upon re-examination of the original CHMP negative opinion. If granted, EMA conditional approval would permit us to market ataluren in the European Union for treatment of nmDMD prior to completion of our confirmatory Phase 3 ACT DMD clinical trial. We plan to complete our confirmatory Phase 3 ACT DMD clinical trial before applying for marketing approval from the FDA. In designing our confirmatory Phase 3 ACT DMD clinical trial for the treatment of nmDMD, we have sought to reflect the views expressed by both the EMA and the FDA in our discussions with these regulatory authorities. We expect that these trial results, if favorable, could serve as the basis for full approval by the EMA and the FDA of ataluren for the treatment of nmDMD. If the trial results are favorable, and based on our estimates of patient enrollment and data availability, we expect to be able to submit applications for full marketing approval of ataluren for the treatment of nmDMD in both the European Union and the United States in 2016.

We have concluded discussions with regulatory authorities concerning our proposed trial protocol for a confirmatory Phase 3 clinical trial of ataluren for nmCF. We plan to begin dosing patients in this trial in the first half of 2014. We also have received scientific advice from the EMA regarding the possibility of submitting an MAA for conditional approval of ataluren for the treatment of nmCF. Our interactions with the FDA regarding the clinical development design options which would have the potential to support an NDA in 2013 did not achieve a consensus between the EMA and FDA views. However, based on these interactions, we nonetheless intend to proceed with our confirmatory Phase 3 clinical trial of ataluren in nmCF in the first half of 2014 consistent with feedback from the EMA on our trial design. Following the conclusion of the re-examination process for our MAA for conditional approval of ataluren in nmDMD, we plan to evaluate the benefit and timing for a potential MAA submission to the EMA for the conditional approval of ataluren in nmCF. There also is substantial risk that the EMA will not grant us conditional approval of ataluren for the treatment of nmCF.

We continue to advance the development of our spinal muscular atrophy collaboration with Roche and the SMA Foundation. The collaboration was initially funded in part by the SMA Foundation. In December 2011, we announced a collaboration with Roche which provided us with an upfront payment of $30 million, the potential for up to $460 million in milestone payments and royalties on any future sales. In August 2013, a development candidate for the program was selected which triggered a $10 million milestone payment to us from Roche. In January 2014, a Phase 1 clinical program was initiated which triggered a $7.5 million milestone payment to us from Roche. Roche is responsible for pursuing clinical development of compounds from the program consistent with a governance structure

that includes representation from us and the SMA Foundation and then commercialization of these compounds.

In addition, we have a pipeline of product candidates that are in preclinical development. Our preclinical and discovery programs are focused on the development of new treatments for multiple therapeutic areas, including neuromuscular disease, oncology and infectious disease. We have discovered all of our compounds currently under development using our proprietary technologies. We plan to develop these compounds both on our own and through selective collaboration arrangements with leading pharmaceutical and biotechnology companies.

Our Strategy

Our goal is to become a leading biopharmaceutical company focused on discovering, developing and commercializing small-molecule therapeutics that target post-transcriptional control processes and address disorders, particularly in the orphan and ultra-orphan areas, with high unmet medical needs. To achieve our goal, we are pursuing the following strategies:

- ***Complete development of and seek marketing approvals for ataluren in lead indications.*** We are devoting a significant portion of our resources and business efforts to completing the development of ataluren for the treatment of nmDMD and nmCF. We have initiated our confirmatory Phase 3 ACT DMD clinical trial and are pursuing a re-examination of our application for conditional approval to market ataluren for the treatment of nmDMD in the European Union prior to completing this trial. We expect that these trial results, if favorable, could serve as the basis for full approval by the EMA and the FDA of ataluren for the treatment of nmDMD. We plan to evaluate the benefit and timing for a potential MAA submission to the EMA for the conditional approval of ataluren in nmCF and, in the first half of 2014, to begin dosing patients for a confirmatory Phase 3 clinical trial of ataluren for the treatment of nmCF.

- ***Maximize commercial potential of ataluren.*** We hold worldwide commercialization rights to ataluren for all indications in all territories. If ataluren receives marketing approval, we plan to commercialize it with our own focused, specialized sales force. We believe that the medical specialists treating Duchenne muscular dystrophy and cystic fibrosis are sufficiently concentrated that we will be able to effectively promote ataluren with targeted sales teams initially in the European Union and the United States and, eventually, in other key territories, such as Asia and Latin America.

- ***Explore additional indications for ataluren.*** We believe that ataluren has the potential to be an important therapy for other genetic disorders for which a nonsense mutation is the cause of the disease. We estimate that, on average, 11% of patients with any genetic disorder resulting from the absence of a single protein, referred to as monogenic disorders, have a nonsense mutation as the cause of the disease. We plan to select additional indications for further clinical development of ataluren consistent with the criteria that we applied in selecting nmDMD and nmCF, such as high unmet medical need and commercially available genotyping. We plan to initiate a proof-of-concept study for a third indication for ataluren in 2014.

- ***Advance the development of our preclinical product candidates and continue to discover and develop small molecules that alter post-transcriptional control processes.*** Our preclinical and discovery programs are focused on new treatments for multiple therapeutic areas, including neuromuscular disease, oncology and infectious disease. We are particularly focused on the development and commercialization of treatments for orphan and ultra-orphan disorders. We are applying several proprietary technologies to identify, chemically optimize and develop small molecules designed to alter post-transcriptional control processes to achieve therapeutic effects. Because post-transcriptional control processes offer many targets for therapeutic intervention and because

drugs that alter these processes have the potential to both increase and decrease protein production, we believe that our approach may be applicable to a broad range of diseases.

- ***Seek third party grants and support and selectively establish strategic alliances.*** We have obtained, and we intend to continue to seek, development funding and other assistance from government entities, non-government and philanthropic organizations and patient advocacy groups for our product candidates. We previously have received grant funding and clinical trial support from the National Institutes of Health, the FDA, the Department of Defense, Defense Threat Reduction Agency, the Muscular Dystrophy Association, Parent Project Muscular Dystrophy, The Wellcome Trust Limited, or Wellcome Trust, Cystic Fibrosis Foundation Therapeutics and the SMA Foundation. In addition, for each of our product candidates, and in particular for product candidates that have high anticipated development costs, address markets requiring a large sales and marketing organization to serve effectively or are directed at indications for which a potential collaborator has a particular expertise, we plan to evaluate the merits of entering into collaboration arrangements with leading pharmaceutical or biotechnology companies.

Our Product Development Programs

The following table summarizes key information about our most advanced product development programs. All of the compounds in these programs are new chemical entities that we identified using our proprietary technologies.

Program	Development status	Development and commercial rights
Ataluren for nmDMD	• Phase 2b clinical trial completed • Confirmatory Phase 3 ACT DMD clinical trial ongoing	PTC
Ataluren for nmCF	• Phase 3 clinical trial completed • Confirmatory Phase 3 clinical trial patient dosing planned for first half of 2014	PTC
Spinal muscular atrophy	• Development candidate selected • Phase 1 clinical program initiated	Roche
Oncology—BMI1	• Preclinical • Lead development compound selected • IND-enabling studies ongoing	PTC
Antibacterial	• Preclinical • Optimization of development compounds ongoing	PTC

We have obtained orphan drug designations from the EMA and from the FDA for ataluren for the treatment of nmDMD and nmCF. We have an effective investigational new drug application, or IND, with the FDA for ataluren for each of nmCF and nmDMD. We plan to submit to the FDA an IND for each of our other product candidates prior to initiating clinical trials for any such product candidate in the United States.

Background on Genetic Disorders and Nonsense Mutations

A significant number of rare genetic disorders are monogenic disorders that occur as a consequence of the absence of a single protein. The restoration of the production of that single protein has the potential to treat the genetic disorder. We estimate that, on average, 11% of patients with any monogenic disorder have a nonsense mutation as the cause of the disease.

Through the post-transcriptional process of translation, a specialized cellular apparatus, called the ribosome, manufactures functional proteins by translating the genetic code contained in the mRNA. This decoding process reads the building blocks of the mRNA, known as nucleotides, in groups of three. Each group of three nucleotides is called a codon. Three of the 64 possible codons contained in mRNA serve as normal stop signals and indicate the end of the protein-coding region of the mRNA. When functioning properly, the stop codons cause the ribosome to halt translation of the mRNA once the mRNA's genetic code has been completely translated into a full-length, functional protein.

There are four basic types of mutations in DNA that can cause a genetic disorder. These are known as insertion, deletion, missense and nonsense mutations. A nonsense mutation is a single nucleotide alteration in the DNA that, when copied to mRNA, is interpreted by the ribosome as a premature stop signal and terminates translation within the protein-coding region of the mRNA. When a ribosome encounters a premature stop codon, the translation process is terminated before a full-length, functional protein is formed. The resulting truncated protein is usually unstable and unable to serve its necessary function. The absence of a full-length, functional protein may cause disease.

Cells have a mechanism that discriminates a normal stop codon from a premature stop codon, although both types of stop codon result in termination of the translation of the genetic code. A group of proteins, known as the termination surveillance complex, can discriminate the proteins downstream of a normal stop codon to regulate normal translational termination. Because these proteins do not appear to be downstream of a premature stop codon, a normal stop codon can be distinguished from a premature stop codon.

Ataluren

Overview

Ataluren is a novel, orally administered small-molecule compound that targets nonsense mutations. We are developing ataluren for the treatment of genetic disorders in which a nonsense mutation is the cause of the disease. We believe that a drug with a mechanism of action that allows the ribosome to read through premature stop codons without affecting the normal termination of protein synthesis may be able to overcome the effects of nonsense mutations.

Ataluren allows the cellular machinery to read through premature stop codons in mRNA and enable the translation process to produce full-length, functional proteins. As described above, certain factors that are located downstream of a normal stop codon are not present at a premature stop codon. We believe that these factors allow ataluren to be active only at premature stop codons without allowing ataluren to read through normal stop codons. Ataluren is from a distinct structural class that does not have antibiotic properties and we believe acts at a different location on the ribosome than gentamicin. Ataluren has been generally well tolerated in all of our clinical trials to date, which involved approximately 600 individuals dosed with ataluren.

The EMA has designated ataluren as an orphan medicinal product for the treatment of nmDMD and nmCF. The FDA has granted orphan drug designation to ataluren for the treatment of nmDMD and nmCF and fast track designation to ataluren for the treatment of nmDMD. There are currently no marketed therapies approved to treat the underlying cause of nmDMD or nmCF.

The following table sets forth information regarding our completed, ongoing and planned Phase 2 and Phase 3 clinical trials of ataluren for the treatment of nmDMD and nmCF.

Phase 2 and Phase 3 clinical trials of ataluren for nmDMD and nmCF

Study	Phase, study design, location	Total patients enrolled	Status	Dates
nmDMD				
nmDMD-004	Phase 2a, open label, United States	38	Completed	December 2005 to May 2007
nmDMD-004e	Phase 2a extension, open label, United States	36 (patients previously in nmDMD-004)	Ended	August 2008 to May 2010
nmDMD-008	Phase 2a, open label, United States	6	Ended	January 2010 to March 2010
nmDMD-007	Phase 2b, double-blind, placebo controlled, Australia, Canada, European Union, Israel, United States	174	Completed	February 2008 to December 2009
nmDMD-007e	Phase 2b extension, open label, Australia, Canada, European Union, Israel, United States	173 (patients previously in nmDMD-007)	Ended	January 2009 to May 2010
nmDMD-016	Phase 3 continuation, open label, United States	Up to 122 (patients previously in nmDMD-004, nmDMD-007 or nmDMD-008)	Ongoing	Initiated in November 2010
nmDMD-019	Phase 3 continuation, open label, Australia, Canada, European Union, Israel	Up to 96 (patients previously in nmDMD-004, nmDMD-007, or nmDMD-008)	Ongoing	Initiated in May 2012
nmDMD-020 (ACT DMD)	Confirmatory Phase 3, double-blind, placebo controlled, planned as Australia, Canada, European Union, Israel, South America, South Korea, Switzerland, Turkey, United States	Approximately 220	Ongoing	Initiated in April 2013
nmDMD-020e	Phase 3 extension, open label, planned as Australia, Canada, European Union, Israel, South America, South Korea, Switzerland, Turkey, United States	Approximately 220 (patients previously in nmDMD-020)	Planned	Plan to begin dosing in the first half of 2014

Study	Phase, study design, location	Total patients enrolled	Status	Dates
nmCF				
nmCF-003	Phase 2, open label, United States	24	Completed	November 2005 to December 2006
nmCF-005	Phase 2, open label, Israel	23	Completed	November 2005 to May 2006
nmCF-005e	Phase 2a extension, open label, Israel	19 (patients previously in nmCF-005)	Completed	January 2007 to June 2007
nmCF-006	Phase 2a, open label, Belgium, France	30	Completed	March 2007 to February 2008
nmCF-009	Phase 3, double-blind, placebo controlled, Canada, European Union, Israel, United States	238	Completed	September 2009 to November 2011
nmCF-009e	Phase 3 extension, open label, Canada, European Union, Israel, United States	191 (patients previously in nmCF-009)	Completed	August 2010 to December 2013
nmCF-021	Confirmatory Phase 3, double-blind, placebo controlled, global trial sites planned	Approximately 210	Planned	Plan to begin dosing patients in the first half of 2014
nmCF-023	Phase 3 open label planned in Canada, European Union, Israel, United States	80 (patients previously in nmCF-009 not using chronic inhaled aminoglycosides)	Planned	Plan to begin enrolling trial sites in the first quarter of 2014

We have completed a Phase 2b clinical trial of ataluren for the treatment of nmDMD and a Phase 3 clinical trial of ataluren for the treatment of nmCF. We did not achieve the primary efficacy endpoint in either trial with the pre-specified level of statistical significance. However, we believe that the collective data from these trials, including retrospective and subgroup analyses that we have performed, provide strong support for concluding that ataluren was active and showed clinically meaningful improvements over placebo in these trials. Accordingly, we initiated our confirmatory Phase 3 ACT DMD clinical trial in April 2013 and expect to initiate an open label extension study to obtain additional safety and efficacy data in patients who completed the double-blind confirmatory Phase 3 ACT DMD clinical trial. We are also planning a confirmatory Phase 3 clinical trial of ataluren for the treatment of nmCF. We believe that our experience in our completed clinical trials has allowed us to enhance the designs of our confirmatory Phase 3 clinical trials and improve our likelihood of success. We plan to begin dosing patients in our confirmatory Phase 3 clinical trial of ataluren for the treatment of nmCF in the first half of 2014. We expect to initiate a separate open label, trial extension study to obtain additional safety and efficacy information in patients who completed the double-blind Phase 3 clinical trial and are not receiving chronic inhaled aminoglycoside antibiotics.

Ataluren is administered orally as granules mixed with permitted liquids or semi-solid foods, such as milk, water, applesauce or yogurt. We designed this formulation because children comprise a significant portion of the patient population for ataluren and often have difficulty swallowing pills or capsules. Ataluren is manufactured in reliable and reproducible synthetic processes from readily available starting materials. Ataluren has been generally well tolerated to date in our Phase 2 and Phase 3 clinical trials.

Duchenne muscular dystrophy

Muscular dystrophies are genetic disorders involving progressive muscle wasting and weakness. Duchenne muscular dystrophy is the most common and one of the most severe types of muscular dystrophy. Duchenne muscular dystrophy occurs when a mutation in the dystrophin gene prevents the

cell from making a functional dystrophin protein. Dystrophin is a muscle membrane associated protein and is critical to the structural and membrane stability of muscle fibers in skeletal, diaphragm and heart muscle. The absence of normally functioning dystrophin results in muscle fragility, such that muscle injury occurs when muscles contract or stretch during normal use. As muscle damage progresses, connective tissue and fat replace muscle fibers, resulting in inexorable muscle weakness.

Because the dystrophin gene is located on the X chromosome, Duchenne muscular dystrophy occurs almost exclusively in young boys. According to Parent Project Muscular Dystrophy, Duchenne muscular dystrophy occurs in approximately 1 in 3,500 live male births. Based on this prevalence data, we estimate that Duchenne muscular dystrophy affects a total of approximately 15,000 boys and adolescents in the United States. Based on data from Orphanet, a public reference portal for information on rare disorders and orphan drugs, we estimate that Duchenne muscular dystrophy affects a total of approximately 19,000 boys and adolescents in the European Union. Genetic tests are available to determine if a patient's Duchenne muscular dystrophy is caused by a nonsense mutation. Based on information from Prior, et al. (1995) in the American Journal of Human Genetics, we estimate that a nonsense mutation is the cause of Duchenne muscular dystrophy in approximately 13% of patients, or approximately 2,000 patients in the United States and 2,500 patients in the European Union.

Children with Duchenne muscular dystrophy typically begin to show symptoms as early as age three, when they develop a waddling gait, may seem clumsy, 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 results in fixations, or contractures, of joints, such as knees, hips, elbows and feet. By the age of eight, most patients have difficulty ascending stairs. By their early teens, patients typically lose walking ability and are confined to wheelchairs. Patients' hearts and respiratory muscles are also affected, typically requiring use of ventilators in their late teens. Further progressive loss of strength and the weakening of heart and lung muscles eventually results in death due to heart and lung failure. The average age of death for Duchenne muscular dystrophy patients is in their mid-twenties.

There is currently no marketed therapy approved for the treatment of the underlying cause of Duchenne muscular dystrophy. Currently available treatments for Duchenne muscular dystrophy are only palliative. These treatments seek to address the symptoms through supportive care measures, such as bracing to give patients some opportunity to remain standing, joint stretching exercises to avoid contractures and tendon release surgery. Corticosteroids are prescribed to mitigate the symptoms of the disease but can cause significant complications because of chronic toxicities. We believe that no other therapy in clinical development for Duchenne muscular dystrophy is designed to treat the underlying cause of nmDMD.

ACT DMD—Phase 3 clinical trial of ataluren for nmDMD

We have initiated our confirmatory Phase 3 ACT DMD clinical trial to evaluate the efficacy and safety of ataluren in patients with nmDMD as confirmed by gene sequencing. This is a multicenter, randomized, double-blind, placebo controlled Phase 3 clinical trial. We dosed the first patient in this trial in April 2013, with enrollment expected to be completed in mid-2014. We plan to conduct this trial in approximately 220 patients at investigational sites worldwide.

The primary objective of this trial is to evaluate the effect of ataluren on ambulation. The primary efficacy endpoint specified in our trial protocol is mean change from baseline over 48 weeks in distance walked during a 6-minute walk test, which we refer to as 6-minute walk distance. The 6-minute walk test is well established as an endpoint for a number of different rare and orphan diseases involving muscle wasting and weakness. Following completion of our Phase 2b clinical trial described below, the

6-minute walk test has become the most common primary endpoint currently used in Duchenne muscular dystrophy clinical trials.

Supportive analyses of ambulation in our trial protocol consist of:

- proportion of patients with at least 10% worsening in 6-minute walk distance at week 48 of the trial compared to baseline;
- time from baseline to persistent 10% worsening in 6-minute walk distance; and
- change from baseline in percent of predicted 6-minute walk distance compared to healthy boys matched for age and height, which we refer to as %-predicted 6-minute walk distance.

Secondary endpoints in the trial consist of change in timed tests of muscle function based on time to climb four stairs, descend four stairs and run/walk 10 meters. Timed function tests are well established in the clinical evaluation of Duchenne muscular dystrophy. Restoration of dystrophin stabilizes muscle membranes, so that the integrity of muscle fibers is maintained, but does not directly increase muscle strength. As a result, we believe that timed function tests provide a more sensitive measure of treatment effect than measures of muscle strength. In addition, because many Duchenne muscular dystrophy patients have very low baseline muscle strength, it is difficult to demonstrate a difference in the rate of decline of muscle strength in these patients.

The trial protocol also includes two secondary endpoints that have not been used previously as outcome measures in published therapeutic clinical trials. The first new endpoint is a functional scale specifically designed for ambulant Duchenne muscular dystrophy patients, referred to as the North Star Ambulatory Assessment, or NSAA. The NSAA is a composite of muscle function tests, such as the ability to rise from the floor, ability to get from lying to sitting, ability to get from sitting to standing and ability to hop, jump and run. The other new endpoint captures patient-reported changes in activities of daily living based on a disease symptom survey that we developed.

The trial protocol specifies the following key inclusion criteria for patients enrolling in the trial:

- the patient must be seven through 16 years of age;
- at baseline, the patient must walk no more than 80% of predicted 6-minute walk distance compared to healthy boys matched for age and height, but have the ability to walk at least 150 meters during the 6-minute walk test; and
- the patient must have used systemic corticosteroids for a minimum of six months prior to start of treatment.

The trial protocol provides for the exclusion of patients from the trial if they have a prior or ongoing clinically significant illness, recently used systemic aminoglycoside antibiotics, recently initiated or changed corticosteroid therapy or previously received ataluren treatment. We will perform study assessments at clinic visits every eight weeks. Patients will undergo 48 weeks of blinded treatment prior to the final analysis.

We plan to stratify patients in this trial based on age, baseline 6-minute walk distance and duration of prior use of corticosteroids. The trial protocol provides that patients will be randomized in a 1:1 ratio to receive either placebo or ataluren at a dosing regimen consisting of 10 mg/kg in the morning, 10 mg/kg at midday and 20 mg/kg in the evening, for a total daily dose of 40 mg/kg. This was the same 10, 10, 20 dose of ataluren that showed beneficial results in our completed Phase 2b clinical trial described below.

We are employing the following methods, among others, to facilitate the recruitment of patients in this trial:

- conducting the trial at sites and with investigators we identify as being well suited for study participation based on access to the targeted patient population, prior clinical trial experience and use of appropriately trained site personnel who are knowledgeable in methods of patient recruitment and retention;

- using technology to increase awareness of the trial in the patient community, including the website at www.clinicaltrials.gov, our corporate website and other online means;
- working with patient groups worldwide to provide trial information to the targeted patient population in local languages;
- collaborating with organizations with strong local expertise to promote region specific recruitment campaigns; and
- providing travel assistance to reduce patient/caregiver burden in traveling to trial sites for study visits.

Based on our estimates regarding patient enrollment, we expect to complete enrollment for this trial in mid-2014 and have initial, top-line data available in mid-2015. At the completion of blinded treatment, an open label continuation trial will be available to patients who successfully complete the trial in countries where ataluren is not commercially available at that time. Patients in the continuation trial will receive ataluren in the same dosing regimen as in the confirmatory Phase 3 ACT DMD clinical trial.

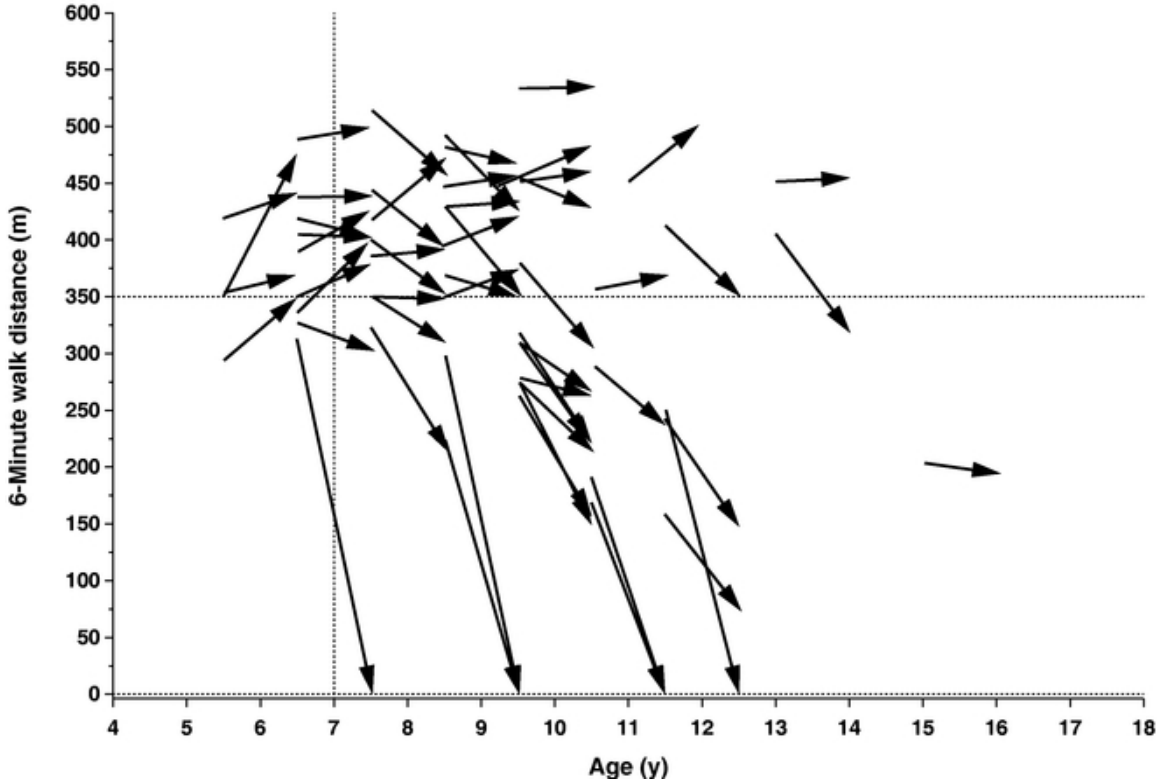
Rationale for design of Phase 3 clinical trial of ataluren for nmDMD

The study population and outcome measures that we are using in our confirmatory Phase 3 ACT DMD clinical trial are based on, and reflect our analysis of the results of, our completed Phase 2b clinical trial for the treatment of nmDMD, including data regarding disease progression, referred to as natural history data, based on patient age and baseline walking ability. Specifically, in our Phase 2b clinical trial:

- Patients who were younger than seven years of age tended to have stable or increasing 6-minute walk distance over 48 weeks. We believe that this reflects the fact that growth and development predominate over disease progression at these ages. Patients seven years of age and older typically had declining 6-minute walk distance over 48 weeks, indicating that they were in the decline phase of the disease. Accordingly, to focus on patients likely to be in the decline phase of the disease, our Phase 3 clinical trial design requires that patients be at least seven years of age.
- The 6-minute walk distance for patients at least seven years of age decreased at different rates over 48 weeks depending on their baseline 6-minute walk distance. Patients whose baseline 6-minute walk distance was greater than 350 meters tended to have stable 6-minute walk distance over 48 weeks. Patients with baseline 6-minute walk distance of less than 350 meters generally declined over 48 weeks, some to the point of becoming non-ambulatory. Accordingly, to focus on patients likely to be in the decline phase of the disease, our Phase 3 clinical trial design requires that patients must walk no more than 80% of predicted 6-minute walk distance compared to healthy boys matched for age and height.

Natural history data from patients in the placebo group in our Phase 2b clinical trial, based on age and baseline 6-minute walk distance, are illustrated in the figure below, in which each placebo-treated patient from the trial is represented by an arrow. The base of the arrow indicates the patient's 6-minute walk distance at baseline, and the tip of the arrow indicates this measurement at week 48 of the trial.

Natural history results from placebo-treated patients in Phase 2b clinical trial



In addition, as discussed in more detail below, we performed a post-hoc, retrospective subgroup analysis of patients from our completed Phase 2b clinical trial who would meet the enrollment criteria for our confirmatory Phase 3 clinical trial. This analysis showed a much larger treatment effect in mean change in 6-minute walk distance over 48 weeks between ataluren and placebo in this subgroup than in the overall population included in the Phase 2b clinical trial.

In light of the natural history data from our Phase 2b clinical trial and this retrospective subgroup analysis, our confirmatory Phase 3 ACT DMD clinical trial is focusing on patients in the decline phase of the disease based on age and baseline 6-minute walk distance. The intent of focusing on patients in the decline phase of the disease is to enhance the demonstration of ataluren's effect to slow decline in walking ability. In addition, we believe that by only enrolling patients who are being treated with systemic corticosteroids, the variability of 6-minute walk distance results will be reduced. Notwithstanding that we expect a larger treatment effect and less variability of results in our Phase 3 ACT DMD clinical trial than in our Phase 2b clinical trial, the sample size of patients in our Phase 3 ACT DMD clinical trial is designed to be large enough to achieve statistical significance even if we achieve the same treatment effect and similar variability as in our Phase 2b clinical trial.

Regulatory status and strategy for nmDMD

EMA. In October 2012, we submitted an MAA to the EMA for conditional approval of ataluren for the treatment of nmDMD. During the review process, the EMA informed us of major objections that would preclude a recommendation for marketing authorization unless adequately addressed. These major objections related to, among other things, the EMA's views regarding insufficient evidence of efficacy based on our single Phase 2b clinical trial, resulting in a negative risk-benefit balance for purposes of conditional approval, and uncertainties about the effective dose. The EMA also questioned

whether our confirmatory Phase 3 ACT DMD clinical trial could be completed if the EMA granted conditional approval. In December 2013, the EMA convened a scientific advisory group, or SAG, meeting as part of the regulatory review process prior to the oral explanation meeting with the CHMP. We believe that both the SAG and oral explanation meetings allowed us and independent experts in the DMD field to provide important information to the SAG and CHMP members on the natural history of DMD as it relates to the primary endpoint of walking a greater distance than patients taking placebo in six minutes, which is referred to as the six minute walk test, the difficulty of utilizing dystrophin as a biomarker, the mechanism of action and dose response curve of ataluren, and the breadth of clinical evidence demonstrating ataluren's activity in nmDMD patients.

In January 2014, the CHMP adopted a negative opinion recommending the refusal of the granting of the conditional marketing authorization for ataluren for the treatment of nmDMD. The CHMP stated that a principal reason for the negative opinion was that the prior Phase 2b clinical trial had failed to demonstrate in the primary analysis that patients taking ataluren could walk a greater distance in six minutes than patients taking placebo, the primary endpoint. Additionally, the CHMP noted that other measures of efficacy provided only limited supportive evidence of the beneficial effects of ataluren. The CHMP acknowledged in communication to us that the post hoc analyses that we presented to the CHMP were performed in line with the most current knowledge about the natural history of the disease and that our definition of the subgroups in the analyses were both clinically and scientifically justified. However, the CHMP concluded that we did not provide sufficiently compelling evidence of efficacy to justify conditional approval. In addition, the CHMP considered that we had not provided sufficient data to determine how ataluren works in the body and how its effects change with dose. Finally, the CHMP expressed concern that the conduct of the confirmatory Phase 3 ACT DMD trial might be affected by the availability of an authorized product and therefore potentially jeopardize the feasibility of completing the trial. Therefore, despite divergent minority positions, the CHMP concluded a favorable risk-benefit balance could not be established at the time of their meeting and adopted a negative opinion. We have requested a re-examination of the CHMP opinion and currently expect a final outcome in the second quarter of 2014.

Based upon the timelines for a re-examination process, we believe that our confirmatory Phase 3 ACT DMD clinical trial will be substantially enrolled at the time the CHMP would consider a revision of their initial opinion as part of the re-examination process. Although it is possible that some later enrolling patients in the European Union may drop out of the trial if ataluren becomes commercially available following conditional approval, we believe that this risk is small, and that the effect on the trial would be minimal because we expect a large number of patients to be enrolled in countries outside the European Union. We also believe that clinical investigators, who may also be the primary physicians for patients in the trial, and patient advocacy groups will encourage patients to remain in the trial.

EMA conditional approval would permit us to market ataluren in the European Union for nmDMD prior to the completion of our confirmatory Phase 3 ACT DMD clinical trial. Conditional approval is valid for one year, with annual renewals required thereafter. Upon granting conditional approval, the EMA specifies the obligations and the timeframe to fulfill them for subsequent full approval.

The EMA will consider conditional marketing approval of a product candidate that is being developed to treat a seriously debilitating or life-threatening disease or that is designated as an orphan medicinal product notwithstanding that one or more additional pivotal clinical trials may be required for full approval. Such a product candidate must satisfy each of the four following requirements: the risk-benefit balance of the product candidate must be positive; the applicant must be likely to provide comprehensive data; the product candidate must fulfill an unmet medical need; and the benefits to public health of the immediate availability of the product candidate must outweigh the risks inherent in the fact that additional data are still required.

We continue to believe that completion of our confirmatory Phase 3 ACT DMD clinical trial and submission of data to the regulatory authorities is the more likely path forward for gaining marketing approval of ataluren. There is substantial risk that the EMA will not grant us this conditional approval even on re-examination. However, we are pursuing this approach because we believe the drug is active and should be made commercially available as soon as possible to patients who have no other treatment options. We plan to complete our confirmatory Phase 3 ACT DMD clinical trial of ataluren for the treatment of nmDMD even if the EMA does not grant conditional approval. We expect that these trial results, if favorable, could serve as the basis for full marketing approval in the European Union, the United States and other territories. If the trial results are favorable, and based on our estimates of patient enrollment and data availability, we expect to be able to submit applications for full marketing approval of ataluren for the treatment of nmDMD in both the European Union and the United States in 2016.

Inspectors acting at the request of the EMA conducted good clinical practice, or GCP, inspections in 2013 of selected clinical sites from our completed Phase 2b clinical trial of ataluren for the treatment of nmDMD and our clinical site relating to our pending MAA for conditional approval of ataluren for the treatment of nmDMD. The reports from these inspections contained a combination of critical and major findings. These findings relate to waivers we granted to admit patients to our completed Phase 2b clinical trial of ataluren for nmDMD in advance of protocol amendments that would have established their eligibility for the trial, as well as our oversight of our trial sites and completeness or sufficiency of trial documentation. We do not believe these findings reflect adversely on the overall integrity of our Phase 2b clinical trial or trial results. Our response to these findings described to the EMA the enhanced internal procedures and controls we have implemented, and the internal quality assurance department we have established, since the conclusion of our Phase 2b clinical trial of ataluren for the treatment of nmDMD. In addition, we proposed corrective action plans to address the inspectors' specific findings. The findings from these inspections, together with our response and inspectors' comments on our response, will be considered by CHMP as it evaluates our MAA and may affect the probability of conditional approval. We have implemented corrective action plans that we believe address the critical and major findings in the inspectors' report in the design and ongoing oversight of our confirmatory Phase 3 clinical trial for ataluren for the treatment of nmDMD.

FDA. Following a meeting with the FDA in November 2009 in which we discussed our submission of a new drug application, or NDA, we submitted to the FDA the final component of an NDA in March 2011 for approval of ataluren for the treatment of nmDMD. The FDA refused to file this NDA on the grounds that the single placebo controlled Phase 2b clinical trial contained in the NDA did not achieve statistical significance in the pre-specified analysis. In December 2011, we filed with the FDA a formal dispute resolution request concerning the NDA. We requested review of the issues related to the FDA's refusal to file the NDA and a prospective resubmission of the NDA with updated information and analyses. In January 2012, the FDA reaffirmed the appropriateness of its earlier decision to refuse to file the NDA. In February 2012, we discussed the design of a proposed Phase 3 clinical trial with the FDA. In that meeting, although the FDA indicated that the adequacy of data for filing and approval of an NDA would remain review issues, the FDA had no objections to key elements of our proposed trial design, including the eligibility criteria for patients based on baseline 6-minute walk distance, use of the 6-minute walk test as the primary efficacy endpoint and inclusion of timed tests of muscle function as key secondary endpoints. Consequently, we plan to include the safety and efficacy data from our confirmatory Phase 3 ACT DMD clinical trial of ataluren for the treatment of nmDMD as part of our application for marketing approval from the FDA if we successfully complete this trial.

Phase 2b clinical trial of ataluren for nmDMD

In March 2010, we announced the results of a randomized, double-blind, placebo controlled, dose ranging Phase 2b clinical trial evaluating the long term efficacy and safety of ataluren in patients with nmDMD as confirmed by gene sequencing. We conducted this clinical trial in 174 patients at 37 investigational sites in 11 countries. Before this clinical trial, there was no established precedent for an appropriate trial design to evaluate the efficacy of ataluren and little clinical experience in the methodologies used to analyze the resulting data. In addition, at the time we designed and initiated this trial, our knowledge of the natural history of Duchenne muscular dystrophy patients was limited. In particular, there were no data available regarding change in 6-minute walk distance over time for patients with Duchenne muscular dystrophy. As a result of this trial, we improved our understanding of the patient population likely to demonstrate the greatest measurable benefit from treatment, the dose of ataluren most likely to demonstrate efficacy and the appropriate statistical plan for analyzing the trial data.

The primary objective of this trial was to evaluate the effect of ataluren on ambulation. The primary efficacy endpoint was the mean change in 6-minute walk distance at week 48 of the trial compared to baseline. Supportive analyses of ambulation consisted of the proportion of patients with at least 10% worsening in 6-minute walk distance at week 48 of the trial compared to baseline and time to persistent 6-minute walk distance 10% worsening from baseline.

We included many secondary and exploratory endpoints in this trial to gain greater understanding of clinical trial design in Duchenne muscular dystrophy and not with the sole objective of showing a treatment effect. Secondary endpoints in the trial included monitoring changes in:

- tests of muscle function based on time to climb four stairs, descend four stairs, run/walk 10 meters and stand from supine;
- muscle strength;
- patient/caregiver reported frequency of accidental falls;
- patient/caregiver reported health related quality of life;
- patient/caregiver reported treatment satisfaction;
- at-home activity as measured by pedometry;
- verbal memory and attention;
- heart rate function;
- creatine kinase, or CK, values as a measure of whole-body muscle fragility; and
- biceps muscle dystrophin expression.

We assessed safety through collection of adverse event information, measurement of laboratory parameters and performance of electrocardiograms, or ECGs. We also evaluated study drug compliance and ataluren plasma concentrations.

Patients enrolled in this trial were at least five years of age, had the ability at baseline to walk at least 75 meters unassisted during a 6-minute walk test, had onset of disease signs/symptoms prior to age nine, had elevated CK levels and had ongoing difficulty with walking. Patients were excluded from the trial if they had a prior or ongoing clinically significant illness, had a positive hepatitis B or hepatitis C test or had recently used systemic aminoglycosides. Patients receiving corticosteroid therapy were required to have initiated therapy more than six months prior to enrollment and to be on a stable dosing regimen for at least three months prior to entering the trial. The trial protocol specified a clinic

visit every six weeks to assess efficacy and safety and an interim laboratory visit every three weeks for the first 24 weeks of the trial. The treatment duration was 48 weeks.

We stratified patients in this trial based on age, baseline 6-minute walk distance and use of corticosteroids. Patients were randomized in a 1:1:1 ratio to receive one of the following:

- placebo;
- ataluren at a dosing regimen consisting of 10 mg/kg in the morning, 10 mg/kg at midday and 20 mg/kg in the evening, for a total daily dose of 40 mg/kg, which we refer to as the 10, 10, 20 dose of ataluren; or
- ataluren at a dosing regimen consisting of 20 mg/kg in the morning, 20 mg/kg at midday and 40 mg/kg in the evening, for a total daily dose of 80 mg/kg, which we refer to as the 20, 20, 40 dose of ataluren.

Pre-specified analysis in ITT population. As specified in the trial protocol, we performed the primary analysis of the mean change in 6-minute walk distance from baseline to 48 weeks in the intent-to-treat, or ITT, population. The ITT population included all 174 randomized patients with a valid 6-minute walk test available at baseline and at least one post-baseline visit.

In this trial, the patients taking the 10, 10, 20 dose of ataluren had notably less decline in their walking ability than the patients taking placebo. The mean change from baseline to 48 weeks in 6-minute walk distance was -42.6 meters, with a standard deviation from the mean of 90.0 meters, in the placebo group, and -12.9 meters, with a standard deviation from the mean of 72.0 meters, in the ataluren 10, 10, 20 dose group. The difference of 29.7 meters between the 10, 10, 20 dose of ataluren and placebo in mean change in 6-minute walk distance over 48 weeks was consistent with the clinically meaningful treatment effect of 30 meters specified in the trial protocol. However, the resulting nominal p-value of 0.149 was not statistically significant at the pre-specified level of less than 0.05. We had targeted a treatment effect of 30 meters because marketed drugs for other genetic disorders that affect muscle activity were approved on the basis of a difference of approximately 30 meters in 6-minute walk distance.

Typically, a trial result is statistically significant if the chance of it occurring when the treatment is like placebo is less than one in 20, resulting in a p-value of less than 0.05. A p-value is called nominal if it is the result of one particular comparison when more than one comparison is possible, such as when two active treatments are compared to placebo or when two or more subgroups are analyzed.

We believe that the principal reasons for the lack of statistical significance for the primary efficacy endpoint in this trial, notwithstanding having achieved the targeted treatment effect, were the higher than expected mean variability in the results of individual patients over 48 weeks, as measured by the standard deviation from the mean, and the heterogeneous population of nmDMD patients based on age and baseline 6-minute walk distance. We believe that the high standard deviation in the 6-minute walk distance data resulted from the substantial variability of disease progression in Duchenne muscular dystrophy in patients in the wide age range that we enrolled in this trial. In particular, we believe that younger patients and patients with higher baseline 6-minute walk distances are less likely to exhibit measurable declines in 6-minute walk distance over 48 weeks. Based on information available at the time we designed this trial, we selected the sample size of the trial based on an assumed standard deviation of 50 meters and enrolled patients between five and 20 years of age. However, the higher actual standard deviation in the trial of between 72 and 90 meters made it difficult to achieve statistical significance without a larger patient population.

In this trial, there was no difference between placebo and the 20, 20, 40 dose of ataluren in the mean change in 6-minute walk distance over 48 weeks. Although unanticipated, this finding is

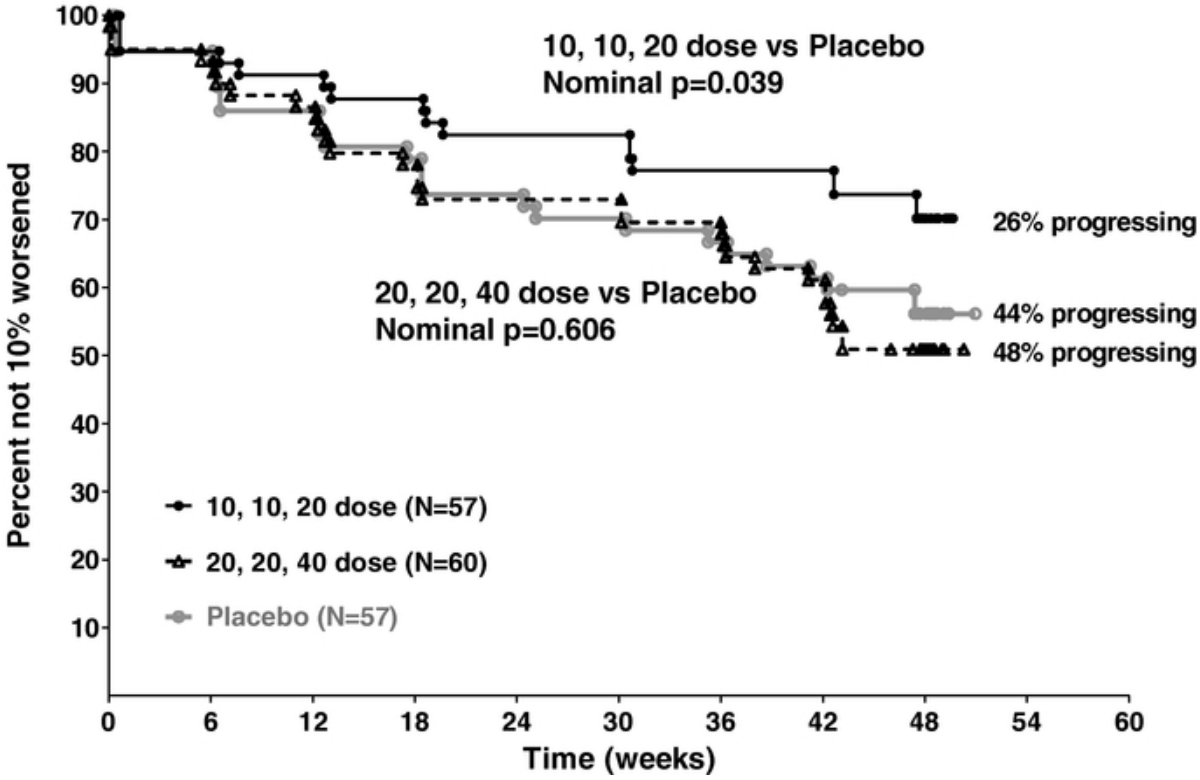
consistent with a bell-shaped dose-response curve that we observed in four subsequent non-clinical studies of ataluren in Duchenne muscular dystrophy and other genetic disorders.

Pre-specified supportive analyses of ambulation. The protocol for our Phase 2b clinical trial included the following two supportive analyses of ambulation:

- an evaluation of the proportion of patients with at least 10% persistent worsening in 6-minute walk distance at week 48 compared to baseline; and
- time to persistent 6-minute walk distance 10% worsening from baseline.

The 10% persistent worsening threshold was defined in advance and reflects the clinical meaningfulness of a 10% change in walking ability in Duchenne muscular dystrophy. Specifically, a change of 10% in walking ability in one year is generally predictive of substantial decline in a patient's clinical status over the following years. The proportion of patients with at least 10% persistent worsening in 6-minute walk distance over the course of the trial is shown in the graph below.

Proportion of patients with persistent 10% worsening in 6-minute walk distance from baseline to week 48 (ITT population)



We believe that this analysis of the 6-minute walk distance indicates a meaningful delay in decline in ambulation for the 10, 10, 20 dose of ataluren compared to placebo and supports the primary analysis of mean change from baseline in 6-minute walk distance in the ITT population.

The analysis of time to 10% persistent worsening indicated that the pre-specified median time to 10% worsening was not reached in any of the three treatment arms of the trial.

Post-hoc analyses of Phase 2b clinical trial data. Based on our further evaluation of the data from our Phase 2b clinical trial after unblinding the results, we identified three issues affecting the

pre-specified statistical analyses. We addressed these issues in a post-hoc, retrospective refinement to the pre-specified statistical analysis plan, resulting in what we refer to as a corrected ITT analysis.

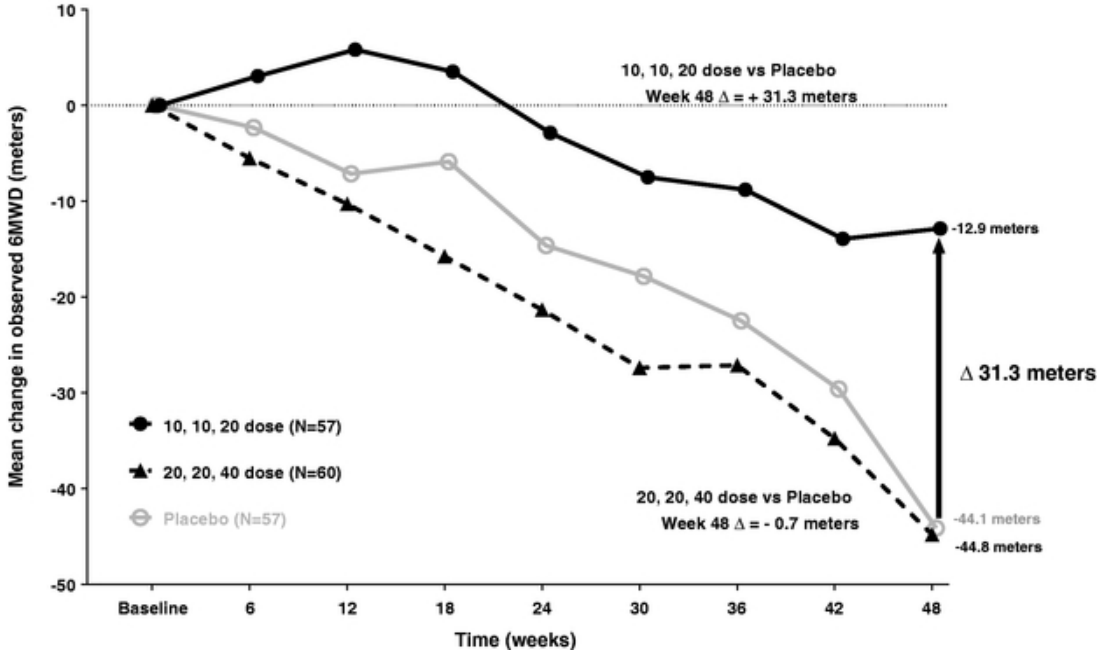
- Our pre-specified statistical model used to calculate the p-value and significance of the trial results omitted a specific statistical term designed to address the potential relationship between the 6-minute walk distance results at baseline and at each subsequent patient visit. As has now become standard practice in analyses of repeated-measures data, we adjusted our statistical model to add this statistical term in preparing the corrected ITT analysis.

- Because the 6-minute walk distance data were non-normally distributed, our pre-specified analysis used rank-transformed data in which the 6-minute walk distance values for each patient were ordered from smallest to largest and ranked from one to 174. However, ranking the data in this way did not fully reflect the large variability as measured in meters that we observed in the original 6-minute walk distance data. In the corrected ITT analysis, we used a re-randomization test, rather than rank transformation of the data, to address non-normality of the trial data. This re-randomization test allowed analysis of the 6-minute walk distance results in meters, rather than ranking the results relative to one another, to more accurately reflect the large variability in walking distances.

- Two patients had lower limb injuries after screening but prior to their baseline assessment. These injuries substantially affected their walking ability and led to aberrantly low baseline 6-minute walk distance values that did not accurately reflect their pre-treatment ambulatory ability. These baseline 6-minute walk tests were incorrectly classified as valid by the investigative site, and the resulting data should not have been included in the ITT analysis. In the corrected ITT analysis, we replaced the baseline values for these two patients with their valid screening values.

The results of our post-hoc analysis of the primary efficacy endpoint of this trial are shown in the graph and the table below.

Mean change in 6-minute walk distance (6MWD) by visit (corrected ITT analysis)



Change in 6-minute walk distance from baseline to week 48 (corrected ITT analysis)

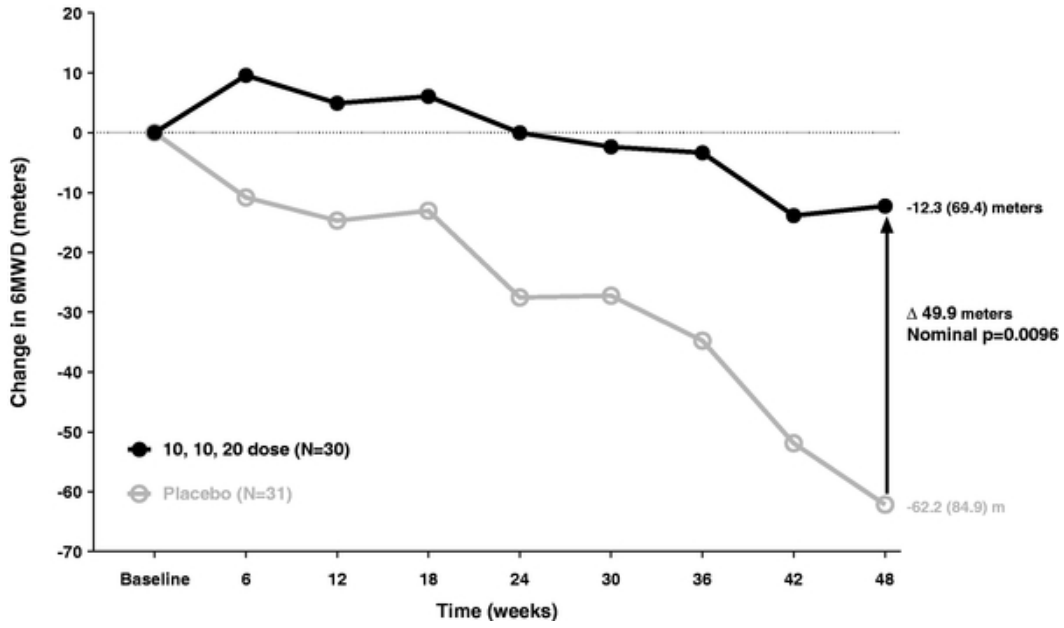
	Treatment arm		
Summary of change from baseline to week 48	**Placebo N=57**	**Ataluren 10, 10, 20 dose N=57**	**Ataluren 20, 20, 40 dose N=60**
Mean (standard deviation), meters	-44.1 (88.0)	-12.9 (72.0)	-44.8 (84.8)
Mean difference from placebo, meters		31.3	-0.7
Nominal p-value (vs. placebo)		0.0281	0.912
Adjusted p-value (vs. placebo)		0.0561	0.991

In the corrected ITT analysis, the difference between the 10, 10, 20 dose of ataluren and placebo in mean change in 6-minute walk distance over 48 weeks was 31.3 meters. We observed clear separation between the 10, 10, 20 dose of ataluren and placebo, with the difference between the arms increasingly favoring the 10, 10, 20 dose of ataluren over time. The resulting nominal p-value for the comparison of mean change in 6-minute walk distance from baseline to week 48 for the 10, 10, 20 dose of ataluren versus placebo was 0.0281. However, because two dose levels were compared to placebo, we were required to apply a multiplicity adjustment, which yielded a final adjusted p-value of 0.0561 for the 10, 10, 20 dose of ataluren versus placebo.

Although we believe that our additional analyses of the trial results were warranted, a retrospective analysis performed after unblinding trial results can result in the introduction of bias if the analysis is inappropriately tailored or influenced by knowledge of the data and actual results. In addition, nominal p-values cannot be compared to the benchmark p-value of 0.05 to determine statistical significance without being adjusted for the testing of multiple dose groups or analyses of subgroups. Because of these limitations, regulatory authorities typically give greatest weight to results from pre-specified analyses and adjusted p-values and less weight to results from post-hoc, retrospective analyses and nominal p-values.

Subgroup analysis based on enrollment criteria for confirmatory Phase 3 clinical trial. Using the corrected ITT analysis, we also performed a post-hoc, retrospective subgroup analysis of patients in the Phase 2b clinical trial who would meet the enrollment criteria for our confirmatory Phase 3 clinical trial. We expect that these patients would be in the decline phase of the disease, based on age and baseline 6-minute walk distance. Patients in this subgroup were seven through 16 years of age, at baseline, walked no more than 80% of predicted 6-minute walk distance compared to healthy boys matched for age and height, but had the ability to walk at least 150 meters during the 6-minute walk test, and had used systemic corticosteroids for a minimum of six months prior to start of treatment. The results of this subgroup analysis are shown in the graph and the table below.

Mean change in 6-minute walk distance (6MWD) in Phase 2b subgroup based on enrollment criteria for confirmatory Phase 3 clinical trial (corrected ITT analysis)



Summary of change from baseline to week 48	Treatment arm: Placebo N=31	Treatment arm: Ataluren 10, 10, 20 dose N=30
Mean (standard deviation), meters	-62.2 (84.9)	-12.3 (69.4)
Mean difference from placebo, meters		49.9
Nominal p-value (vs. placebo)		0.0096

In this subgroup analysis, the difference between the 10, 10, 20 dose of ataluren and placebo in mean change in 6-minute walk distance over 48 weeks was 49.9 meters (nominal p = 0.0096). Because all patients in this subgroup were receiving corticosteroids, the variability was reduced compared to the mixed population in the Phase 2b clinical trial of corticosteroid users and non-users.

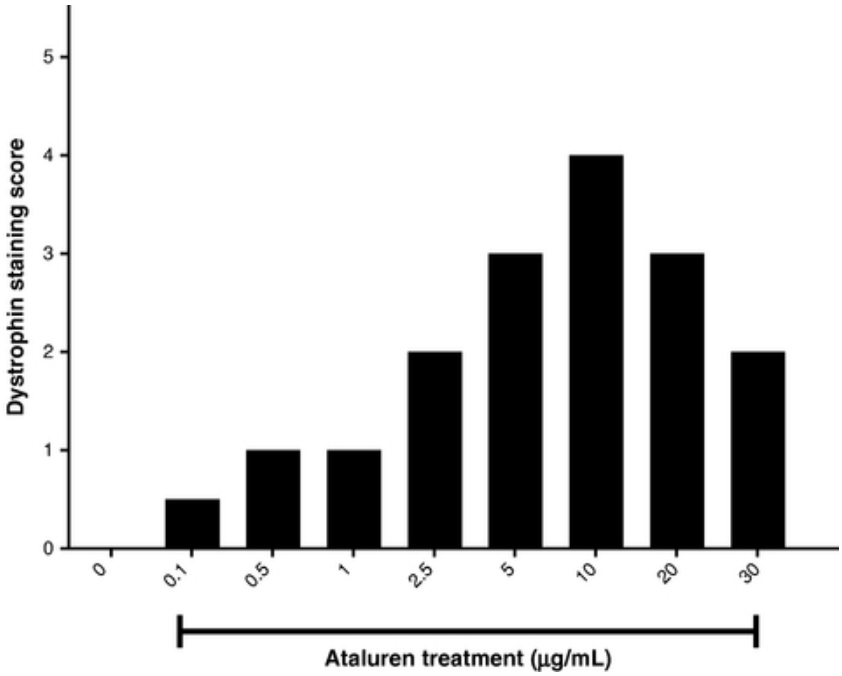
Dose-response curve. In our Phase 2b clinical trial, although the 10, 10, 20 dose of ataluren showed clinically meaningful improvements over placebo, the 20, 20, 40 dose of ataluren generally showed little or no difference from placebo. Based on our current understanding of the ribosome's structure, we believe that the 10, 10, 20 dose of ataluren associates with a particular site on the ribosome that allows the ribosome to read through a premature stop signal. We believe that this allows the ribosome to make the full-length, functional dystrophin protein and modulate the defect in muscular dystrophy. At higher doses, such as the 20, 20, 40 dose, we believe that ataluren may also interact with a second site on the ribosome that interferes with the ability of the ribosome to read through the premature stop signal. Therefore, we believe that at higher doses ataluren no longer enables the ribosome to make the full-length, functional dystrophin protein.

The results of our Phase 2b clinical trial are consistent with a bell-shaped dose-response in which the response to treatment initially increases with higher drug concentrations and then subsequently decreases at even higher drug concentrations. We also observed a bell-shaped dose-response to ataluren in non-clinical studies involving mouse and human cellular models of nmDMD and a mouse cellular

model of the genetic disorder Hurler's Disease and in two extension trials of ataluren that we conducted.

Mouse model of nmDMD. In a mouse model of nmDMD, ataluren increased dystrophin production in muscle cells grown in the laboratory, referred to as myotubes, with maximal activity at a concentration of 10 micrograms per milliliter, or µ g/ml. In this study, we observed decreased dystrophin production at concentrations of ataluren ranging from 20 µ g/ml to 30 µ g/ml, indicating a bell-shaped dose-response curve. We assessed dystrophin production based on staining of muscle samples with antibodies as observed under a microscope. The figure below shows the results from this mouse model.

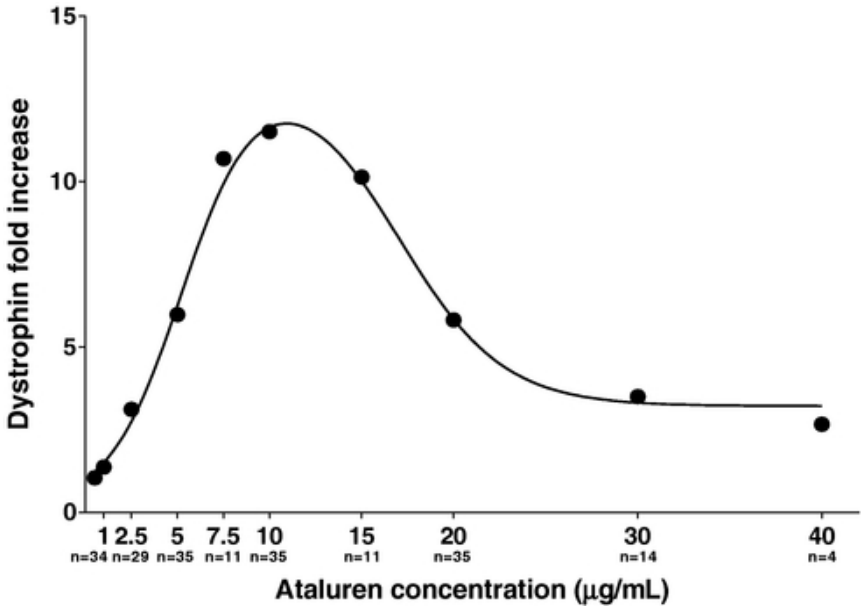
Effect of ataluren on dystrophin staining scores in myotubes isolated from nmDMD mice



Myotubes from nmDMD patients. In non-clinical studies with human myotubes grown from 35 different nmDMD patients, ataluren also exhibited a bell-shaped dose-response curve with maximal dystrophin staining observed at 10 µ g/ml of ataluren. At concentrations above 10 µ g/ml, there was diminishing response to treatment. The figure below shows the results from these non-clinical studies. In this figure, the values on the vertical axis represent changes in dystrophin expression relative to untreated myotube cultures from patients with nmDMD.

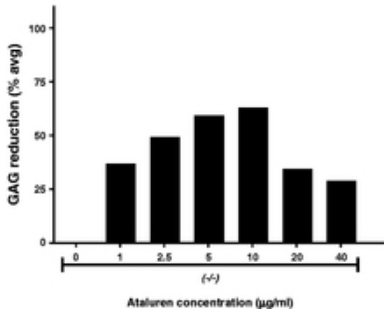
***In vitro* dystrophin expression concentration-response in cultured myotubes from nmDMD patients**

Mean increase relative to control

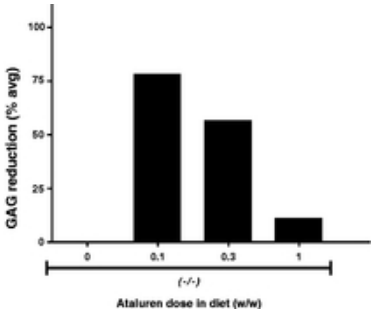


Mouse model of nonsense mutation Hurler's disease. In addition, ataluren also showed a bell-shaped dose-response in two experiments in a mouse model that we developed for the genetic disorder Hurler's disease in which the mice harbor a nonsense mutation. In cells taken both from the mouse model exposed to increasing concentrations of ataluren, shown in the first figure below, and in spleen samples from mice given increasing doses of ataluren, shown in the second figure below, we observed a bell-shaped dose-response in the reduction in the levels of glycosaminoglycans, or GAGs, elevated levels of which are a hallmark of Hurler's disease.

In *vitro* mouse cells



In *vivo* mouse spleen

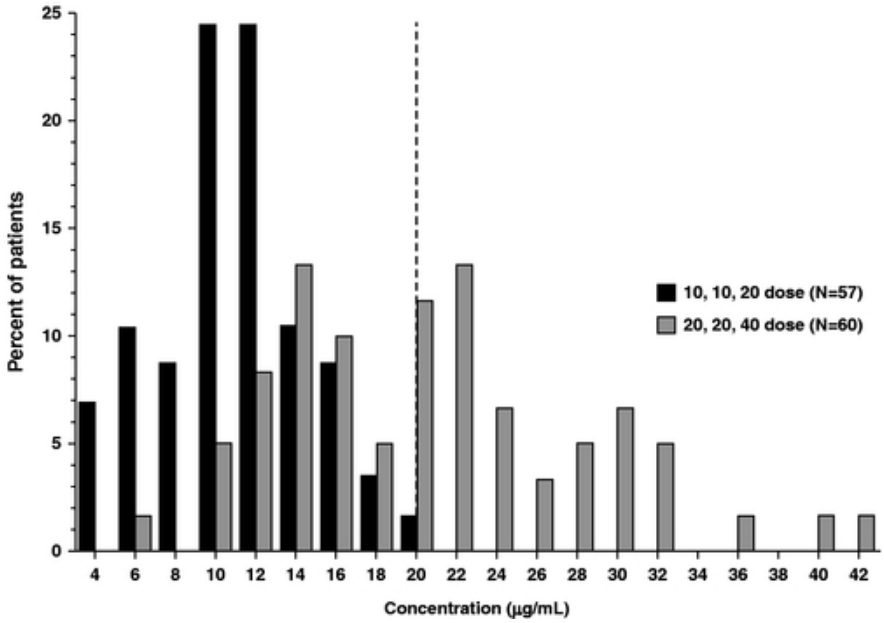


Zebrafish model of nonsense mutation DMD. In addition, ataluren also showed a bell-shaped dose-response in experiments performed by an independent academic research laboratory using nonsense-containing dystrophin mutation DMD zebrafish. In this research, ataluren significantly improved skeletal muscle function and demonstrated improvement dystrophin expression, and the dose-dependency was bell-shaped.

Clinical trial data. To gather additional evidence of a bell-shaped dose-response curve, we analyzed the data from our clinical trials based on ataluren plasma concentration. In our Phase 2b

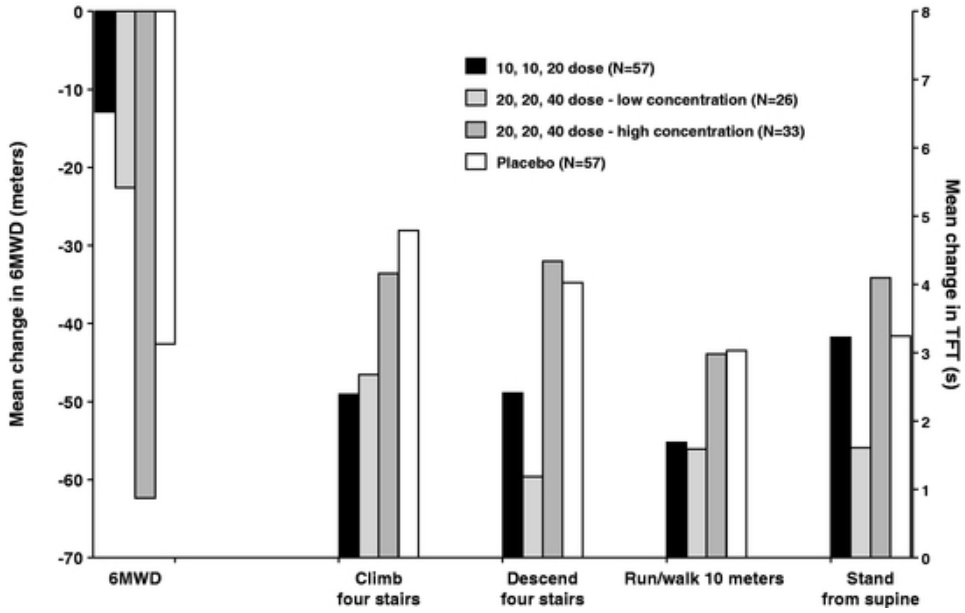
clinical trial, we measured ataluren plasma concentrations prior to the morning dose, or C_{0h} , and two hours after the morning dose, or C_{2h} , at each visit. All patients receiving the 10, 10, 20 dose of ataluren had a maximal mean plasma concentration of less than 20 µ g/ml. Approximately 40% of patients receiving the 20, 20, 40 dose had mean plasma concentrations in a low concentration range of less than 20 µ g/ml, and approximately 60% of these patients had mean plasma concentrations in a high concentration range of 20 µ g/ml or greater. The figure below shows mean C_{2h} ataluren data from our Phase 2b clinical trial.

Mean 2-hour ataluren plasma concentrations



In our Phase 2b clinical trial, we also analyzed 6-minute walk distance and timed function tests by mean C_{0h} and C_{2h} across all visits. Patients who received the 20, 20, 40 dose of ataluren and had mean plasma concentrations in a low concentration range of less than 20 µ g/ml had better results in 6-minute walk distance and time function tests than patients who received the 20, 20, 40 dose of ataluren but had mean plasma concentrations in a high concentration range of 20 µ g/ml or greater. The figure below shows these results.

Mean change in 6-minute walk distance (6MWD) and timed function tests (TFT(s)) by concentration



We performed similar concentration-response analyses, based on $C_{0h,}$ in our Phase 2a and Phase 2b open label extension trials in which only the 20, 20, 40 dose of ataluren was evaluated. In both trials, patients with mean plasma concentrations in a low concentration range of less than 20 µ g/ml had better results in 6-minute walk distance and timed function tests than patients with mean plasma concentrations in a high concentration range of 20 µ g/ml or greater. This indicates that the plasma concentration range associated with the 10, 10, 20 dose is the active concentration range of ataluren.

Secondary endpoints. Our analyses of the data from the secondary efficacy endpoints of this Phase 2b clinical trial are summarized below. There was little or no prior experience with several of these secondary endpoints in Duchenne muscular dystrophy therapeutic trials. In addition, this trial was powered based upon the primary endpoint, 6-minute walk distance, and not to detect statistically significant differences in these secondary endpoints. However, patients in the 10, 10, 20 ataluren dose group trended better than the placebo group in several of these secondary endpoints.

- *Timed tests of muscle function.* Patients treated with ataluren showed less decline in muscle function over 48 weeks, as evidenced by smaller increases in the times to climb four stairs, descend four stairs and run/walk 10 meters, relative to placebo. These trends were more prominent with the 10, 10, 20 dose of ataluren and exceeded the clinically meaningful threshold of 1.5 seconds for stair-climbing and stair-descending in the ITT analysis and for running/walking in the corrected ITT analysis. In a supine to stand test, we did not observe any difference between ataluren and placebo.

- *Muscle strength.* We performed myometric evaluations, in which muscle strength is measured in knee flexion, knee extension, elbow flexion, elbow extension and shoulder abduction. Over 48 weeks, patients treated with ataluren generally showed slightly less decline in muscle strength, as evidenced by smaller decreases in most myometry parameters, relative to placebo. These trends were more prominent with the 10, 10, 20 dose of ataluren, although differences were below a threshold considered to be clinically meaningful.

- *Frequency of accidental falls.* The frequency of falls was measured based on a diary kept by patients/caregivers. Trial results showed trends in reductions in accidental falling for ataluren

compared to placebo. Accidental falls are a major concern of patients and their families, since they can lead to fractures and, in some cases, loss of ambulation.

- *Patient-reported health related quality of life and treatment satisfaction.* We observed positive trends favoring the 10, 10, 20 dose of ataluren compared to placebo in the patient reported physical functioning aspect of the health related quality of life measurement, although differences were below a threshold considered to be clinically meaningful.

- *At-home activity as measured by pedometry.* In an assessment of time spent at different activity levels in daily life, the largest differences between ataluren and placebo in mean changes at week 48 were observed with the 10, 10, 20 dose of ataluren, which showed trends toward less time spent at no activity and more time spent at medium activity. We performed this assessment on the basis of the number of steps taken per minute as measured by a pedometer worn on the ankle. In conjunction with this step activity monitoring, patients receiving the 10, 10, 20 dose of ataluren showed trends toward less increase in wheelchair use over 48 weeks as compared to placebo.

- *Biceps muscle dystrophin expression.* Because muscular dystrophy is caused by the absence of the dystrophin protein, we sought to collect quantitative data with respect to muscle dystrophin expression as we had observed in our Phase 2a clinical trial described below. However, we were unsuccessful in doing so, in part, because a majority of muscle biopsy samples that we collected were compromised, which precluded meaningful interpretation of the data. In addition, we have since concluded that a sensitive and reliable method is not currently available for quantifying dystrophin at the low levels seen in patients with Duchenne muscular dystrophy and that muscle sampling is problematic because of the variation in dystrophin levels within either the same muscle or between different muscles.

- *Other secondary endpoints.* Changes in other secondary efficacy endpoints were generally small, and we did not observe any clear differentiation between ataluren and placebo.

Safety and tolerability. Ataluren was generally well tolerated at both dose levels in our Phase 2b clinical trial. There were no study discontinuations due to adverse events. Most treatment-emergent adverse events were mild or moderate in severity. Investigators' attributions of drug-related adverse effects were generally similar across the placebo and ataluren arms. The most common adverse events in this trial were vomiting (46.6% overall), headache (29.3%), diarrhea (24.1%), nasopharyngitis (20.7%), fever (19.0%), cough (19.0%) and upper abdominal pain (17.8%). These events were generally balanced across treatment arms and are typical of pediatric illnesses. Adverse events with at least a 10% incidence in any treatment arm that were seen with increased frequency from the placebo group to the ataluren 10, 10, 20 dose group to the ataluren 20, 20, 40 dose group were nausea (12.3% for placebo, 14.0% for the ataluren 10, 10, 20 dose and 16.7% for the ataluren 20, 20, 40 dose), abdominal pain (7.0% for placebo, 12.3% for the ataluren 10, 10, 20 dose and 16.7% for the ataluren 20, 20, 40 dose), pain in extremity (10.5% for placebo, 12.3% for the ataluren 10, 10, 20 dose and 13.3% for the ataluren 20, 20, 40 dose), flatulence (7.0% for placebo, 8.8% for the ataluren 10, 10, 20 dose and 11.7% for the ataluren 20, 20, 40 dose) and nasal congestion (7.0% for placebo, 8.8% for the ataluren 10, 10, 20 dose and 10.0% for the ataluren 20, 20, 40 dose). An overview of adverse events in this trial is shown in the table below.

Overview of treatment-emergent adverse events in Phase 2b clinical trial (as-treated population)

Parameter	Treatment arm: Placebo N=57	Ataluren 10, 10, 20 dose N=57	Ataluren 20, 20, 40 dose N=60	All patients N=174
Patients with o 1 adverse event	56 (98.2)%	55 (96.5)%	57 (95.0)%	168 (96.6)%
Adverse events by severity				
Grade 1 (mild)	21 (36.8)%	16 (28.1)%	20 (33.3)%	57 (32.8)%
Grade 2 (moderate)	26 (45.6)%	31 (54.4)%	27 (45.0)%	84 (48.3)%
Grade 3 (severe)	9 (15.8)%	8 (14.0)%	10 (16.7)%	27 (15.5)%
Grade 4 (life-threatening)	—	—	—	—
Adverse events by relatedness				
Unrelated	14 (24.6)%	8 (14.0)%	11 (18.3)%	33 (19.0)%
Unlikely	16 (28.1)%	17 (29.8)%	13 (21.7)%	46 (26.4)%
Possible	20 (35.1)%	25 (43.9)%	29 (48.3)%	74 (42.5)%
Probable	6 (10.5)%	5 (8.8)%	4 (6.7)%	15 (8.6)%
Discontinuations due to adverse events	—	—	—	—
Serious adverse events	3 (5.3)%	2 (3.5)%	2 (3.3)%	7 (4.0)%
Deaths	—	—	—	—

There were no serious adverse events observed during the trial that were considered possibly or probably related to ataluren. Determination of relatedness of the serious adverse event to ataluren was made by the trial investigator, based on his or her judgment.

Open label continuation trials of ataluren for nmDMD

We are currently conducting two open label continuation trials to evaluate the safety and tolerability of ataluren in patients with nmDMD who previously participated in one of our other clinical trials. We are conducting one of these continuation trials in the United States and the other in countries outside the United States. We plan to enroll up to 122 patients in the U.S. trial and approximately 96 patients in the other trial. We initiated the U.S. trial in November 2010 and the other trial in May 2012. As of September 1, 2013, we had enrolled 107 patients in the U.S. trial and 79 patients in the other trial. Patients in these trials receive the 10, 10, 20 dose of ataluren at morning, midday and evening. Study assessments are performed at clinic visits every 12 weeks. As of September 1, 2013, available data from these continuation trials indicated no change in the safety profile for ataluren in patients with nmDMD.

Phase 2a clinical trial of ataluren for nmDMD

In October 2007, we announced the results of an open label Phase 2a clinical trial evaluating ataluren in 38 patients with nmDMD as confirmed by gene sequencing. We conducted this trial at three academic centers in the United States.

The primary objective of this trial was to obtain indications of pharmacological activity. The primary efficacy endpoint in this trial was the change from baseline measurement of dystrophin levels in a muscle in the foot known as the extensor digitorum brevis, or EDB. In this trial, the entire EDB muscle was removed from one foot prior to treatment and the entire EDB muscle was removed from the other foot after treatment. An increase from baseline in study participants' dystrophin levels in the EDB muscle biopsy indicates suppression of the nonsense mutation. We evaluated dystrophin protein levels using immuno-fluorescent staining. Secondary endpoints of the trial included serum CK levels, changes in muscle strength, time taken to perform specified functions such as walking and climbing stairs and compliance with ataluren treatment. The trial also assessed dose-response and the safety and pharmacokinetic profiles of ataluren.

Patients enrolled in this trial were at least five years of age, were diagnosed with nonsense mutation Duchenne muscular dystrophy, had increased levels of serum CK and had absent or diminished dystrophin protein on muscle biopsy.

Participants in the trial were divided into three groups, with all participants in each group receiving ataluren treatment for 28 days. The first group comprised the first six participants in the trial, who received a dosing regimen of ataluren consisting of 4 mg/kg in the morning, 4 mg/kg at midday and 8 mg/kg in the evening. The second group comprised the next 20 participants in the trial, who received the 10, 10, 20 dose of ataluren. The third group comprised the final 12 participants in the trial, who received the 20, 20, 40 dose of ataluren.

We tested the effects of ataluren on trial participants at the end of the 28-day treatment period and conducted a follow-up assessment four weeks after the last dose administration.

In this trial, ataluren induced a mean 11.0% increase in muscle dystrophin expression over the 28 days of treatment, with 23 of the 38 patients (61%) showing an increase from baseline. We observed serum CK reductions in 35 of the 38 patients (92%) at the end of treatment. With cessation of ataluren treatment, mean serum CK concentrations reverted toward baseline. Changes in myometry scores and timed function tests were small and not statistically significant with 28 days of ataluren treatment. Anecdotal reports from the parents and teachers of several boys noted evidence of greater activity, increased endurance and less fatigue during ataluren administration. Pharmacokinetic results from this trial indicated that both the 10, 10, 20 dose and the 20, 20, 40 dose regimens achieved plasma concentrations of ataluren that were predicted to have a therapeutic effect, based on preclinical data. The 4, 4, 8 dose regimen did not consistently achieve these levels, and as a result we did not include this dosing regimen in our subsequent Phase 2b clinical trial.

We observed mild treatment emergent adverse events of transient headache and gastrointestinal complaints, which appeared consistent with background symptoms commonly observed in clinical trials. There were no clearly dose dependent increases in frequency or severity of adverse events. No drug related serious adverse events were reported. Patients received approximately 99% of the planned ataluren doses, and no patient discontinued ataluren due to an adverse event.

Cystic fibrosis

Cystic fibrosis is among the most common life-threatening genetic disorders worldwide. According to the Cystic Fibrosis Foundation, cystic fibrosis occurs in approximately one of every 3,500 live births in the United States, with approximately 1,000 new cases diagnosed each year in the United States. Commercially available genetic testing can determine if a patient's cystic fibrosis is caused by a nonsense mutation. The Cystic Fibrosis Foundation estimates that approximately 83% of the active patients in their National Patient Registry have been genotyped. According to the Cystic Fibrosis Foundation, the disease affects approximately 30,000 adults and children in the United States. Based on data from the Journal of Cystic Fibrosis, we believe the disease affects between approximately 37,000 and 42,000 adults and children in the European Union. Based on information from the Cystic Fibrosis Foundation, we estimate that nonsense mutations are the cause of cystic fibrosis in approximately 10% of patients, or approximately 3,000 patients in the United States and approximately 3,700 to 4,200 patients in the European Union.

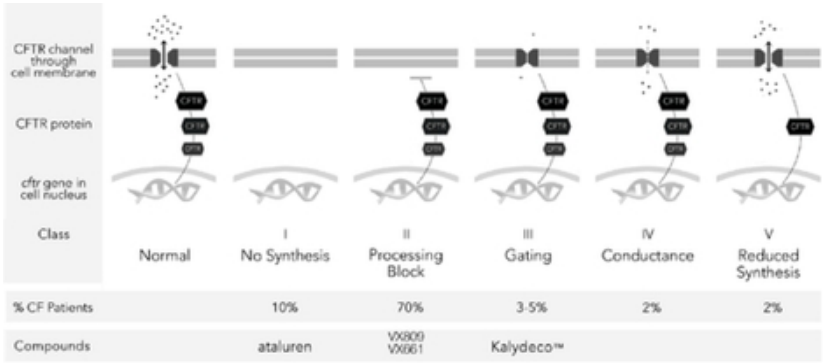
Cystic fibrosis is caused by defects in a single gene known as the cystic fibrosis transmembrane conductance regulator, or CFTR. The CFTR gene encodes the CFTR protein, which is used by the body to transport chloride across cell membranes. Genetic mutations that result in the loss of function of the CFTR protein cause the body to produce abnormally thick and sticky mucus that clogs multiple organs, including the lungs, pancreas and liver. In particular, the absence or very low levels of CFTR leads to progressive loss of lung function, potentially life-threatening lung infections, permanent pancreatic damage and malnutrition because digestive enzymes from the pancreas do not reach the

intestines to help break down and absorb food. Because patients with cystic fibrosis have malabsorption and a high calorie expenditure from breathing, their body weights are often low.

Complications from lung infections are the primary cause of death from cystic fibrosis. From as early as four months of age, patients with cystic fibrosis may begin to develop airway obstruction and inflammation. Over time, most patients develop chronic bacterial infections in the airways, resulting in repeated episodes of pneumonia. Ultimately, progressive lung dysfunction leads to respiratory failure and death. According to the Cystic Fibrosis Foundation's National Patient 2011 Registry, the median predicted age of survival for a cystic fibrosis patient in the United States is approximately 37 years. The median predicted age of survival is the age to which half of the current patients in this registry are expected to survive based on the ages of patients in the registry and the distribution of deaths in 2011. However, the average age of death for cystic fibrosis patients in 2011 was approximately 27 years.

Mutations causing cystic fibrosis are categorized in five different classes, Class I through Class V, as represented in the figure below. Class I consists of nonsense mutations and is the most severe because there is absence of CFTR production and no CFTR on the surface of the lung cells. Patients from six to 18 years of age with two Class I mutations, one on each of a pair of genes, have on average 10% lower forced expiratory volume in one second, or FEV_1 , measures than patients with two Class II mutations. FEV_1 is a measure of the volume of air that has been exhaled at the end of the first second of forced expiration. Ataluren targets Class I mutations. Class II mutations are targeted by corrector drugs, which promote the production or movement of CFTR protein from within the cell to the cell surface. In contrast, the milder mutations, Class III, IV and V, are targeted by potentiator drugs, which enhance the effect of abnormal CFTR that is already present on the cell surface. The FDA recently approved Kalydeco, developed by Vertex Pharmaceuticals, as a treatment for patients with a Class III mutation known as G551D that occurs in approximately 3% to 5% of cystic fibrosis patients. Ataluren and Kalydeco have not been tested in combination in any clinical trials.

Different types of genetic mutations cause cystic fibrosis



There is currently no marketed therapy approved to correct defective CFTR production and function in patients with nmCF. For nmCF patients, available treatments do not address the underlying cause of the disease and are designed only to alleviate the symptoms of the disease. These treatments include chest physical therapy to clear the thick mucus from the lungs, antibiotics to treat lung infections and a mucus-thinning drug designed to reduce the number of lung infections and improve lung function. In addition, the majority of cystic fibrosis patients take pancreatic enzyme supplements to assist with food absorption in digestion.

Planned Phase 3 clinical trial of ataluren for nmCF

We are planning a multicenter, randomized, double-blind, placebo controlled Phase 3 clinical trial to evaluate the efficacy and safety of ataluren in approximately 210 patients with cystic fibrosis caused

by a nonsense mutation as confirmed by gene sequencing. We expect to dose the first patient in this trial in the first half of 2014. We expect that the primary objective of this trial will be to evaluate the effect of ataluren on pulmonary function relative to placebo based on a primary efficacy endpoint of relative change in percent of predicted FEV_1 . Percent of predicted FEV_1 , or %-predicted FEV_1 , is based on a comparison to healthy individuals matched for age, height and gender. We expect that secondary efficacy endpoints in the trial will include the following:

- pulmonary exacerbation rate, based on specified signs and symptoms; and
- other pulmonary function measures as assessed by lung capacity and expiratory flow.

We expect to require that patients in this trial be at least six years of age and have %-predicted FEV_1 within a specified range, sweat chloride in excess of a specified level as evidence of the severity of the disease and documentation of a nonsense mutation in at least one copy of the CFTR gene. We expect to exclude patients from the trial if they are receiving chronic inhaled aminoglycoside antibiotics, have any change in treatment or prophylaxis for cystic fibrosis related conditions within four weeks prior to screening, have recently been treated with intravenous antibiotics or have major complications of lung disease. We expect to perform study assessments of FEV_1 at clinic visits every eight weeks and that patients will undergo 48 weeks of blinded treatment prior to the final analysis.

We plan to stratify patients based on age, screening %-predicted FEV_1 and chronic use of inhaled antibiotics. We plan to randomize patients in a 1:1 ratio to receive either placebo or ataluren at a dosing regimen of 10 mg/kg in the morning, 10 mg/kg at midday and 20 mg/kg in the evening, for a total daily dose of 40 mg/kg. At the completion of blinded treatment, we plan to make an open label extension trial available to patients who successfully complete the double-blind trial and are not in countries where ataluren is commercially available at that time.

Based on our estimates regarding initiation of the trial and patient enrollment, we expect to complete this trial and have initial, top-line data available in 2016.

Regulatory status and strategy for nmCF

EMA. We have received scientific advice from the EMA regarding the possibility of submitting an MAA for conditional approval of ataluren for the treatment of nmCF and the protocol design of a post-approval confirmatory trial. The EMA recognized that there is an unmet medical need and advised us that it would consider an MAA for conditional approval of ataluren for patients with nmCF. Following the conclusion of the re-examination process for our MAA for conditional approval of ataluren in nmDMD, we plan to evaluate the benefit of and timing for a potential MAA submission to the EMA for the conditional approval of ataluren in nmCF. Approval of our MAA will depend on the EMA's assessment of the relative risks and benefits of conditional approval and our ability to provide comprehensive clinical data from a post-approval confirmatory trial. The EMA has informed us that the benefit from ataluren that we observed in our completed Phase 3 clinical trial would have been more demonstrative if we had used absolute change in %-predicted FEV_1 rather than relative change in %-predicted FEV_1 as the primary efficacy endpoint, although the EMA also acknowledged that relative change in %-predicted FEV_1 can nonetheless be considered an acceptable primary endpoint in our planned Phase 3 clinical trial. We may not be able to demonstrate the required relative risk-benefit profile or the likelihood that we can provide the required confirmatory trial data for ataluren for this indication. There is substantial risk that the EMA will not grant us conditional approval of ataluren for the treatment of nmCF.

In particular, the EMA has advised us that we may need to address the following additional matters in our MAA.

- *The clinical relevance of the relative change in %-predicted FEV_1 that we observed in our completed Phase 3 clinical trial after taking into account all possible biases and confounders.* In this trial, the

difference between ataluren and placebo in relative change in %-predicted FEV_1 at week 48 in the ITT population was not statistically significant. We believe that use of the inhaled antibiotic tobramycin confounded the results of the trial by interfering with ataluren's mechanism of action. For a subgroup of patients not receiving chronic inhaled aminoglycoside antibiotics, there was a substantial difference in mean relative changes from baseline in %-predicted FEV_1 at the end of the trial favoring ataluren in comparison with placebo. In addition, we believe that even a modest slowing of the decrease in FEV_1 in nmCF patients over time may be clinically meaningful.

- *Consideration of alternatives to explain the lack of statistical significance in relative change in %-predicted FEV_1 in our Phase 3 clinical trial other than the plausible explanation that the inhaled antibiotic tobramycin interfered with ataluren's mechanism of action.* We believe that other possible explanations of the tobramycin effect can be discounted because the patients in our trial treated with tobramycin are similar clinically based on signs and symptoms of the disease to patients not treated with tobramycin, so that differences between the patient subgroups would not be expected to explain a difference in outcomes.

- *Lack of clear support of treatment effect from secondary or tertiary endpoints in our completed Phase 3 clinical trial.* The results for the secondary endpoint of pulmonary exacerbation were consistent with the primary endpoint in the ITT population and in the subgroups with and without tobramycin. The tertiary endpoints did not clearly support the primary endpoint. However, some of these endpoints were novel, and although tertiary endpoints included pharmacodynamic measurements, there is no established surrogate biomarker in cystic fibrosis.

- *The imbalance in the baseline %-predicted FEV_1 in favor of ataluren.* We believe that the numeric difference between baseline %-predicted FEV_1 for ataluren and placebo (63% for ataluren and 59% for placebo) is small and would not be expected to affect the trial results. Furthermore, our review of scientific literature indicates that a higher baseline FEV_1 is associated with greater decline in FEV_1 than a lower baseline FEV_1 , and therefore the imbalance, if it caused any effect, would favor placebo over ataluren.

- *The evolution of the relative change in %-predicted FEV_1 over 48 weeks in the placebo group being worse than expected.* The relative change in %-predicted FEV_1 over 48 weeks in the placebo group in our Phase 3 clinical trial was -5.5%. Although this decrease is larger than expected in 48 weeks in general for patients with cystic fibrosis, we believe that the greater severity of the disease for patients with nmCF as compared to patients with cystic fibrosis caused by other mutations explains the unexpected result.

- *The lack of analysis of patients based on body weight and height.* We plan to provide to the EMA an analysis based on body weight that has been previously performed. We believe that height is not a common outcome measure in clinical trials for cystic fibrosis, although we could perform an analysis if requested by the EMA.

- *The statistical analysis that we employed.* To address concerns about the statistical methodology that we used, we plan to provide to the EMA the results of sensitivity analyses of the primary endpoint.

FDA. We met with the FDA in July 2012 to discuss the results of our completed Phase 3 clinical trial of ataluren for the treatment of nmCF. The FDA indicated that in its view the data from our completed Phase 3 clinical trial and other data from our development program in cystic fibrosis do not by themselves support an NDA submission. Consequently, the FDA informed us that additional clinical data would be required to establish the evidence required to support eventual filing of an NDA for the use of ataluren to treat nmCF. We had additional interactions with the FDA in 2013 regarding the clinical development design which would have the potential to support an NDA, but we did not achieve

a consensus between the EMA and FDA views. While we have incorporated feedback from the FDA into our proposed trial design, we believe that certain key recommendations from the FDA are not appropriate. Two of the key recommendations that we are in disagreement with are the designation of FEV1, CF pulmonary exacerbations and body mass index as three co-primary endpoints for the trial and a suggested three-year trial duration. We plan to make FEV1 the primary endpoint with CF pulmonary exacerbations and body mass index key secondary endpoints, which is consistent with other clinical trials currently ongoing in cystic fibrosis and FDA's earlier recommendation. Additionally, we believe that extending the study duration to three years would result in a number of complications that would ultimately limit the robustness of the data and conclusions that could be drawn from the results. Based on these interactions, we nonetheless intend to proceed with our Phase 3 clinical trial of ataluren in nmCF in the first half of 2014 consistent with feedback from the EMA on our trial design.

Completed Phase 3 clinical trial of ataluren for nmCF

In June 2012, we announced the results of a multicenter, international, randomized, double-blind, placebo controlled Phase 3 clinical trial assessing the effects of ataluren in 238 patients with cystic fibrosis caused by a nonsense mutation as confirmed by gene sequencing. The primary objective of this trial was to evaluate the effect of ataluren on pulmonary function relative to placebo. The primary efficacy endpoint was relative change in %-predicted FEV_1. The trial assessed pulmonary exacerbation rate as a secondary efficacy endpoint.

Patients enrolled in this trial were at least six years of age, weighed at least 16 kilograms and had a %-predicted FEV_1 between 40% and 90%, sweat chloride in excess of a specified level, a minimum level of resting oxygen saturation in the blood and documentation of a nonsense mutation in at least one copy of the CFTR gene. We excluded patients from the trial if they had any change in treatment or prophylaxis for cystic fibrosis related conditions within four weeks prior to start of study treatment, had evidence of pulmonary exacerbation or acute upper or lower respiratory tract infection, were treated with intravenous antibiotics or had major complications of lung disease.

We stratified patients in this trial based on age, baseline %-predicted FEV_1 and chronic use of inhaled antibiotics. Patients were randomized in a 1:1 ratio to receive placebo or ataluren at a dosing regimen of 10 mg/kg in the morning, 10 mg/kg at midday and 20 mg/kg in the evening, for a total daily dose of 40 mg/kg. The trial protocol specified a clinic visit every eight weeks to assess FEV_1. The treatment duration was 48 weeks.

We designed the trial to detect a mean relative change in %-predicted FEV_1 from baseline to end of treatment at week 48 that was at least 6% greater in the ataluren arm than in the placebo arm. Of the 238 total patients, 120 patients received ataluren and 118 patients received placebo, with 34 patients withdrawing prematurely, including 20 patients on ataluren and 14 patients on placebo. Of these 34 patients, nine withdrew because of adverse events, one was lost to follow-up for unexplained reasons, 18 withdrew consent, one was withdrawn based on an investigator decision, two were withdrawn because of protocol noncompliance and three withdrew for other unspecified reasons. One patient completed 48 weeks of blinded therapy but did not have evaluable FEV_1 data at week 48. This resulted in 203 patients completing the 48-week treatment period with FEV_1 data available at week 48. As specified in the trial protocol, the ITT population included all randomized patients who had FEV_1 data available at baseline and at least one post-baseline visit, resulting in 116 patients on ataluren and 116 patients on placebo being included in the ITT population.

The percent of the initial total value that was changed is referred to as relative change. The change in percentage that is representative of the difference alone is referred to as absolute change. For example, when 50% changes to 55%, the result is a 10% relative change and a 5% absolute change. The results from this trial are shown in the table below. The table shows information about

relative change, which was the primary analysis, and absolute change in %-predicted FEV_1 from baseline to week 48.

Change in %-predicted FEV_1 from baseline to week 48 (ITT population)

	Placebo N=116		Ataluren 10, 10, 20 dose N=116	
Relative change in %-predicted FEV_1 at week 48				
Mean (standard deviation)	-5.5%	(12.56)	-2.5%	(13.25)
Mean difference from placebo			3.0%	
p-value			0.124	
Relative change in %-predicted FEV_1 averaged over 48 weeks				
Mean	-4.3%		-1.8%	
Mean difference from placebo			2.5%	
p-value			0.0478	
Absolute change in %-predicted FEV_1 at week 48				
Mean (standard deviation)	-3.1%	(7.39)	-1.3%	(8.50)
Mean difference from placebo			1.8%	
p-value			0.136	

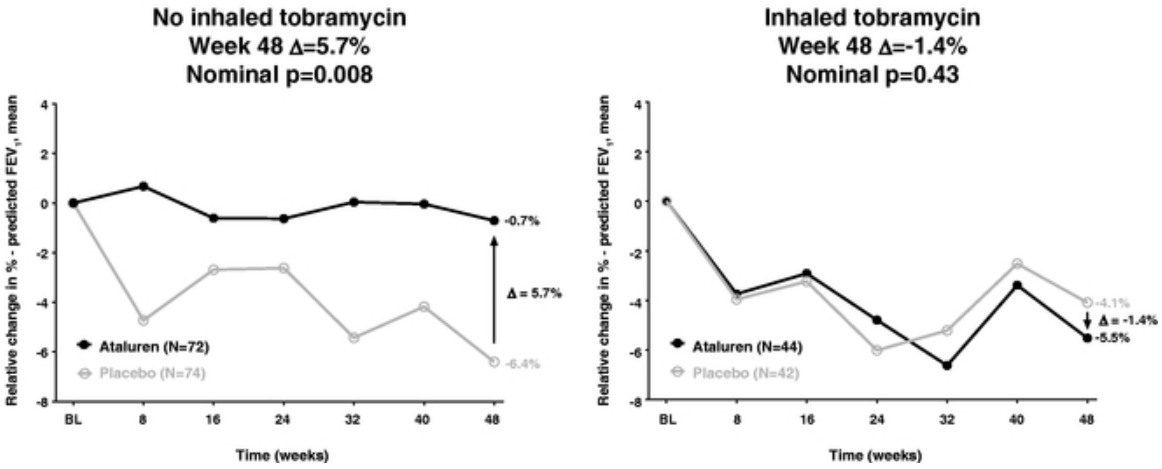
The primary analysis of relative change in %-predicted FEV_1 in this trial showed a 3.0% difference (2.5% decrease on ataluren, 5.5% decrease on placebo) at week 48 favoring ataluren (p=0.124), which was not statistically significant. An analysis of relative change in %-predicted FEV_1 based on the average treatment effect across all post-baseline visits showed a statistically significant difference of 2.5% favoring ataluren compared to placebo (1.8% decrease on ataluren, 4.3% decrease on placebo; p=0.0478). The analysis of treatment effect across all visits was part of the pre-specified statistical model for this trial and has served as the primary analysis of FEV_1 data in other cystic fibrosis therapeutic trials conducted by other companies. The analysis of absolute change in %-predicted FEV_1 at week 48 showed a 1.8% difference (1.3% decrease on ataluren, 3.1% decrease on placebo; p=0.136).

Subgroup analysis of patients not receiving inhaled antibiotics. As described above, we pre-specified three stratification factors in this trial: age, baseline FEV_1 and chronic use of inhaled antibiotics. In this trial, there was a statistically significant interaction (nominal p=0.0072) between treatment and chronic inhaled antibiotic use. As discussed in more detail below, we believe that the inhaled antibiotic tobramycin interfered with ataluren's mechanism of action. The interactions between treatment and age and between treatment and baseline %-predicted FEV_1 were not significant.

For the subgroup of patients not receiving chronic inhaled antibiotics, the difference in mean relative changes from baseline in %-predicted FEV_1 at week 48 was 6.7% favoring ataluren (nominal p=0.013). The average treatment effect across all post-baseline visits was 5.6% (nominal p=0.0006). For absolute change in %-predicted FEV_1 , the average treatment effect across all post-baseline visits was 2.4% (nominal p=0.037). In contrast, patients that received chronic inhaled antibiotics and ataluren did not exhibit a difference compared to patients that received chronic inhaled antibiotics and placebo.

Approximately 37% of patients in the trial were receiving the chronic inhaled antibiotic tobramycin, and approximately 45% of patients were receiving no chronic inhaled antibiotic. Other chronic inhaled antibiotics that patients received were colistin or aztreonam. We performed analyses comparing patients not receiving chronic inhaled tobramycin to patients receiving chronic inhaled tobramycin. The results for patients not receiving chronic inhaled tobramycin and patients receiving chronic inhaled tobramycin are depicted in the following graphs.

Mean relative change in %-predicted FEV_1 at week 48 by baseline chronic inhaled tobramycin use



In patients not receiving chronic inhaled tobramycin, the difference in mean relative change from baseline in %-predicted FEV_1 at week 48 was 5.7% favoring ataluren (nominal p=0.008), consistent with the targeted treatment effect size. Patients receiving chronic inhaled tobramycin did not show a benefit for ataluren compared to placebo in %-predicted FEV_1 . In contrast, the treatment effect was similar in patients receiving colistin or aztreonam compared to patients not receiving colistin or aztreonam.

Both tobramycin and ataluren act through modulation of the ribosomal machinery. We believe that the binding of tobramycin to the ribosome may interfere with ataluren's mechanism of action. We explored this hypothesis in a functional cell-based translation assay. In this experiment, ataluren-induced read-through of premature stop codons was diminished when the cells were exposed to ataluren together with tobramycin or gentamicin, but not when ataluren was administered together with colistin or aztreonam, both of which are non-aminoglycosides.

Pulmonary exacerbation rate. The secondary endpoint in this trial was pulmonary exacerbation rate, which is a measure of frequency of lung infections related to cystic fibrosis. FEV_1 and pulmonary exacerbation rate are the two most clinically important outcome measures in cystic fibrosis trials. In the ITT population, we observed a 23% lower pulmonary exacerbation rate in patients receiving the 10, 10, 20 dose of ataluren than placebo (p=0.099). This result was not statistically significant. However, we also saw the tobramycin subgroup effect in this endpoint. Patients not receiving chronic inhaled tobramycin had a 41% lower pulmonary exacerbation rate on ataluren than placebo (nominal p=0.005). Patients receiving chronic inhaled torbramycin did not show a benefit in pulmonary exacerbation rate on ataluren as compared to placebo.

Tertiary Endpoints. In this trial, we assessed CFTR function by nasal transepithelial difference, or TEPD, and sweat chloride concentration as tertiary endpoints. TEPD is assessed by means of a standardized, though complex, minimally invasive procedure. In the procedure, a small plastic catheter is used to assess electrical differences across the outer cell membrane of nasal mucosa cells in the nostril. Nasal TEPD is physiologically meaningful because nasal mucosa closely reflects CFTR activity in the lung epithelium. Because of the role of the CFTR protein in transporting chloride across cell membranes and because of the absence of this protein in cystic fibrosis patients, these patients have an abnormal TEPD chloride conductance. Sweat chloride concentration is a commonly used test to diagnose cystic fibrosis and is a measurement of CFTR activity in the sweat gland.

A number of clinical trials for CFTR restoration therapies have used sweat chloride concentration and nasal TEPD as pharmacodynamic endpoints. However, these two endpoints can exhibit varying

results, likely because of differences in CFTR regulation and function in the sweat glands as compared to the nasal or lung mucosa, or variation in tissue penetration of different drugs.

Nasal TEPD results were positive in our prior Phase 2 clinical trials discussed below, but sweat chloride testing was not positive in either Phase 2 clinical trial or in our Phase 3 clinical trial. In contrast with our Phase 2 clinical trials, in which we assessed TEPD at a small number of experienced sites, in the Phase 3 clinical trial, TEPD assessments were performed at all centers. This trial was the first time most centers had performed TEPD assessments. In this trial, TEPD results showed high variability and an unexpectedly high response rate on placebo.

The other tertiary endpoints in this trial were hourly cough rate, respiratory domain score from a questionnaire, inflammatory markers and lung computed tomography. Differences between ataluren and placebo for each of these endpoints were small and not statistically significant.

Safety and tolerability. Ataluren was generally well tolerated in this clinical trial, and there were generally similar adverse event profiles in patients treated with ataluren and patients treated with placebo. Most serious adverse events were cystic fibrosis pulmonary exacerbations unrelated to study drug treatment. Most treatment-emergent adverse events were mild or moderate in severity. Investigators' attributions of severity and drug-relatedness were generally similar across the placebo and ataluren arms. The most common adverse events during this trial were cystic fibrosis pulmonary exacerbation (78.2% overall), cough (25.6%) and viral upper respiratory tract infection (21.0%). These events were slightly more frequent in the placebo arm and are typical of cystic fibrosis. Adverse events with at least a 10% incidence in any treatment arm that were seen with higher frequency in the ataluren arm were headache (11.9% for placebo and 16.7% for ataluren), abdominal pain (12.7% for placebo and 15.0% for ataluren), sinusitis (11.9% for placebo and 12.5% for ataluren) and vomiting (8.5% for placebo and 11.7% for ataluren). Eleven patients prematurely discontinued treatment because of adverse events, including eight in the ataluren arm and three in the placebo arm.

There were 19 patients with at least one treatment-emergent renal adverse event, including 15 patients receiving ataluren and 4 patients receiving placebo. In the ataluren arm, five adverse events that involved the renal system led to discontinuation. As compared to the placebo group, the ataluren treatment arm also had a higher incidence of adverse events of creatinine elevations, which can be an indication of impaired kidney function. These adverse events of creatinine elevations were generally mild and transient. In the ataluren treatment arm, clinically meaningful creatinine elevations of grade 3 or grade 4 were reported in conjunction with cystic fibrosis pulmonary exacerbations. These creatinine elevations were associated with concomitant treatment with antibiotics associated with impaired kidney functions, such as aminoglycosides or vancomycin. This led to the subsequent prohibition of concomitant use of ataluren and these potentially nephrotoxic antibiotics, which was successful in addressing this issue. The incidence of new-onset kidney stones was similar in both arms, with five patients in the ataluren arm and four patients in the placebo arm.

An overview of adverse events in this trial is shown in the table below.

Overview of treatment-emergent adverse events in Phase 3 clinical trial (as-treated population)

Parameter	Treatment arm: Placebo N=118	Treatment arm: Ataluren N=120	All patients N=238
Patients with o 1 adverse event	115 (97.5)%	118 (98.3)%	233 (97.9)%
Adverse events by severity			
Grade 1 (mild)	20 (16.9)%	18 (15.0)%	38 (16.0)%
Grade 2 (moderate)	65 (55.1)%	81 (67.5)%	146 (61.3)%
Grade 3 (severe)	30 (25.4)%	19 (15.8)%	49 (20.6)%
Grade 4 (life-threatening)	—	—	—
Adverse events by relatedness			
Unrelated	42 (35.6)%	30 (25.0)%	72 (30.3)%
Unlikely	31 (26.3)%	39 (32.5)%	70 (29.4)%
Possible	35 (29.7)%	34 (28.3)%	69 (29.0)%
Probable	7 (5.9)%	15 (12.5)%	22 (9.2)%
Discontinuations due to adverse events	3 (2.5)%	8 (6.7)%	11 (4.6)%
Serious adverse events	48 (40.7)%	45 (37.5)%	93 (39.1)%
Deaths	—	—	—

The serious adverse events observed during the trial that were considered possibly related to ataluren were biliary colic, elevated creatinine, pancreatitis, renal failure, urinary tract infection and urinary retention. Determination of relatedness of the serious adverse event to ataluren was made by the trial investigator, based on his or her judgment.

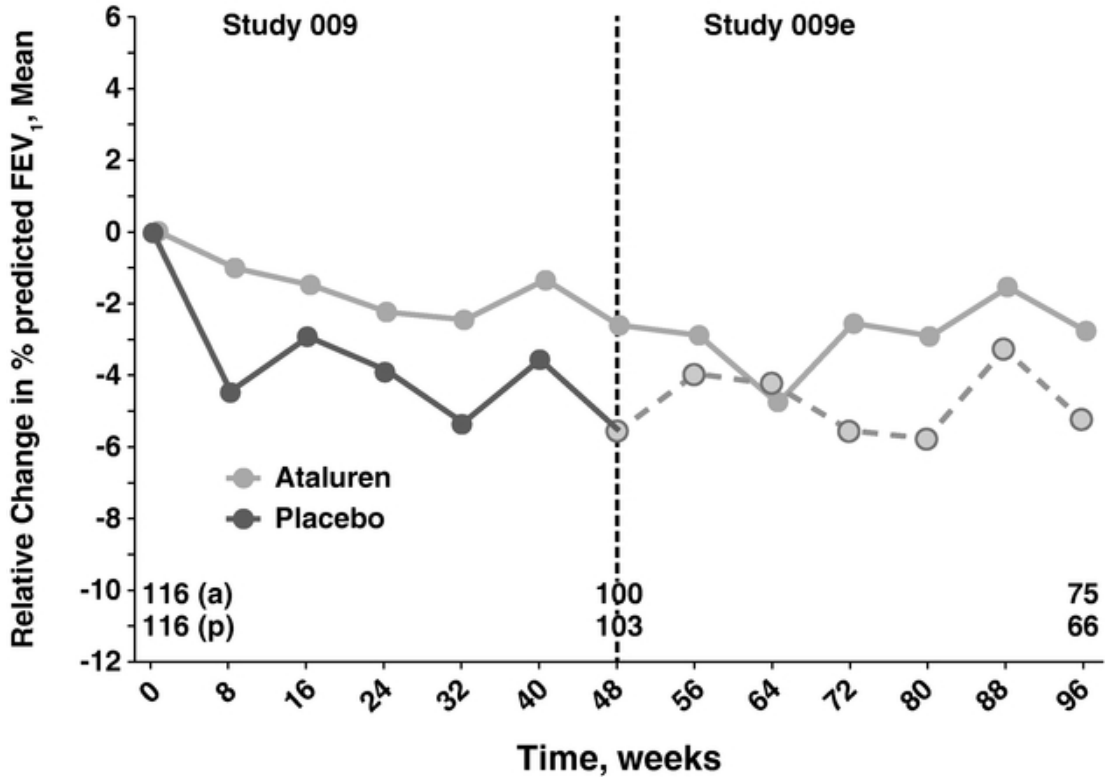
Open label extension trial of ataluren for treatment of nmCF

We recently completed an open label, extension trial that is providing additional safety information for the long term administration of ataluren in patients with cystic fibrosis who successfully completed 48 weeks of treatment in our completed Phase 3 clinical trial. In addition, this trial was designed to provide supportive long-term efficacy information to better understand the long-term effects of ataluren on pulmonary function and pulmonary exacerbations. This trial enrolled 191 of the patients who completed the double-blind Phase 3 clinical trial described above. Patients in this trial received 10 mg/kg in the morning, 10 mg/kg at midday and 20 mg/kg in the evening of ataluren for a 96 week treatment period. Study assessments were performed at clinic visits every eight weeks to sixteen weeks. Currently available data on FEV_1 in patients who have completed a total of 96 weeks of treatment are shown in the figure below. In patients who have received ataluren since the beginning of the Phase 2b clinical trial, FEV_1 has been generally maintained over the course of 96 weeks. In patients who transitioned from placebo to ataluren at the beginning of the open label, extension trial, FEV_1 has remained stable since their transition to ataluren. We expect complete study results to be available in the first quarter of 2014. We are planning a separate open label, extension trial to obtain additional safety and efficacy information in patients who completed the double-blind Phase 3 clinical trial and are not receiving chronic inhaled aminoglycoside antibiotics. We plan to begin dosing patients in this trial in the first half of 2014.

The most common adverse events during the recently completed open label, extension trial were cystic fibrosis pulmonary exacerbation (79.1%), cough (27.2%) and viral upper respiratory tract infection (25.7%). These are the same common adverse events, and are similar in frequency, as those seen in our completed Phase 3 clinical trial. The serious adverse events observed during this trial that were considered possibly related to ataluren were abdominal pain, back pain, difficulty urinating, hydronephrosis, interstitial nephritis, kidney stones, pancreatitis and renal failure. Determination of

relatedness of the serious adverse event to ataluren was made by the trial investigator, based on his or her judgment.

Change in %-predicted FEV_1 through week 96



Phase 2 clinical trials of ataluren for treatment of nmCF

In 2006, we completed two open label Phase 2 clinical trials of ataluren for the treatment of nmCF in adult patients. In these two trials, we enrolled a combined total of 47 patients age 18 years or older who were diagnosed with cystic fibrosis resulting from a nonsense mutation in the CFTR gene. We conducted the first trial at one site in Israel and the second trial at four sites in the United States. In 2008, we completed a third open label Phase 2 clinical trial of ataluren for the treatment of nmCF in pediatric and adolescent patients. We enrolled 30 patients between 6 and 18 years of age who were diagnosed with cystic fibrosis resulting from a nonsense mutation in the CFTR gene. We conducted this third trial at one site in France and two sites in Belgium. Each of these three trials had a treatment duration of 28 days. We also conducted an open label, extension trial with a treatment duration of three months for the patients who completed the 28-day trial in Israel. The goal of each of these trials was to obtain indications of pharmacological activity and to assess dose-response, safety and pharmacokinetics.

The trial designs for the three Phase 2 clinical trials with 28-day treatment durations were comparable and included two treatment cycles. Each cycle consisted of a two-week period of continuous ataluren treatment, and then a two-week follow-up period without ataluren treatment. During the two weeks of ataluren treatment one of the cycles, participants received ataluren at doses of 4 mg/kg in the morning, 4 mg/kg at midday and 8 mg/kg in the evening, for a total daily dose of 16 mg/kg. During the two weeks of ataluren treatment in the other cycle, the same participants received ataluren at doses of 10 mg/kg in the morning, 10 mg/kg at midday and 20 mg/kg in the evening, for a total daily dose of

40 mg/kg. We evaluated trial participants at the beginning and end of each two-week treatment period and follow-up period in each cycle. In the trial with a treatment duration of three months, patients received either ataluren at doses of 4 mg/kg in the morning, 4 mg/kg at midday and 8 mg/kg in the evening, for a total daily dose of 16 mg/kg, or ataluren at doses of 10 mg/kg in the morning, 10 mg/kg at midday and 20 mg/kg in the evening, for a total daily dose of 40 mg/kg.

The objective in each of these trials was to determine the change in CFTR-mediated chloride conductance in respiratory cells as measured between the beginning and end of treatment for each study participant. To make this determination, we measured the patient's TEPD. TEPD values are expressed in millivolts, or mV. A chloride conductance equal to or more electrically negative than -5.0 mV is generally considered to be in the normal range.

In the trials conducted in adults in Israel and in children and adolescents in France and Belgium, there were statistically significant improvements at the end of the ataluren treatment period in mean total chloride conductance and in the percentage of patients with a total chloride conductance response of at least a -5.0 mV improvement. There were also improvements in the percentage of patients with a chloride conductance in the normal range at the end of treatment. These results indicated the presence of pharmacological activity. These improvements were generally followed in the adult trials by reversions toward baseline with cessation of treatment during the follow-up period. In the trial conducted in the United States, we did not observe improvements in mean total chloride conductance.

Ataluren was generally well tolerated in these trials. Only one serious adverse event was considered possibly related to ataluren. Adverse events that were potentially drug-related were generally mild in severity. These adverse events included pain during urination in several patients. This issue resolved successfully with increased hydration. There were no clinically meaningful safety concerns identified in patients' physical examinations, vital sign measurements or electrocardiograms.

Phase 1 clinical trials of ataluren

We have completed two Phase 1 clinical trials of ataluren involving a total of 62 healthy volunteers. The first Phase 1 clinical trial was a single-dose, safety and pharmacokinetic study with a placebo component, conducted in a total of 31 healthy volunteers between 18 and 30 years of age. In the first stage of the trial, subjects were enrolled at escalating dose levels ranging from 3 to 200 mg/kg. In this study, we determined that 100 mg/kg is the maximum tolerated dose based on the observation of increased frequency of headaches, dizziness and mild gastrointestinal events, such as nausea, vomiting and diarrhea, at the 150 mg/kg and 200 mg/kg doses. The drug was palatable, with no obvious odor or taste. In the second stage of this trial, we assessed the effect of food on the safety and pharmacokinetic profiles of ataluren at a dose of 50 mg/kg. This study provided us with pharmacokinetic data that indicated minimal alterations in the pharmacokinetic profile when ataluren was taken after a meal and supported giving ataluren with food to maintain plasma concentrations. The study also provided pharmacokinetic information allowing us to predict ataluren blood exposure levels in future studies.

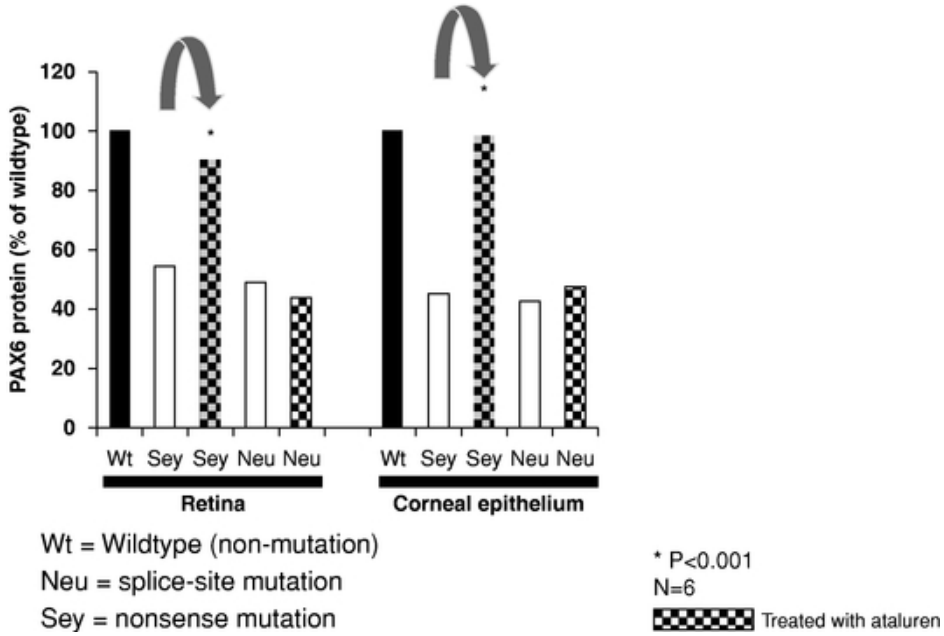
The second Phase 1 clinical trial was a multiple-dose, open label safety and pharmacokinetic study conducted in a total of 31 healthy volunteers between 18 and 30 years of age. In the first stage of the trial, subjects were enrolled at escalating twice-daily doses ranging from 10 to 50 mg/kg per dose taken with food for seven consecutive days. In the second stage of this trial, subjects were enrolled at a twice-daily dose of 50 mg/kg per dose for 14 days. In this study, there were no clinically significant adverse events reported at any dose tested, although we observed modest elevations of liver enzymes in some subjects. These elevated enzyme levels did not require cessation of ataluren administration, and enzyme levels typically normalized after completion of the treatment phase. As in the single-dose study, we were able to achieve and maintain plasma concentrations of ataluren that were predicted to have a therapeutic effect based on preclinical data. In the multiple-dose trial, as in the single-dose study, we sought to determine whether ataluren promoted improper read-through of normal stop codons. We

assessed this by observing whether the trial participants produced improperly large forms of specified proteins. We did not observe any such improper protein formation.

Ataluren preclinical studies

In addition to our preclinical work on ataluren, in the last six years multiple independent investigators have conducted preclinical studies in which ataluren enabled readthrough of the premature stop codons from a large set of nonsense mutations across a diverse group of experimental models exhibiting various genetic disorders. The studies evaluated ataluren's ability to read through premature stop codons in mRNA in cell-free systems, transfected cell lines, mouse models and patient cells. For example, investigators studying aniridia, a genetic disorder due to mutations in the PAX6 gene associated with loss of eyesight and other symptoms in which it is estimated that half of all cases are due to a nonsense mutation, have published a paper finding that ataluren exhibited readthrough activity in a nonsense mutation aniridia mouse model. In this research, ataluren treatment in mice resulted in a significant increase in the relevant protein. The investigators found that ataluren not only inhibited disease progression, but also stably reversed corneal, lens and retinal malformation defects and restored electrical and behavioral responses of the retina. Ataluren treatment resulted in a significant increase in the PAX6 protein in an nonsense mutation PAX6 gene but not in a PAX6 gene harboring a splice-site mutation, as shown in the graph below:

Ataluren increases PAX6 in PAX6 Sey mice



In another example, investigators studying mucopolysaccharidosis type I (MPS I), a progressive multisystem disorder resulting from a mutation in the IDUA gene in which the majority of cases are due to a nonsense mutation, studied ataluren in a mouse model. In this model of the Hurler's form of the disorder, administration of ataluren for two weeks resulted in near normal levels of a protein that is a biomarker of the disorder in the brain, spleen, liver and heart tissues.

Our spinal muscular atrophy collaboration

Spinal muscular atrophy is a genetic neuromuscular disease characterized by muscle wasting and weakness. The disease generally manifests early in life. Spinal muscular atrophy is caused by defects in

the Survival Motor Neuron 1, or SMN1, gene that encodes the survival motor neuron, or SMN, protein. The SMN protein is critical to the health and survival of the nerve cells in the spinal cord responsible for muscle contraction. A second gene, SMN2, is very similar to SMN1, except that SMN2 produces SMN protein that is less effective because, unlike SMN1, SMN2 does not include a particular nucleotide sequence known as exon 7. According to the SMA Foundation, spinal muscular atrophy is the leading genetic cause of death in infants and toddlers. The SMA Foundation estimates that spinal muscular atrophy affects approximately 10,000 to 25,000 children and adults in the United States and that one in 10,000 children are born with the disease. There is currently no marketed therapy approved to treat the underlying cause of spinal muscular atrophy. Currently available treatments for spinal muscular atrophy are only palliative.

Using our alternative splicing technology, we have identified small molecule splicing modifiers that at very low concentrations in non-clinical studies involving cells from patients with spinal muscular atrophy increased both the inclusion of exon 7 in the SMN2 mRNA and the levels of SMN protein produced by SMN2. Importantly, in studies of mice with only the SMN2 gene, these compounds are orally bioavailable, penetrate the blood-brain barrier and increase full-length SMN mRNA and protein in various tissues. In these same mouse studies, treatment with these compounds resulted in increased survival, restoration of body weight, prevention of motor neuron loss and improved motor function.

We have entered into a collaboration agreement with Roche and the SMA Foundation for the development and commercialization of these compounds. Roche is responsible for pursuing clinical development of compounds from the research program under the collaboration and then commercializing any resulting products. In November 2011, we signed a licensing agreement with Roche which included a $30 million upfront payment, the potential for up to $460 million in milestone payments and royalties on net sales. A lead development compound was selected to move into IND-enabling studies in August 2013, triggering a milestone payment to us from Roche of $10 million. In January 2014, a Phase 1 clinical program was initiated, triggering a milestone payment to us from Roche of $7.5 million. We also previously received $13.3 million in sponsored research funding for this program from the Spinal Muscular Atrophy Foundation.

Scientific Background of Post-Transcriptional Control Processes

Post-transcriptional control processes are the events that occur in cells following the transcription of DNA to make mRNA. These processes regulate how long an mRNA molecule lasts in the cell and how efficiently the mRNA is used to produce its protein.

The majority of human protein-encoding genes are not contiguous but have an interrupted structure consisting of nucleotides that comprise the mRNA, called exons. The genetic information, encoded by exons, is interrupted by stretches of nucleotides called introns that are removed immediately after the gene is transcribed from DNA to the precursor messenger RNA, or pre-mRNA. The process of intron removal is called splicing.

The mRNA contains multiple regions that have specific functions. Although the protein coding region of mRNA contains the instructions to manufacture the protein, portions of mRNA that do not directly code for proteins, known as untranslated regions, or UTRs, are unique to specific mRNAs and are directly involved in the post-transcriptional control of protein production. Interactions of factors in the cell with the UTRs on the mRNA can modulate the translational efficiency of mRNA and how mRNA is degraded and eliminated from the cell.

Our Approach

Our approach to drug discovery and development is to systematically target post-transcriptional control processes that can be modulated by small-molecule therapeutics. We believe that focusing on post-transcriptional control processes will enable us both to address known drug targets through new mechanisms of action and to pursue a broad range of targets that have previously not been amenable

to drug discovery. We believe that a large number of promising post-transcriptional control drug targets remain unexploited, providing a significant opportunity for our integrated and systematic approach to drug discovery. This technology also has broad applicability to address intractable drug targets in a wide variety of diseases for which there is an unmet medical need, including genetic disorders, cancer, and musculoskeletal disorders, as well as inflammation, metabolic disorders, cardiovascular conditions and neurological disorders.

Our RNA-Focused Small Molecule Technology Platform

We have developed and assembled an integrated set of proprietary technologies focused on our understanding of RNA biology for the discovery of small molecules that target post-transcriptional control processes. Our technologies allow us to screen our compound library against targets in many different therapeutic areas in an expeditious and cost-effective manner. Our efforts span from target identification and characterization to the identification of selective lead molecules. From these lead molecules, our research team undertakes a chemical optimization program designed to select an appropriate development candidate. We refer to our technologies as GEMS, alternative splicing and nonsense suppression.

GEMS

We use our GEMS technology to identify molecules that modulate gene expression by targeting the post-transcriptional control processes that act through the UTRs of mRNA molecules. The UTRs of mRNA can have important roles in regulating protein production because they contain the instructions for determining the protein production efficiency and how long a given mRNA molecule will live within the cell.

We identify target proteins of potential biological and medical relevance to human disease and assess their regulation through UTRs and clinical feasibility. For targets that we select, we precisely identify the UTRs of the target gene.

We use proprietary assays to test our library of approximately 240,000 compounds to identify those that are likely to enhance or inhibit expression of the target gene by modulating the post-transcriptional control processes that act through that target's UTRs.

Alternative splicing

We use our alternative splicing technology to identify molecules that modulate mRNA splicing. Pre-mRNA splicing is a multi-step biochemical reaction. Approximately 94% of all human genes undergo splicing. In addition, through alternative splicing, one gene can often generate several mRNA products by including or excluding exons that can result in the mRNA being regulated differently or a different protein being produced. Altered regulation of alternative splicing is the direct cause of many human diseases, including many forms of cancer, Riley-Day syndrome (familial dysautonomia), myotonic dystrophy and spinal muscular atrophy.

We have developed a powerful high-throughput drug discovery technology that enables us to identify small molecule modifiers of pre-mRNA splicing. The technology relies on a sensitive quantification of mRNA directly in human cells or tissue samples. Using this technology, we have successfully identified orally bioavailable small molecules that correct splicing of the Survival Motor Neuron 2, or SMN2, gene, which is implicated in the genetic disorder spinal muscular atrophy. Based on this experience, we believe that other small molecule drug candidates can be rapidly identified that correct alternative splicing of genes, promote inclusion of specific exons into mRNA or force skipping of undesired exons from the mature mRNA. We believe that this technology is potentially widely applicable to a large number of target genes in all therapeutic areas.

Nonsense suppression

We use our nonsense suppression technology to identify molecules that promote or enhance nonsense suppression. The presence of a premature stop codon results in translation termination before a full-length protein can be produced. Our nonsense suppression technologies identify small molecules that increase nonsense suppression at the premature stop codon to produce a full-length protein. In addition to increasing read-through, small molecules that stabilize nonsense-containing mRNAs can enhance the effect of a compound that acts through the nonsense suppression mechanism.

Nonsense suppression also can be designed to identify molecules that can enhance the nonsense suppression effect of ataluren and other nonsense suppression agents to prevent the decay of nonsense-containing mRNAs, which we refer to as nonsense mediated decay. We have developed a high throughput screen to identify molecules that increase the level of nonsense-containing mRNAs. We can evaluate the effect of these molecules alone and in combination with ataluren in cell-based models of disease, identify lead compounds and initiate a chemical optimization program. We are currently in the process of evaluating compounds in preparation for an optimization program.

Preclinical Development Programs

Oncology—BMI1 program

We have selected a development candidate, PTC596, for the treatment of chemotherapy resistant cancers through the targeting of cancer stem cells. We are currently conducting IND-enabling preclinical studies with PTC596. We have received grant funding of $5.4 million for our BMI1 program from Wellcome Trust.

Cancer stem cells have been identified in numerous tumor types as a subpopulation of tumor cells that have the ability to initiate a tumor, produce other cancer cell types, move freely and proliferate throughout the body without attaching to other cells or surfaces and resist chemotherapy and radiotherapy. Many researchers believe that the resistance of cancer stem cells to chemotherapy and radiotherapy is a key factor in the failure of current cancer treatments. The BMI1 protein, which is overexpressed in many tumor subtypes, is a critical component of the polycomb repressive complex 1, or PRC1. PRC1 modulates gene expression that is important for cancer stem cell survival, maintenance, stabilization and differentiation. PRC1 is epigenetic, meaning that it is able to modify DNA directly to modulate gene expression without altering the nucleotide sequence in the genetic code. As a critical component of PRC1, the BMI1 protein regulates the self-renewal of adult blood and central nervous system stem cells that regulate cell growth.

PTC596 is an orally active small molecule that targets tumor stem cell populations by reducing the function, activity and amount of BMI1. PTC596 acts by altering and destroying the BMI1 protein through a process called phosphorylation. PTC596 has potently inhibited BMI1 function in multiple tumor cell lines. In *in vitro* tests, PTC596 has preferentially targeted chemotherapy resistant cancer stem cells. Specifically, PTC596 preferentially depleted cancer stem cells in assays with tumor cell lines from fibrosarcoma, prostate and colon cancers. Conversely, the cytotoxic chemotherapies carboplatin, temozolomide, methotrexate and indibulin enriched the population of cancer stem cells in this assay.

In animal cancer models using human tumors, weekly oral dosing of PTC596 provided tumor control, including reduction of tumor size. PTC596 and the commonly used chemotherapy paclitaxel were both effective at controlling tumor growth in these animal models. However, PTC596, but not paclitaxel, decreased BMI1 levels, indicating a reduction in cancer stem cells. Consistent with this reduction in BMI1 levels, after transplanting tumor cells from one animal to another, the resulting tumors treated with PTC596 had lower levels of cancer stem cells than either untreated tumors or tumors treated with paclitaxel. PTC596 has been well tolerated at effective doses in animals. Preliminary data from these animal models suggest that PTC596 may preferentially target cancer stem cells without targeting normal stem cells.

Antibacterial program

We have identified and are chemically optimizing several small molecule compounds for the treatment of life-threatening infections caused by multidrug-resistant Gram-negative bacteria. Our goal is to select lead development compounds that can be formulated for both intravenous and oral administration. Wellcome Trust awarded us a $5.0 million grant for this program, of which we have received approximately $3.4 million as of December 31, 2013.

The increasing prevalence of infections caused by multidrug-resistant bacteria is a global health problem and represents a critical unmet medical need. Many infections caused by multidrug-resistant pathogens occur in patients receiving medical care for serious conditions in hospitals, long-term acute care facilities, such as those providing wound care or ventilation, or nursing homes. Infections acquired in these settings, commonly referred to as nosocomial infections, frequently result in severe pneumonia and infections of the urinary tract and bloodstream. The majority of these cases of pneumonia and infections of the urinary tract and bloodstream are caused by Gram-negative bacteria.

We have identified a novel structural class of molecules that kill bacteria by targeting bacterial DNA synthesis. When tested using *in vitro* minimum inhibitory concentration, or MIC, assays, our compounds have demonstrated broad spectrum antibacterial activity against numerous Gram-negative bacteria, including *E. coli., A. baumannii, K. pneumoniae, H. influenzae, M. catarrhalis, N. gonorrhoeae, and Staphylococcus aureus.* We believe that the key differentiating factor of our compounds is their potent antibacterial activity against multidrug-resistant bacteria that are refractory to current drugs, including carbapenems and fluoroquinolones. Through chemical optimization, we have improved MIC levels 100-fold against Gram-negative pathogens and expanded the spectrum of activity to include select Gram-positive species, such as *Staphylococcus aureus* . We also have identified what we believe to be the key structural feature that contributed to activity against drug-resistant pathogens. In animal studies, several analogs within this class of molecules have exhibited good exposure upon intravenous administration and protected mice against lethal *E. coli* infection. We have also identified chemotypes within the broad structural class that selectively inhibits *Neisseria* species. All isolates of *Neisseria gonorrhoeae* tested in vitro, including quinolone-resistant and multi-drug resistant strains, are sensitive to our compounds. These molecules demonstrated that these molecules have been effective in a mouse model of gonorrhea after a single oral dose. Antibiotic resistant *N. gonorrhoeae* is an increasing world-wide threat. The Centers for Disease Control and Protection identified it as one of the top three urgent threats to public health. Gonorrhea is estimated to affect greater than 800,000 people yearly in the United States.

Our Collaborations and Funding Arrangements

We currently have ongoing collaborations with Roche and the SMA Foundation. We also have received grant funding from Wellcome Trust pursuant to funding agreements under which we have continuing obligations. In addition to these material collaboration and funding agreements, which are described in more detail below, we have an early stage collaboration and discovery agreement with AstraZeneca AB for the discovery and development of potential new therapies for cancer and other diseases.

Roche and the SMA Foundation

In November 2011, we entered into a license and collaboration agreement with Roche and the SMA Foundation pursuant to which we are collaborating with Roche and the SMA Foundation to further develop and commercialize compounds identified under our spinal muscular atrophy sponsored research program with the SMA Foundation, as described below, and to research, develop and commercialize other small molecule compounds with potential for therapeutic use in patients with spinal muscular atrophy. Pursuant to the license and collaboration agreement, Roche paid us an

upfront non-refundable payment of $30.0 million. Roche has additional financial obligations described below.

Research and development. The agreement provides for a research and development collaboration under which we and Roche will conduct a program designed to further research and develop specified compounds from our pre-existing collaboration with the SMA Foundation, as described below, and to discover and develop new small molecule compounds that result in increased levels of SMN1 mRNA and protein based on the conversion of SMN2 RNA to SMN1 mRNA. During the research term, Roche has agreed to provide us with funding, based on an agreed-upon full-time equivalent rate, for an agreed-upon number of full-time equivalent employees that we contribute to the research program. The research term is for a minimum of two years from the effective date of the agreement and can be terminated by Roche any time thereafter upon 90 days' notice. Roche is responsible for pursuing worldwide clinical development of compounds from the research program.

Joint steering committee. The collaboration is governed by a joint steering committee consisting of an equal number of representatives of us, the SMA Foundation and Roche. We, the SMA Foundation and Roche have agreed that the members of the joint steering committee will act in good faith to cooperate with one another and seek agreement with respect to issues to be decided by the joint steering committee. In addition, we, the SMA Foundation and Roche have agreed to endeavor to make decisions by consensus, but if the joint steering committee cannot reach agreement after following a specified decision resolution procedure, Roche's decision will control. However, Roche may not exercise its final decision-making authority with respect to certain specified matters, including any decision that would increase our or the SMA Foundation's obligations, reduce our or the SMA Foundation's rights, expand Roche's rights, or reduce Roche's obligations under the license and collaboration agreement.

Commercialization. Roche is responsible for commercializing compounds and products from the collaboration. We have granted Roche worldwide exclusive licenses, with the right to grant sublicenses, to our patent rights and know-how with respect to such compounds and products.

We are eligible to receive up to an aggregate of $135 million in payments if specified development and regulatory milestones are achieved and up to an aggregate of $325 million in payments if specified sales milestones are achieved. To date, we have earned $17.5 million of these development and regulatory milestone payments based on the progression of the collaboration from the pre-clinical stage to Phase 1 trials in healthy volunteers. We are also entitled to tiered single-digit to mid-teen royalties on worldwide net product sales of products developed pursuant to the collaboration. Roche's obligation to pay us royalties will expire generally on a country-by-country basis at the latest of the expiration of the last-to-expire patent covering a product in the given country, the expiration of regulatory exclusivity for that product in such country or 10 years from the first commercial sale of that product in such country. However, the royalties payable to us may be decreased in certain circumstances. For example, the royalty rate in a particular country is reduced if the product is not protected by patents in that country and no longer entitled to regulatory exclusivity in that country. We remain responsible for making any payments to the SMA Foundation that may become due under our pre-existing sponsored research agreement with the SMA Foundation.

Exclusivity. Roche has the exclusive right to develop and commercialize compounds from the collaboration. Furthermore, until November 2014, except in specified circumstances involving termination or certain acquisitions, neither we nor Roche is permitted, outside the collaboration, to use alternative splicing to identify any small molecule compound that results in increased levels of SMN1 mRNA and protein based on the conversion of SMN2 RNA to SMN1 mRNA or to engage in any research, development, manufacture or commercialization of any compound that such party knows or believes to be such a small molecule compound identified with alternative splicing.

Termination. Unless terminated earlier, the license and collaboration agreement will expire on the date when no royalty or other payment obligations are or will become due under the agreement.

Roche's termination rights under the license and collaboration agreement include the following:

- the right to terminate the agreement at any time after November 22, 2013 on a product-by-product and country-by-country basis upon three months' notice before the launch of the applicable product or upon nine months' notice thereafter; and

- the right to terminate the agreement in specified circumstances following a change of control of us.

The license and collaboration agreement provides that we or Roche may terminate the agreement in the event of an uncured breach by the other party of a material provision of the agreement, or in the event of the other party's bankruptcy or insolvency.

Upon termination of the collaboration agreement by Roche for convenience or termination by us as a result of Roche's breach, bankruptcy, change of control or patent challenge, we have the right to assume the development and commercialization of product candidates arising from the license and collaboration agreement. In that event, we may become obligated to pay royalties to Roche on sales of any such product.

SMA Foundation

In June 2006, we entered into a sponsored research agreement with the SMA Foundation under which we and the SMA Foundation have collaborated in the research and preclinical development of small molecule therapeutics for spinal muscular atrophy. Pursuant to the sponsored research agreement, as amended, the SMA Foundation provided us with $13.3 million in funding. The SMA Foundation is not obligated to provide any further funding under this agreement.

Research collaboration. The agreement established a research collaboration under which we identified and optimized compounds with the potential to treat spinal muscular atrophy by increasing production of the survival motor neuron, or SMN, protein. We expect to designate one of the compounds from the research program as a development candidate in the first half of 2013, and several other compounds from the research program have been designated as potential back-up compounds. As discussed above, we are also collaborating with the SMA Foundation and Roche to further develop these compounds.

Development and commercialization. We have agreed to use commercially reasonable efforts to develop and commercialize at least one product from compounds we advance from the research program, including performing specified activities within agreed timelines. As discussed above, we are also collaborating with the SMA Foundation and Roche to further develop these compounds.

Continuing financial obligations. We may become obligated to pay the SMA Foundation single-digit royalties on worldwide net product sales of any collaboration product that we successfully develop and subsequently commercialize or, if we outlicense rights to a collaboration product, a specified percentage of certain payments we receive from our licensee. As discussed above, we have outlicensed rights to Roche pursuant to a license and collaboration agreement. We are not obligated to make such payments unless and until annual sales of a collaboration product exceed a designated threshold. Our obligation to make such payments would end upon our payment to the SMA Foundation of a specified amount, which we refer to as the repayment amount.

Reversion rights. In specified circumstances, including those involving our decision to discontinue development or commercialization of a collaboration product, our uncured failure to meet agreed timelines or those that might arise following our change of control, we may be obligated to grant the SMA Foundation exclusive or non-exclusive sublicensable rights under our intellectual property, in

certain collaboration products, among other rights, to assume the development and commercialization of such collaboration products and to provide the SMA Foundation with other transitional assistance, which we refer to as a reversion. In some such cases, we may be entitled to receive licensing fee payments from the SMA Foundation and single-digit royalties on sales of the applicable collaboration product, which amounts we collectively refer to as reversion payments. In other cases, the SMA Foundation is not required to make any payments to us in connection with the licenses it receives from us.

Termination. Unless terminated earlier, the sponsored research agreement will continue until the earliest of the SMA Foundation's receipt of the repayment amount or, if there was a reversion, either our receipt of all reversion payments that the SMA Foundation may be obligated to make to us or, if the SMA Foundation is not obligated to make reversion payments, the expiration of the last-to-expire patent we licensed to the SMA Foundation in connection with such reversion. The sponsored research agreement provides that either party may terminate the agreement in the event of an uncured material breach by the other party or in the event of the other party's bankruptcy or insolvency.

Wellcome Trust (BMI1 for oncology)

In May 2010, we entered into a funding agreement with Wellcome Trust for the research and development of small molecule compounds that selectively decrease the production of BMI1 expression in tumor stem cells. Pursuant to the funding agreement, Wellcome Trust awarded us a $5.4 million grant, of which approximately $0.9 million was paid in connection with execution of the agreement and the balance of which was paid based on our achievement of specified milestones.

Research program. We have agreed to use reasonable efforts to achieve each specified research program milestone on or before its corresponding agreed target date. We have designated PTC596 as an experimental drug candidate. The research program term began on the effective date and ends on the earlier of completion of the research program or three years after the effective date.

Development and commercialization. We own all intellectual property that arises from the conduct of the research program, which we refer to as program intellectual property, and are responsible for developing and commercializing the program intellectual property, including PTC596 and other compounds. However, we will require Wellcome Trust's written consent prior to any such development or commercialization. If Wellcome Trust withholds such consent and we and Wellcome Trust are not able to resolve Wellcome Trust's concerns, the parties have agreed to follow a specified dispute resolution procedure that gives neither party final decision-making authority.

Continuing financial obligations. To the extent that we develop and commercialize program intellectual property on a for-profit basis ourselves, we may become obligated to pay to Wellcome Trust development and regulatory milestone payments of up to an aggregate of $35.6 million and single-digit royalties on sales of any research program product. Our obligation to pay such royalties would continue on a country-by-country basis until the longer of the expiration of the last patent in the program intellectual property in such country covering the research program product and the expiration of market exclusivity of such product in such country. To the extent that we develop and commercialize program intellectual property on a for-profit basis through outlicensing, we will be obligated to pay to Wellcome Trust a specified share of any consideration we receive from our licensee. We would incur no payment obligations to Wellcome Trust to the extent that we elect to develop and commercialize program intellectual property on a non-profit basis.

Reversion rights. If we fail to take reasonable steps to develop or commercialize program intellectual property during specified timeframes, we may be obligated to grant exclusive rights to Wellcome Trust or its nominee under the program intellectual property, along with non-exclusive rights under our background intellectual property, so that Wellcome Trust or its nominee can assume such

development and commercialization. If we grant such a license, we would be entitled to a share of any consideration received by Wellcome Trust in connection with any subsequent development or commercialization of program intellectual property on a for-profit basis, which share would be proportionate to our contribution to the development and commercialization.

Termination. Unless terminated earlier, the funding agreement will continue until the research program has ended, the last-to-expire of the patents in the program intellectual property has expired, any agreement entered into for the exploitation of the program intellectual property or our background intellectual property has expired, and there are no remaining payment obligations relating to the exploitation of the program intellectual property or certain of our other intellectual property.

Wellcome Trust's rights under the funding agreement include the right to terminate the agreement under specified circumstances, including if:

- according to a team of experts from Wellcome Trust, an uncorrected serious failure exists in the progress, management or conduct of the research program, or an uncorrected major external scientific, technical or commercial barrier exists that means the research program is unlikely to succeed in its objectives;
- we cease or threaten to cease to carry on our business or operations necessary for the completion of our obligations under the funding agreement;
- in Wellcome Trust's reasonable opinion, an act or omission by us is incompatible with or has an adverse effect on Wellcome Trust's charitable objectives or reputation or on our ability to comply with our obligations under the funding agreement;
- we enter into any transaction involving the program intellectual property or our background intellectual property without Wellcome Trust's prior written consent;
- specified events take place relating to our principal investigator for the research program; or
- specified situations exist following a change of control of us.

The funding agreement provides that either party may terminate the agreement in the event of an uncured material breach by the other party or in the event of the other party's bankruptcy or insolvency.

Except as noted below, certain specified rights and obligations of the parties will generally survive termination of the funding agreement, including Wellcome Trust's right to receive payments from us with respect to development and commercialization of program intellectual property on a for-profit basis.

If the funding agreement terminates prior to the end of the research program, we are obligated to return all funding we received from Wellcome Trust that is unspent at the date of termination, after deduction of costs and non-cancellable commitments incurred prior to such date.

If Wellcome Trust terminates the funding agreement in specified circumstances, including as a result of our material breach, bankruptcy or insolvency, or following our change of control, we may be obligated to assign to Wellcome Trust ownership of the program intellectual property, grant to Wellcome Trust royalty-free non-exclusive rights under our background intellectual property for the continuation of the research program, if applicable, and the development and commercialization of program intellectual property, and provide Wellcome Trust with other specified transitional assistance.

If we terminate the funding agreement in specified circumstances, including as a result of Wellcome Trust's uncured material breach or bankruptcy or insolvency, Wellcome Trust's right to receive payments from us with respect to development and commercialization of program intellectual property on a for-profit basis, as well as certain other specified rights, will terminate.

Wellcome Trust (antibacterial)

In December 2011, we entered into an additional funding agreement with Wellcome Trust for the research and development of small molecule compounds that target life-threatening infections caused by multidrug-resistant Gram-negative bacteria. Pursuant to the funding agreement, Wellcome Trust awarded us a $5.0 million grant, of which approximately $1.7 million was paid in connection with execution of the agreement and $1.6 million was paid in 2013 in connection with the achievement of a specified milestone. The balance of the grant is payable based on our achievement of two additional specified milestones.

Research program. We have agreed to use reasonable efforts to achieve each specified research program milestone on or before its corresponding agreed target date. The research program term began on the effective date of the agreement and ends on the earlier of completion of the research program or three years after the effective date.

Development and commercialization. We own all intellectual property that arises from the conduct of the research program, which we refer to as program intellectual property, and have the first right to develop and commercialize the program intellectual property, including compounds, provided that we obtain Wellcome Trust's written consent prior to any such development or commercialization. If Wellcome Trust withholds such consent and we and Wellcome Trust are not able to resolve Wellcome Trust's concerns, the parties have agreed to follow a specified dispute resolution procedure that gives neither party final decision-making authority.

Continuing financial obligations. To the extent that we develop and commercialize program intellectual property on a for-profit basis ourselves, we may become obligated to pay to Wellcome Trust development and regulatory milestone payments of up to an aggregate of $33.3 million and single-digit royalties on sales of any research program product. Our obligation to pay such royalties would continue on a country-by-country basis until the longer of the expiration of the last patent in the program intellectual property in such country covering the research program product and the expiration of market exclusivity of such product in such country. To the extent that we develop and commercialize program intellectual property on a for-profit basis through outlicensing, we will be obligated to pay to Wellcome Trust a specified share of any consideration we receive from our licensee. We would incur no payment obligations to Wellcome Trust to the extent that we elect to develop and commercialize program intellectual property on a non-profit basis.

Reversion rights. If we fail to take reasonable steps to develop or commercialize program intellectual property during specified timeframes, we may be obligated to grant exclusive rights to Wellcome Trust or its nominee under the program intellectual property, along with non-exclusive rights under our background intellectual property, so that Wellcome Trust or its nominee can assume such development and commercialization. If we grant such a license, we would be entitled to a share of any consideration received by Wellcome Trust in connection with any subsequent development or commercialization of program intellectual property on a for-profit basis, which share would be proportionate to our contribution to the development and commercialization.

Termination. Unless terminated earlier, the funding agreement will continue until we have received the full amount of the grant, the research program has ended, the last-to-expire of the patents in the program intellectual property has expired, any agreement entered into for the exploitation of the program intellectual property or our background intellectual property has expired, and there are no remaining payment obligations relating to the exploitation of the program intellectual property or our background intellectual property.

Wellcome Trust's termination rights under the funding agreement include the right to terminate the funding agreement under specified circumstances, including if:

- according to a team of experts from Wellcome Trust, an uncorrected serious failure exists in the progress, management or conduct of the research program, or an uncorrected major external scientific, technical or commercial barrier exists that means the research program is unlikely to succeed in its objectives;
- we cease or threaten to cease to carry on our business or operations necessary for the completion of our obligations under the funding agreement;
- in Wellcome Trust's reasonable opinion, an act or omission by us is incompatible with or has an adverse effect on Wellcome Trust's charitable objectives or reputation or on our ability to comply with our obligations under the funding agreement;
- we enter into any transaction involving the program intellectual property or our background intellectual property without Wellcome Trust's prior written consent;
- specified events take place relating to our principal investigator for the research program; or
- specified situations exist following a change of control of us.

The funding agreement provides that either party may terminate the agreement in the event of an uncured material breach by the other party or in the event of the other party's bankruptcy or insolvency.

Except as noted below, certain specified rights and obligations of the parties will generally survive termination of the funding agreement, including Wellcome Trust's right to receive payments from us with respect to development and commercialization of program intellectual property on a for-profit basis.

If the funding agreement terminates prior to the end of the research program, we are obligated to return all funding we received from Wellcome Trust that is unspent at the date of termination (after deduction of costs and non-cancellable commitments incurred prior to such date).

If Wellcome Trust terminates the funding agreement in specified circumstances, including as a result of our material breach, bankruptcy or insolvency, or following our change of control, we may be obligated to assign to Wellcome Trust ownership of the program intellectual property, grant to Wellcome Trust royalty-free non-exclusive rights under our background intellectual property for the continuation of the research program (if applicable) and the development and commercialization of program intellectual property, and provide Wellcome Trust with other specified transitional assistance.

If we terminate the funding agreement in specified circumstances, including as a result of Wellcome Trust's uncured material breach or bankruptcy or insolvency, Wellcome Trust's right to receive payments from us with respect to development and commercialization of program intellectual property on a for-profit basis, as well as certain other specified rights, will terminate.

Intellectual Property

Patents and trade secrets

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business, where patent protection is available. We also rely on trade secrets,

know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of January 28, 2014, we owned or exclusively licensed a total of 65 U.S. patents and 74 U.S. patent applications, including original filings, continuations and divisional applications, as well as numerous foreign counterparts to many of these patents and patent applications. Our patent portfolio includes patents and patent applications with claims directed to the composition of matter, pharmaceutical formulation and methods of use of many of our compounds, including ataluren.

The patent rights relating to ataluren owned by us consist of 15 issued U.S. patents relating to composition of matter, methods of use, formulation and methods of manufacture and multiple pending patent applications relating to composition of matter, methods of use, formulation, dosing and methods of manufacture. We do not license any material patent rights relating to ataluren. The issued U.S. patents relating to composition of matter are currently scheduled to expire in 2024, including patent term adjustment, and all U.S. patents that issue from U.S. patent applications relating to composition of matter would also be scheduled to expire in 2024. An issued U.S. patent relating to therapeutic method of use is currently scheduled to expire in 2027, including patent term adjustment. All of these patent rights are also the subject of pending counterpart patent applications in a number of other jurisdictions, including Europe and Japan. We own two issued European patents relating to dosing and methods of manufacture of ataluren, and multiple pending European patent applications relating to composition of matter, methods of use, formulation, dosing and methods of manufacture of ataluren. The issued European patents are currently scheduled to expire in 2026 and 2027, and any European patent that issues from the pending European patent application relating to composition of matter would currently be expected to expire in 2024. Except as indicated above, the anticipated expiration dates referred to above are without regard to potential patent term extension, patent term adjustment or other market exclusivity that may be available to us.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a U.S. patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval, or PMA, may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug may be extended.

Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors.

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology

systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

License agreements

We are a party to a number of license agreements under which we license patents, patent applications and other intellectual property from third parties. We enter into these agreements to augment our proprietary intellectual property portfolio. The licensed intellectual property covers some of the compounds that we are researching and developing, some post-transcriptional control targets and some of the scientific processes that we use. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of ataluren or for the compounds that we are testing in our preclinical programs. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and any products that we may develop, other than small amounts of compounds that we synthesize ourselves for preclinical testing.

We obtain our supply of the bulk drug substance for ataluren from two third-party manufacturers. We engage a separate manufacturer to provide fill and finish services for the finished product that we are using in our ongoing clinical trials of ataluren. We are in the process of qualifying an additional manufacturer for fill and finish services for our future clinical trials of ataluren. We obtain our supplies of the product candidates from these manufacturers pursuant to agreements that include specific supply timelines and volume expectations. If any of these manufacturers should become unavailable to us for any reason, we believe that there are a number of potential replacements, although we might incur some delay in identifying and qualifying such replacements.

All of our drug candidates are organic compounds of low molecular weight, generally called small molecules. We have selected these compounds not only on the basis of their potential efficacy and safety, but also for their ease of synthesis and reasonable cost of their starting materials. In particular, ataluren is manufactured in reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale up and does not require unusual equipment in the manufacturing process. We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies and private and public research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining

regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop. In addition, our ability to compete may be affected because in some cases insurers or other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers.

The competition for ataluren includes the following:

- ***Ataluren for nmDMD.*** There are currently no marketed therapeutics approved to treat the underlying cause of nmDMD. Current treatments seek to address symptoms through supportive care measures, such as bracing, joint stretching exercises, tendon release surgery, wheelchair use and assisted ventilation. Corticosteroids, such as prednisone and deflazacort are often prescribed to treat some of the symptoms of the disease. We believe that ataluren is the only product candidate in clinical trials that is designed to treat the underlying cause of nmDMD by restoring dystrophin activity. Other biopharmaceutical companies are developing treatments for Duchenne muscular dystrophy based on a different scientific approach known as exon-skipping. Prosensa Therapeutics is developing a product candidate, PRO051, based on exon-skipping that recently completed a Phase 3 clinical study in collaboration with GlaxoSmithKline. Sarepta Therapeutics is developing a product candidate, Eteplirsen, based on exon-skipping that is currently in Phase 2b clinical development. We do not believe that either PRO051 or Eteplirsen is applicable for the treatment of patients with nmDMD. Summit Corporation also has a product candidate in early clinical development designed to increase the production of the protein utrophin, which is functionally similar to dystrophin, to treat Duchenne muscular dystrophy. In addition, Pfizer has a potentially muscle-enhancing product candidate in Phase 2 clinical development for muscular dystrophy.

- ***Ataluren for nmCF.*** There are currently no marketed therapeutics approved to treat the underlying cause of nmCF. In 2012, the FDA approved Kalydeco (ivacaftor), a CFTR potentiator developed by Vertex Pharmaceuticals, as a treatment for cystic fibrosis in patients six years of age and older who have a type of mutation in the CFTR gene known as a gating mutation. We do not believe that Kalydeco, which is designed for the treatment of patients with a mutation other than a nonsense mutation, is applicable for the treatment of patients with nmCF, except possibly in very rare instances in which a patient is heterozygous with both a nonsense mutation and a gating mutation. Other current treatments for cystic fibrosis are designed to alleviate the symptoms of the disease and depend upon the stage of the disease and the organs involved. Clearing mucus from the lungs is an important part of the daily cystic fibrosis treatment regimen. Chest physical therapy is a form of airway clearance that involves vigorous clapping on the back and chest to dislodge the thick mucus from the lungs. Other treatments for cystic fibrosis include TOBI (tobramycin), an aerosolized antibiotic used to treat lung infections that is marketed by Chiron Corporation, and Pulmozyme, a mucus-thinning drug shown to reduce the number of lung infections and improve lung function, that is marketed by Genentech, Inc. We believe that ataluren is the only product candidate in clinical trials that is designed to treat the underlying cause of nmCF by restoring CFTR activity. Vertex Pharmaceuticals also is developing two other product candidates for the treatment of cystic fibrosis in patients who have a type of mutation in the CFTR gene known as a processing block mutation, one of which is in Phase 2 clinical development in combination with Kalydeco.

The key competitive factors affecting the success of ataluren are likely to be its efficacy, safety, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

Sales and marketing

If we receive regulatory approval for our product candidates, we plan to commence commercialization activities by building our own focused sales and marketing organization in selected territories complemented by selective distribution, co-promotion and other arrangements with leading pharmaceutical or biotechnology collaborators.

We generally expect to retain commercial rights for our product candidates for which we receive marketing approvals in situations in which we believe it is possible to access the market through focused, specialized sales force. In particular, we believe that such a sales force could address the community of pulmonologists and neurologists who are the key specialists in treating cystic fibrosis and Duchenne muscular dystrophy, for which we are developing ataluren. Accordingly, if ataluren is approved, we plan to initially build our own internal sales teams to target these specialists.

We also plan to continue building key capabilities, such as marketing, market access, sales management and medical affairs, to implement marketing and medical strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with thought leaders in relevant fields of medicine.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, approval, manufacturing, labeling, post-approval monitoring and reporting, packaging, promotion, storage, advertising, distribution, marketing and export and import of pharmaceutical products such as those we are developing. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. government regulation

In the United States, the information that must be submitted to the FDA in order to obtain approval to market a new drug varies depending upon whether the drug is a new product whose safety and efficacy have not previously been demonstrated in humans or a drug whose active ingredients and certain other properties are the same as those of a previously approved drug. A New Drug Application, or NDA, is the vehicle through which the FDA approves a new pharmaceutical product for sale and marketing in the United States.

The NDA approval process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and implementing regulations. Failures to comply with the applicable FDA requirements at any time during the product development process or approval process may result in a delay of approval or administrative or judicial sanctions. These sanctions could include the FDA's imposition of a clinical hold on trials, refusal to approve pending applications, withdrawal of an approval, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

To market a new drug, a sponsor generally must undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies under the FDA's good laboratory practices regulations;
- submission to the FDA of an investigational new drug application, or IND, for clinical testing, which must become effective before clinical trials may begin and which must include independent Institutional Review Board, or IRB, approval before the trials may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with GCP to establish the safety and efficacy of the product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA Advisory Committee meeting, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, which require that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND applicant must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some preclinical testing may continue after the IND is submitted. The IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. In other words, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB must approve the protocol and amendments.

All research subjects or their legally authorized representatives must provide their informed consent in writing.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Phase 1 clinical trials usually involve the initial introduction of the investigational drug into human subjects. Phase 1 clinical trials may be conducted in patients or healthy volunteers to evaluate the product's safety, dosage tolerance and pharmacokinetics and, if possible, seek to gain an early indication of its effectiveness.

Phase 2 clinical trials usually involve controlled trials in a larger but still relatively small number of subjects from the relevant patient population to:

- evaluate dosage tolerance and appropriate dosage;
- identify possible short-term adverse effects and safety risks; and
- provide a preliminary evaluation of the efficacy of the drug for specific indications.

Phase 2 clinical trials are sometimes denoted by companies as Phase 2a or Phase 2b clinical trials. Phase 2a clinical trials typically represent the first human clinical trial of a drug candidate in a smaller patient population and are designed to provide earlier information on drug safety and efficacy. Phase 2b clinical trials typically involve larger numbers of patients or longer durations of therapy and may involve comparison with placebo, standard treatments or other active comparators.

Phase 3 clinical trials usually further evaluate clinical efficacy and test further for safety in an expanded patient population. Phase 3 clinical trials usually involve comparison with placebo, standard treatments or other active comparators. These trials are intended to establish the overall risk-benefit profile of the product and provide an adequate basis for physician labeling. Phase 3 clinical trials are usually larger, more time consuming, more complex and more costly than Phase 1 and Phase 2 clinical trials.

Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. Furthermore, the FDA or we may suspend or terminate clinical trials at any time on various grounds, including a finding that the subjects are or would be exposed to an unreasonable and significant risk of illness or injury. Similarly, an IRB can suspend or terminate approval of a clinical trial if the trial is not being conducted in accordance with the IRB's requirements or if the research has been associated with unexpected serious harm to patients. The FDA typically requires that an NDA include data from two adequate and well-controlled clinical trials, but approval may be based upon a single adequate and well-controlled clinical trial plus confirmatory evidence. In some cases, the FDA may condition approval of an NDA on the applicant's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after NDA approval. Such post-approval trials are typically referred to as Phase 4 studies.

The FDA's accelerated approval process allows for potentially faster development and approval of certain drugs intended to treat serious or life-threatening illnesses that provide meaningful therapeutic benefit to patients over existing treatments. Under the accelerated approval process, the adequate and well-controlled clinical trials conducted with the drug establish that the drug has an effect on a "surrogate" endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical benefit other than survival or irreversible morbidity. Drugs approved through the accelerated approval process are subject to certain post-approval requirements, including that the applicant complete Phase 4 clinical trials to demonstrate the drug's clinical benefit. If the trials fail to verify the clinical benefit of the drug, the FDA may withdraw approval of the application through a streamlined process.

The FDA has explained in draft guidance that some drugs are dependent upon the use of an *in vitro* diagnostic test, such as when the use of the drug is limited to a specific patient subpopulation that can be identified by using the test. The draft guidance refers to the diagnostic tests used with these types of drugs as *in vitro* companion diagnostic devices. According to the draft guidance, *in vitro* companion diagnostic devices ordinarily will be considered to be high risk and, therefore, will require the approval of a premarket approval application before they are marketed. Some *in vitro* companion diagnostic devices, however, could potentially be cleared through a 510(k) premarket notification submission. The draft guidance states that the FDA may decline to approve a drug that is dependent upon the use of an *in vitro* companion diagnostic device if no such device is FDA-approved or -cleared for the relevant indication. According to the draft guidance, however, the FDA may approve such a drug without an approved or cleared *in vitro* companion diagnostic device when the drug is intended to treat a serious or life-threatening condition for which no satisfactory alternative treatment exists and the FDA determines that the benefits from the use of drug with an unapproved or uncleared *in vitro* companion diagnostic device are so pronounced as to outweigh the risks from the lack of an approved or cleared *in vitro* companion diagnostic device. The draft guidance is subject to change and is not binding on the FDA or the public.

Assuming successful completion of the required clinical testing, the results of the preclinical studies and of the clinical trials, together with other detailed information, including proposed labeling and information on the chemistry, manufacture and composition of the product, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. In most cases, the NDA must be accompanied by a substantial user fee. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the FDA's threshold determination that it is sufficiently complete to permit a substantive review. If the FDA determines that the NDA is incomplete, the FDA may refuse to file the application. If the FDA refuses to file an NDA, the applicant may request an informal conference with the FDA about whether the application should be filed. The applicant also may appeal the decision through the FDA's formal dispute resolution process, which involves appealing the decision through the Center for Drug Evaluation and Research and, ultimately, to the Commissioner of Food and Drugs if necessary. After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether a product is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity.

Under the Pediatric Research Equity Act of 2003, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. PREA compliance may be required if approval is sought for other indications for which the drug has not received orphan designation.

The FDA will typically inspect one or more clinical sites to assure compliance with GCP before approving an NDA. The FDA also will inspect the facility or the facilities at which the product is manufactured before the NDA is approved. The FDA will not approve the product unless cGMP compliance is satisfactory. The FDA may also take into account results of inspections performed by certain counterpart foreign regulatory agencies in assessing compliance with GCP or GMP. The FDA has entered into international agreements with foreign agencies, including the EMA, in order to facilitate this type of information sharing. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The testing and approval process requires substantial time, effort and financial resources, and each may take years to complete. Data obtained from clinical trials are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

We may encounter difficulties or unanticipated costs in our efforts to secure necessary FDA approvals, which could delay or preclude us from marketing our products. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The advisory committee process may cause delays in the approval timeline. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully, particularly any negative recommendations or limitations, when making drug approval decisions.

The FDA may limit the indications for use, approve narrow labeling relegating a drug to second-line or later-line use, add limitations of use to the labeling or place other conditions on

approvals, which could restrict the marketing of the products. After approval, some types of changes to the approved product, such as adding new indications, which may itself require further clinical testing, or changing the manufacturing process are subject to further FDA review and approval.

Post-approval requirements

After FDA approval of a product is obtained, we are required to comply with a number of post-approval requirements. Holders of an approved NDA must report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information, and comply with requirements concerning advertising and promotional labeling for their products. As a condition of approval of an NDA, the FDA may require post marketing testing and surveillance to monitor the product's safety or efficacy.

The FDA also has the authority to require a drug-specific risk evaluation and mitigation strategy, or REMS, to ensure the safe use of the drug. In determining whether a REMS is necessary, the FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the drug's risks, limitations on who may prescribe or dispense the drug, or other measures that the FDA deems necessary to assure the safe use of the drug. In addition, the REMS must include a timetable to assess the strategy at 18 months, three years, and seven years after the strategy's approval. The FDA may also impose a REMS requirement on an approved drug if the FDA determines, based on new safety information, that a REMS is necessary to ensure that the drug's benefits outweigh its risks.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Although physicians may prescribe a drug for off-label uses, manufacturers may only promote for the approved indications and in accordance with the approved labeling. 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, that 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.

Also, quality control and manufacturing procedures must continue to conform to cGMP after approval. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes certain procedural, substantive and recordkeeping requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Future FDA inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing.

Newly discovered or developed safety or effectiveness data or other information may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established that could delay or prevent FDA approval of our products under development or negatively impact the marketing of any future approved products.

Orphan drug designation

We have received orphan drug designation from the FDA for ataluren for the treatment of nmCF, nmDMD and spinal muscular atrophy. The FDA may grant orphan drug designation to drugs intended to treat a "rare disease or condition," which is defined as a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Orphan drug designation can provide opportunities for grant funding towards clinical trial costs, tax advantages and FDA user-fee benefits. In addition, if a product which has an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors may receive approval of different drugs or biologics for the indications for which the orphan product has exclusivity.

Fast track designation

We have obtained fast track designation from the FDA for our product candidate ataluren for the treatment of nmDMD. The FDA's fast track program is a process designed to facilitate the development and review of new drugs that are intended to treat serious or life threatening conditions and that demonstrate the potential to address unmet medical needs for the conditions. Fast track designation applies to the product for the specific indication for which it is being studied. Thus, it is the development program for a specific drug for a specific indication that receives fast track designation. The sponsor of a product designated as being in a fast track drug development program may engage in close early communication with the FDA including through timely meetings and feedback on clinical trials. Products in the fast track drug development program also may receive priority review or accelerated approval, and sponsors may be able to submit portions of an application on a rolling basis rather than as one complete submission. The FDA may notify a sponsor that its program is no longer classified as a fast track development program if the fast track designation is no longer supported by emerging data or the designated drug development program is no longer being pursued.

Hatch-Waxman exclusivity

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety. During the exclusivity period, the FDA generally may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company that references the previously approved drug. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

The FDCA also provides three years of market exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity

Pediatric exclusivity is another type of non-patent market exclusivity in the United States and, if granted, provides for the attachment of an additional six months of market protection to the term of any existing Orange Book-listed patents or regulatory exclusivity, including the non-patent exclusivity periods described above. This six-month exclusivity may be granted based on the voluntary completion of a pediatric study or studies in accordance with an FDA-issued "Written Request" for such a study or studies.

Regulation outside the United States

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

Regulation in the European Union

We have obtained an orphan medicinal product designation from the European Commission, following an evaluation by the EMA's Committee for Orphan Medicinal Products, for ataluren for the treatment of nmDMD, Becker muscular dystrophy and nmCF. The European Commission can grant orphan medicinal product designation to products for which the sponsor can establish that it is intended for the diagnosis, prevention, or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the European Union, or (2) a life threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that sales of the drug in the European Union would generate a sufficient return to justify the necessary investment. In addition, the sponsor must establish that there is no other satisfactory method approved in the European Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation is not a marketing authorization. It is a designation that provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized E.U. marketing authorization, as well as 10 years of market exclusivity following a marketing authorization. During this market exclusivity period, neither the European Medicines Agency, nor the European Commission nor the Member States can accept an application or grant a

marketing authorization for a 'similar medicinal product.' A 'similar medicinal product' is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, a competing similar medicinal product may in limited circumstances be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to our product. Our product can lose orphan designation, and the related benefits, prior to us obtaining a marketing authorization if it is demonstrated that the orphan designation criteria are no longer met.

To obtain regulatory approval of a drug under the European Union's regulatory systems and authorization procedures, an applicant may submit MAAs under a centralized, decentralized, or national procedure. The centralized procedure is compulsory for certain medicinal products, including orphan medicinal products, like ataluren for the treatment of nmDMD and nmCF, and medicinal products produced by certain biotechnological processes, and optional for certain other innovative products. The centralized procedure enables applicants to obtain a marketing authorization that is valid in all E.U. member states based on a single application. Under the centralized procedure, the EMA's Committee for Human Medicinal Products, or CHMP, is required to adopt an opinion on a valid application within 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions. More specifically, on day 120 of the procedure, once the CHMP has received the preliminary assessment reports and opinions from the rapporteur and co-rapporteur, it prepares a list of potential outstanding issues, referred to as "other concerns" or "major objections". These are sent to the applicant together with CHMP's recommendation. The CHMP can make one of two recommendations: (1) the marketing authorization could be granted provided that satisfactory answers are given to the "other concerns" and/or "major objections" identified and that all conditions outlined in the list of outstanding issues are implemented and complied with; or (2) the product is not approvable since there are "major objections".

Applicants have three months from the date of receiving the potential outstanding issues to respond to the CHMP, and can request a three-month extension if necessary. The granting of a marketing authorization will depend on the recommendations and potential major objections identified by the CHMP as well as the ability of the applicant to adequately respond to these findings. An accelerated assessment can be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, 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. After the adoption of the CHMP opinion, a decision on the MAA must be adopted by the European Commission, after consulting the European Union member states, which in total can take more than 60 days.

An applicant for an MAA may request a re-examination in the event of a negative opinion, in connection with which CHMP appoints new rapporteurs. Within 60 days of receipt of the negative opinion, the applicant must submit a document explaining the basis for its request for re-examination. The CHMP has 60 days to consider the applicant's request for re-examination. The applicant may request an oral explanation before the CHMP, which is routinely granted, following which CHMP will adopt a final opinion. The final opinion, whether positive or negative, is published by the CHMP shortly following the CHMP meeting at which the oral explanation takes place.

In specific circumstances, E.U. legislation enables applicants to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for products designated as orphan medicinal products, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the

applicant will be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs, and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization. The granting of conditional marketing authorization will depend on the applicant's ability to fulfill the conditions imposed within the agreed upon deadline.

Prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the paediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver, or (3) a deferral for one or more of the measures included in the PIP. In the case of orphan medicinal products, completion of an approved PIP can result in an extension of the aforementioned market exclusivity period from ten to twelve years.

In the European Union, independently generated data submitted as part of a full marketing authorization application dossier are protected by regulatory data protection ('data exclusivity') for a period of eight years from the granting of a marketing authorization for a 'reference product'. This means that for a period of eight years, competent authorities may not accept marketing authorization applications that rely on the independently generated data in the marketing authorization dossier of the reference product. Generic medicinal products that rely on the independently generated data of the reference product may not be placed on the market for 10 years from the granting of the initial marketing authorization for the reference medicinal product. These periods of data exclusivity and market exclusivity do not prevent other companies from obtaining a marketing authorization based on their own independently generated data.

If we obtain authorization for a medicinal product in the European Union, we will be required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. We will, for example, have to comply with the E.U.'s stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. Other requirements relate to, for example, the manufacturing of products and active pharmaceutical ingredients in accordance with good manufacturing practice standards. E.U. regulators may conduct inspections to verify our compliance with applicable requirements, and we will have to continue to expend time, money and effort to remain compliant. Non-compliance with E.U. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties in the E.U. Similarly, failure to comply with the E.U.'s requirements regarding the protection of individual personal data can also lead to significant penalties and sanctions. Individual E.U. member states may also impose various sanctions and penalties in case we do not comply with locally applicable requirements.

The EMA is responsible for coordinating inspections to verify compliance with the principles of GCP, good manufacturing practice, or GMP, good laboratory practice, or GLP, and good pharmacovigilance practice, or GVP. These inspections are also intended to verify compliance with other aspects of the supervision of authorized medicinal products in use in the European Union. The EMA coordinates any inspection requested by the CHMP in connection with the assessment of MAAs or matters referred to these committees. Inspections may be routine or triggered by issues arising during the assessment of the dossier or by other information, such as previous inspection experience.

Inspections usually are requested during the initial review of an MAA, but could arise post-authorization.

Inspectors are drawn from member states of the European Union and the European Economic Area. Following an inspection, the inspectors provide a written inspection report to the inspected site or applicant and provide an opportunity for response. Some inspection reports require follow-up and may result in additional adverse consequences due to critical or major findings. The inspectors and the CHMP will comment on any response from an inspected site or applicant and may monitor future compliance with any proposed corrective action plan.

In the GCP area, inspectors grade their findings according to the following scale:

- Critical: Conditions, practices or processes that adversely affect the rights, safety or well being of the subjects or the quality and integrity of data. Observations classified as critical may include a pattern of deviations classified as major.

- Major: Conditions, practices or processes that might adversely affect the rights, safety or well-being of the subjects and/or the quality and integrity of data. Observations classified as major may include a pattern of deviations or numerous minor observations.

- Minor: Conditions, practices or processes that would not be expected to adversely affect the rights, safety or well being of the subjects or the quality and integrity of data. Minor observations indicate the need for improvement of conditions, practices and processes.

- Comments: Suggestions on how to improve quality or reduce the potential for a deviation to occur in the future.

Possible consequences of critical and major findings include rejection of clinical trial data, causing significant delays in obtaining final marketing authorization, or other direct action by national regulatory authorities.

Early access programs

Many jurisdictions allow the supply of unauthorized medicinal products in the context of strictly regulated and exceptional early access programs, and some countries may provide reimbursement for drugs provided in the context of such programs. In the European Union, the legal basis for early access programs, also referred to as named-patient and compassionate use programs, is set out in the E.U. legislation regulating the authorization, manufacture, distribution and marketing of medicinal products. Detailed regulatory requirements applicable to early access programs have been adopted and implemented by E.U. member states in their national laws. The promotion, advertising and marketing of unauthorized medicinal products is generally prohibited, and authorization for early access programs must generally be obtained from national competent authorities, which might not grant such authorization. Obtaining authorization for an early access program in one country does not ensure that authorization will be obtained in another country. U.S. law permits "expanded access" (also known as compassionate use and treatment use) for certain patients with serious diseases who have no comparable alternative treatment options. To provide expanded access, sponsors must submit detailed regulatory information to the FDA. FDA authorization depends on several different factors, including whether expanded access will interfere with related clinical trials or drug development. Sponsors may not promote products as safe or effective for expanded-access uses.

Pharmaceutical Pricing and Reimbursement

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of pharmaceuticals have been a focus of this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing

cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 expanded Medicare coverage for drug purchases by the elderly and changed the way Medicare covers and pays for pharmaceutical products. Cost reduction initiatives and other provisions of this law may decrease the coverage and reimbursement rate that we may receive for any approved products. Likewise, healthcare reform measures under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, referred to together as the Affordable Care Act, contain provisions that may reduce the profitability of drug products by increasing rebates for covered outpatient drugs sold to Medicaid programs, extending the Medicaid rebate to Medicaid managed care plans, mandating discounts for certain Medicare Part D beneficiaries, and imposing annual fees based on pharmaceutical companies' share of sales to federal healthcare programs, among other provisions.

In this healthcare regulatory climate, there may be significant delays in and impediments to obtaining coverage and reimbursement for newly approved drugs. Coverage by federal healthcare programs may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities' coverage of the same products. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the extent to which the costs of the products will be covered and reimbursed by third-party payors, including government healthcare programs such as Medicare and Medicaid, private health insurers and other organizations. Obtaining reimbursement for orphan drugs may be particularly difficult because of the higher prices typically associated with drugs directed at smaller populations of patients. In addition ,third-party payors are likely to impose strict requirements for reimbursement in the use of a higher priced drug.

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 may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA approved products for a particular indication. Third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. Our product candidates may not be considered cost-effective. In the future, we may need to conduct direct head-to-head studies to demonstrate clinical superiority and cost-effectiveness. Our product candidates may not be considered clinically superior and cost-effective to competitor products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and other third-party payors fail to provide adequate coverage and reimbursement. In addition, there is an increasing emphasis on managed care in the United States that may negatively impact pharmaceutical pricing.

In some countries, particularly 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. In addition, there can be considerably pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various E.U. member states, and parallel distribution (arbitrage between low-priced and high-priced member states), can further reduce prices. In some countries we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidate to other available therapies in order to obtain reimbursement or pricing approval.

U.S. Fraud and Abuse Laws

Any present or future arrangements with third-party payors, healthcare providers and professionals and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may restrict certain marketing and contracting practices. These laws include, and are not limited to, anti-kickback and false claims statutes.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, in cash or kind, to induce or reward either the referral of an individual for, or the purchase, or order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others.

The federal False Claims Act imposes civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for 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 government and *qui tam* relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be presented to the government. There is also a separate false claims provision imposing criminal penalties.

The Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

HIPAA also imposes criminal liability for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services.

The federal Physician Sunshine Act requirements under the Affordable Care Act, and its implementing regulations, require 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 made to covered recipients, such as physicians and teaching hospitals, and physician ownership and investment interests. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law.

A number of states also have statutes or regulations similar to the federal Anti-Kickback Statute and False Claims Act that apply to items and services reimbursed under Medicaid and other state programs. Some states have anti-kickback statutes that apply to all payors and not just government payors.

Employees

As of December 31, 2013, we had 137 employees, of whom 133 were employed on a full-time basis, including a total of 54 employees with M.D. or Ph.D. degrees. Of our workforce, 91employees are engaged in research and development. None of our employees is represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on March 31, 1998, under the name PTC Therapeutics, Inc. Our principal executive offices are located at 100 Corporate Court, South Plainfield, New Jersey 07080. Our telephone number is (908) 222-7000. We maintain a website at www.ptcbio.com.

Additional Information

We make available, free of charge on our website, www.ptcbio.com, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file those reports with, or furnish them to, the Securities and Exchange Commission, or SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. Such reports, proxy statements and other information may be obtained through the SEC's website (www.sec.gov) or by visiting the Public Reference Room of the SEC at 100 F Street, N.E., Washington D.C. 20549 or calling the SEC at 1-800-SEC-0330. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K.

Item 1A. Risk Factors

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

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

Since inception, we have incurred significant operating losses. As of December 31, 2013, we had an accumulated deficit of $328.8 million. To date, we have financed our operations primarily through the issuance and sale of our common stock in public offerings, the private placements of our preferred stock, collaborations, bank debt, convertible debt financings, grant funding and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates.

We have devoted substantially all of our efforts to research and development, including clinical trials. We have not completed development of any drugs. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. The net losses we incur may fluctuate significantly from quarter to quarter.

We anticipate that our expenses will increase substantially in connection with initiating and completing confirmatory Phase 3 clinical trials for our lead product candidate, ataluren, for the treatment of patients with Duchenne muscular dystrophy caused by nonsense mutations, or nmDMD, and patients with cystic fibrosis caused by nonsense mutations, or nmCF, commencing early access programs for ataluren for nmDMD patients in selected territories and seeking marketing approval for

ataluren for these indications in the European Union and the United States. In October 2012, we submitted a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for conditional approval of ataluren for the treatment of nmDMD. In January 2014, the EMA's Committee for Medicinal Products for Human Use, or CHMP, adopted a negative opinion recommending the refusal of the granting of the conditional marketing authorization for ataluren for the treatment of nmDMD. We have requested a re-examination of the CHMP opinion and currently expect a final outcome in the second quarter of 2014. EMA conditional approval would permit us to market ataluren in the European Union for treatment of the applicable indication prior to completion of the confirmatory Phase 3 clinical trial for that indication. If we obtain marketing approval of ataluren for either nmDMD or nmCF, we also expect to incur significant sales, marketing, distribution and manufacturing expenses. The timing of commercialization expenses for ataluren depends in part on whether we receive conditional approval for ataluren for either or both of nmDMD and nmCF.

In addition, our expenses will increase if and as we:

- initiate or continue the research and development of ataluren for additional indications and of our other product candidates;
- seek to discover and develop additional product candidates;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

Our ability to generate profits from operations and remain profitable depends on our ability to successfully develop and commercialize drugs that generate significant revenue. Based on our current plans, we do not expect to generate significant revenue unless and until we obtain marketing approval for, and commercialize, ataluren for the treatment of nmDMD or nmCF. This will require us to be successful in a range of challenging activities, including:

- obtaining approval to market ataluren for the treatment of either or both of nmDMD and nmCF;
- successfully initiating and completing confirmatory Phase 3 clinical trials of ataluren for the treatment of either or both of nmDMD and nmCF;
- protecting our rights to our intellectual property portfolio related to ataluren;
- contracting for the manufacture of commercial quantities of ataluren;
- negotiating and securing adequate reimbursement from third-party payors for ataluren; and
- establishing sales, marketing and distribution capabilities to effectively market and sell ataluren in the European Union and the United States.

We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to generate profits from operations. Even if we do generate profits from operations, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to generate profits from operations 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 product offerings or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment in our company.

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.

We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we initiate and continue confirmatory Phase 3 clinical trials of ataluren for the treatment of nmDMD and nmCF, continue our research activities in our preclinical programs and initiate clinical development of other product candidates. In addition, if we obtain regulatory approval for ataluren or any of our other product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. We also expect to incur expenses in connection with commencing early access programs for ataluren for nmDMD patients in selected territories. Furthermore, since the closing of our initial public offering in June 2013, we have begun 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 could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We believe that our existing cash and cash equivalents, including the net proceeds from our initial public offering and our public offering of common stock that we completed in February 2014 as well as research funding that we expect to receive under our collaborations and marketable securities will be sufficient to enable us to fund our operating expenses, debt service obligations and capital expenditure requirements through the fourth quarter of 2016. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate assumes, among other things, that we do not receive conditional approval to market ataluren for nmDMD or nmCF in the European Union prior to completing a confirmatory Phase 3 clinical trial for the applicable indication and, as a result, that we do not incur significant related commercialization expenses prior to such time. Our future capital requirements will depend on many factors, including:

- the progress and results of confirmatory Phase 3 clinical trials of ataluren for nmDMD and nmCF;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for ataluren for additional indications and for our other product candidates;
- the number and development requirements of other product candidates that we pursue;
- the costs, timing and outcome of regulatory review of ataluren and our other product candidates;
- the costs and timing of commercialization activities, including product sales, marketing, distribution and manufacturing, for any of our product candidates that receive marketing approval;
- subject to receipt of marketing approval, revenue received from commercial sales of ataluren or any of our other product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining, and protecting our intellectual property rights and defending against intellectual property-related claims;
- the extent to which we acquire or invest in other businesses, products and technologies; and
- our ability to establish and maintain collaborations, including our collaborations with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche, Inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or the SMA Foundation, and our ability to obtain research funding and achieve milestones under these agreements.

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 regulatory 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 products that we are not planning to have commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. In addition, we may seek additional capital due to favorable market conditions or based on strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. Additional financing may not be available to us on acceptable terms or at all.

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

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; grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates; and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our shareholders ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution 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 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.

Our limited operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability.

Our operations to date have been limited to organizing and staffing our company, developing and securing our technology, raising capital and undertaking preclinical studies and clinical trials of our product candidates. We have not yet demonstrated our ability to successfully complete development of any product candidates, 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. Consequently, any predictions our stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Risks related to the development and commercialization of our product candidates

We depend heavily on the success of our lead product candidate, ataluren, which we are developing for nmDMD and nmCF. All of our other product candidates are still in preclinical development. If we are unable to commercialize ataluren, or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of ataluren for nmDMD and nmCF. Our ability to generate product revenues, which may not occur for

several years, if ever, will depend heavily on the successful development and commercialization of ataluren. The success of ataluren will depend on a number of factors, including the following:

- successful completion of confirmatory Phase 3 clinical trials of ataluren;
- receipt of marketing approvals for ataluren in the European Union and the United States, including possible receipt of conditional approval to market ataluren in the European Union prior to completion of confirmatory Phase 3 clinical trials;
- establishing commercial manufacturing arrangements with third-party manufacturers;
- building an infrastructure capable of supporting product sales, marketing and distribution of ataluren in territories where we pursue commercialization directly;
- launching commercial sales of ataluren, if and when approved, whether alone or in collaboration with others;
- acceptance of ataluren, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- a continued acceptable safety profile of ataluren following approval;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity; and
- protecting our rights in our intellectual property portfolio.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize ataluren, which would materially harm our business.

If clinical trials of our product candidates, such as our confirmatory Phase 3 clinical trials of ataluren, fail to demonstrate safety and efficacy to the satisfaction of the EMA or the U.S. Food and Drug Administration, or FDA, or do not otherwise produce favorable results, we may experience delays in completing, or ultimately be unable to complete, the development and commercialization of ataluren or any other product candidate.

In connection with seeking marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

For example, we did not achieve the primary efficacy endpoint with the pre-specified level of statistical significance in a Phase 2b clinical trial of ataluren for the treatment of nmDMD that we completed in 2009 or in a Phase 3 clinical trial of ataluren for the treatment of nmCF that we completed in 2011. Although we believe that the collective data from these trials, including retrospective and subgroup analyses that we have performed, provide strong support for concluding that ataluren was active and showed clinically meaningful improvements over placebo in these trials, we may similarly fail to achieve the primary efficacy endpoint in confirmatory Phase 3 clinical trials of ataluren for these indications. If the results of our confirmatory Phase 3 clinical trials are not favorable, we may need to conduct additional clinical trials at significant cost or altogether abandon development of

ataluren for either or both of nmDMD and nmCF. We also did not achieve the primary objective in one of four prior Phase 2 clinical trials that we conducted for ataluren for the treatment of nmCF in which we measured change in chloride conductance in nasal cells over the course of treatment.

If we are required to conduct additional clinical trials or other testing of ataluren or any other product candidate that we develop beyond those that we contemplate; if we are unable to successfully complete our clinical trials or other testing; if the results of these trials or tests are not positive or are only modestly positive; or if there are safety concerns, we 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 safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements or restrictions; or
- have the product removed from the market after obtaining marketing approval.

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

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, 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 anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- we may be unable to enroll a sufficient number of patients in our trials to ensure adequate statistical power to detect any statistically significant treatment effects;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, institutional review boards or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may have to 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;
- regulators, institutional review boards or independent ethics committees may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; or

- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, institutional review boards or independent ethics committees to suspend or terminate the trials.

Our product development costs will increase if we experience delays in testing or marketing approvals. 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 may have the exclusive right to commercialize our product candidates, allow our competitors to bring products to market before we do, or impair our ability to successfully commercialize our product candidates, and so may harm our business and results of operations.

Our conclusions regarding the activity and potential efficacy of ataluren in our completed Phase 2b clinical trial of ataluren for the treatment of nmDMD and in our completed Phase 3 clinical trial of ataluren for nmCF are based on retrospective analyses of the results of these trials and nominal p-values, which are generally considered less reliable indicators of efficacy than pre-specified analyses and adjusted p-values.

After determining that we did not achieve the primary efficacy endpoint with the pre-specified level of statistical significance in our completed Phase 2b clinical trial of ataluren for the treatment of nmDMD and in our completed Phase 3 clinical trial of ataluren for nmCF, we performed retrospective and subgroup analyses that we believe provide strong support for concluding that ataluren was active and showed clinically meaningful improvements over placebo in these trials. Although we believe that these additional analyses of the results of these trials were warranted, a retrospective analysis performed after unblinding trial results can result in the introduction of bias if the analysis is inappropriately tailored or influenced by knowledge of the data and actual results. Some of our favorable statistical data from these trials also are based on nominal p-values that reflect only one particular comparison when more than one comparison is possible, such as when two active treatments are compared to placebo or when two or more subgroups are analyzed. Nominal p-values cannot be compared to the benchmark p-value of 0.05 to determine statistical significance without being adjusted for the testing of multiple dose groups or analyses of subgroups.

Because of these limitations, regulatory authorities typically give greater weight to results from pre-specified analyses and adjusted p-values and less weight to results from post-hoc, retrospective analyses and nominal p-values. This diminishes the likelihood that the EMA will grant conditional approval of ataluren for either of these indications and, even if we successfully complete our confirmatory Phase 3 clinical trials, could negatively impact the evaluation by the EMA or the FDA of our anticipated applications for full marketing approval for ataluren for the applicable indication.

If our request for re-examination of the negative opinion on our MAA for the grant of conditional approval of ataluren for the treatment of nmDMD is not successful in changing the negative opinion , our potential commercialization of this product candidate and receipt of related revenues will be delayed.

On January 24, 2014, the EMA's Committee for Medicinal Products for Human Use, or CHMP, adopted a negative opinion on our MAA for conditional approval of ataluren for nmDMD. We have requested a re-examination of the opinion and will be required, within 60 days of receipt of the negative opinion, to submit a document explaining the basis for our request for re-examination. The CHMP will have 60 calendar days to consider the request for re-examination. If the re-examination does not successfully change the negative opinion, we will be required to submit a new MAA at a later date and our potential commercialization of this product candidate and the receipt of related revenues will be delayed.

There is substantial risk that the re-examination request and any conditional approval for which we have applied will not be successful until we have completed a confirmatory Phase 3 clinical trial for this indication, which would delay the potential commercialization of this product candidate and our receipt of related revenues. We expect to face similar risks if we apply for conditional approval of ataluren for the treatment of nmCF prior to completing a confirmatory Phase 3 clinical trial for this indication. In particular, conditional approval of ataluren for the treatment of nmCF will depend on the EMA's assessment of the relative risks and benefits of conditional approval and our ability to provide comprehensive clinical data from a post-approval confirmatory trial.

Our confirmatory Phase 3 clinical trials of ataluren for nmDMD and nmCF, even if successfully completed, may not be sufficient for approval of ataluren for the applicable indication.

It is possible that the EMA or the FDA may not consider the results of our confirmatory Phase 3 clinical trials of ataluren for nmDMD or nmCF, once completed and even if successful, to be sufficient for approval of ataluren for such indication. The FDA typically requires two adequate and well-controlled pivotal clinical trials to support marketing approval of a product candidate for a particular indication. The EMA or the FDA could determine that the results of our trials are not sufficiently robust, are subject to confounding factors or are not adequately supported by other trial endpoints. In addition, although we have had discussions with the FDA regarding our proposed confirmatory Phase 3 clinical trial of ataluren for the treatment of nmCF, the FDA may not consider our proposed trial design acceptable. For example, in 2012, the FDA indicated that in its view the data from our completed Phase 3 clinical trial and other data from our development program in cystic fibrosis do not by themselves support an NDA submission and, consequently, the FDA informed us that additional clinical data would be required to establish the evidence necessary to support eventual filing of an NDA for the use of ataluren to treat nmCF. We had additional interactions with the FDA in 2013 regarding the clinical development design which would have the potential to support an NDA, but we did not achieve a consensus between the EMA and FDA views. While we have incorporated feedback from the FDA into our proposed trial design, we believe that certain key recommendations from the FDA are not appropriate. Two of the key recommendations that we are in disagreement with are the designation of FEV_1 , CF pulmonary exacerbations and body mass index as three co-primary endpoints for the trial and a suggested three-year trial duration. We plan to make FEV_1 the primary endpoint with CF pulmonary exacerbations and body mass index key secondary endpoints, which is consistent with other clinical trials currently ongoing in cystic fibrosis and FDA's earlier recommendation. Additionally, we believe that extending the study duration to three years would result in a number of complications that would ultimately limit the robustness of the data and conclusions that could be drawn from the results. Based on these interactions, we nonetheless intend to proceed with our Phase 3 trial of ataluren in nmCF in the first half of 2014 consistent with feedback from the EMA on our trial design. If the FDA does not consider our proposed trial designs acceptable, we may need to conduct more than one confirmatory clinical trial and our ability to receive marketing approval for this indication could be delayed or prevented.

Because we are developing product candidates for the treatment of diseases in which there is little clinical experience and, in some cases, using new endpoints or methodologies, there is increased risk that the outcome of our clinical trials will not be favorable.

There are no marketed therapies approved to treat the underlying cause of nmDMD or nmCF. In addition, there has been limited historical clinical trial experience generally for the development of drugs to treat either of these diseases. As a result, the design and conduct of clinical trials for these diseases, particularly for drugs to address the underlying nonsense mutations causing these diseases in some subsets of patients, is subject to increased risk.

Prior to our conducting the Phase 2b clinical trial of ataluren for nmDMD, there was no established precedent for an appropriate trial design to evaluate the efficacy of ataluren for nmDMD, and little clinical experience in the methodologies used to analyze the resulting data. Although we believe that we now understand the issues of concern with the pre-specified statistical analyses of our Phase 2b clinical trial results, and that we have designed our confirmatory Phase 3 clinical trial of ataluren for nmDMD in an appropriate fashion, we may nonetheless experience similar or other unknown complications with our confirmatory Phase 3 clinical trial because of the limited clinical experience in this indication. As a result, we may not achieve the pre-specified endpoint with statistical significance in our confirmatory Phase 3 clinical trial, which would make approval of ataluren for this indication unlikely. Among other endpoints in our confirmatory Phase 3 clinical trial of ataluren for nmDMD, the trial protocol includes two secondary endpoints that have not been used previously as outcome measures in published therapeutic clinical trials of nmDMD. These endpoints, in particular, may produce results that are unpredictable or inconsistent with other trial results.

With regard to nmCF, we believe that we now understand subgroup effects that we observed in our completed Phase 3 clinical trial and that we have designed our confirmatory Phase 3 clinical trial of ataluren for nmCF to take these effects into account. However, we may nonetheless experience unknown complications with our confirmatory Phase 3 clinical trial. As a result, we may not achieve the pre-specified endpoint with statistical significance in our confirmatory Phase 3 clinical trial, which would make approval of ataluren for this indication unlikely.

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

We may not be able to initiate or continue clinical trials for our product candidates, including our confirmatory Phase 3 clinical trials of ataluren, if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials. For example, both nmDMD and nmCF are characterized by relatively small patient populations, which could result in slow enrollment of clinical trial participants. In addition, our competitors have ongoing clinical trials for product candidates that could be competitive with our product candidates. As a result, potential clinical trial sites may elect to dedicate their limited resources to participation in our competitors' clinical trials and not ours, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is affected by other factors including:

- severity of the disease under investigation;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of the company to decline and limit our ability to obtain additional financing. Our inability to enroll a sufficient number of patients in our confirmatory Phase 3 clinical trials of ataluren or any of our other clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

If serious adverse or inappropriate side effects are identified during the development of ataluren or any other product candidate, we may need to abandon or limit our development of that product candidate.

All of our product candidates are in clinical or preclinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development 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 side effects that prevented further development of the compound.

For example, although we did not observe a pattern of liver enzyme elevations in our Phase 2 or Phase 3 clinical trials of ataluren, we did observe modest elevations of liver enzymes in some subjects in one of our Phase 1 clinical trials. These elevated enzyme levels did not require cessation of ataluren administration, and enzyme levels typically normalized after completion of the treatment phase. We did not observe any increases in bilirubin, which can be associated with serious harm to the liver, in the Phase 1 clinical trial.

In addition, in our completed Phase 3 clinical trial of ataluren for the treatment of nmCF, five adverse events in the ataluren arm of the trial that involved the renal system led to discontinuation. As compared to the placebo group, the ataluren treatment arm also had a higher incidence of adverse events of creatinine elevations, which can be an indication of impaired kidney function. In the ataluren treatment arm, more severe clinically meaningful creatinine elevations were reported in conjunction with cystic fibrosis pulmonary exacerbations. These creatinine elevations were associated with concomitant treatment with antibiotics associated with impaired kidney functions, such as aminoglycosides or vancomycin. This led to the subsequent prohibition of concomitant use of ataluren and these antibiotics, which was successful in addressing this issue in the clinical trial. If patients in the ataluren arm of a confirmatory Phase 3 clinical trial for the treatment of nmCF exhibit clinically meaningful creatinine elevations, the EMA or the FDA might not approve ataluren for this indication or could require that we instruct physicians to frequently monitor patients for these abnormalities or impose other conditions, which may be an impediment to the use of ataluren because of concerns related to its safety and convenience.

Further, in 2011, we suspended development of our oncology product candidate PTC299, an inhibitor of production of vascular endothelial growth factor, or VEGF, in part because of two cases of severe liver toxicity that occurred in our clinical trials of PTC299 and in part because of our limited resources available at that time.

Our focus on the discovery and development of product candidates that target post-transcriptional control processes is unproven, and we do not know whether we will be able to develop any products of commercial value.

Our scientific approach focuses on the discovery and development of product candidates that target post-transcriptional control processes. While a number of commonly used drugs and a growing body of research validate the importance of post-transcriptional control processes in the origin and progression of a number of diseases, no existing drugs have been specifically designed to alter post-transcriptional control processes in the same manner as ataluren or our other product candidates. As a result, our focus on targeting these processes may not result in the discovery and development of commercially viable drugs that safely and effectively treat genetic disorders or other diseases. In addition, even if we are successful in developing and receiving regulatory approval for a commercially viable drug that treats an approved indication by targeting a particular post-transcriptional control process, we may not receive regulatory approval for additional indications. Furthermore, we may not

receive regulatory approval for product candidates that target different post-transcriptional control processes. If we fail to develop and commercialize viable drugs, we will not achieve commercial success.

Even if ataluren or any other product candidate 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.

If ataluren or any of our other product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. 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 potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects;
- the ability to offer our product candidates for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- any restrictions on concomitant use of other medications, such as a restriction that nmCF patients taking ataluren not also use chronic inhaled aminoglycoside antibiotics.

Our ability to negotiate, secure and maintain third-party coverage and reimbursement may be affected by political, economic and regulatory developments in the United States, the European Union and other jurisdictions. Governments continue to impose cost containment measures, and third-party payors are increasingly challenging prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. These and other similar developments could significantly limit the degree of market acceptance of ataluren or any of our other product candidates that receive marketing approval.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be successful in commercializing ataluren or any other product candidate if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale or marketing 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 establish our own sales and marketing capabilities and promote ataluren in the European Union and the United States with a targeted sales force if and when it is approved. There are risks involved with establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales and marketing services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little 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 and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and any products we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

Currently available treatments for Duchenne muscular dystrophy are only palliative. Although there are currently no marketed therapeutics approved to treat the underlying cause of nmDMD, there are other biopharmaceutical companies, including Prosensa Therapeutics and Sarepta Therapeutics, that are developing treatments for Duchenne muscular dystrophy based on a different scientific approach known as exon-skipping. Summit Corporation also has a product candidate in early clinical development designed to increase the production of the protein utrophin, which is functionally similar to dystrophin, to treat Duchenne muscular dystrophy. We believe that ataluren is the only product candidate in clinical trials that is designed to treat the underlying cause of nmDMD by restoring dystrophin activity.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products to manage the symptoms and side effects of cystic fibrosis. These products include Chiron Corporation's TOBI and Genentech, Inc.'s Pulmozyme. Although there are currently no marketed products approved to treat the underlying cause of nmCF, Vertex Pharmaceuticals' CFTR potentiator drug Kalydeco is approved by the FDA as a treatment for cystic fibrosis in patients six years of age and older who have a type of mutation in the CFTR gene known as a gating mutation. Vertex Pharmaceuticals also is developing two other product candidates for the treatment of cystic fibrosis in patients who have a type of mutation in the CFTR gene known as a process block mutation. We believe that ataluren is the only product candidate in clinical trials that is designed to treat the underlying cause of nmCF by restoring CFTR activity.

Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Our competitors may

develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. Our competitors may also obtain marketing approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

We believe that many competitors are attempting to develop therapeutics for the target indications of our product candidates, including academic institutions, government agencies, public and private research organizations, large pharmaceutical companies and smaller more focused companies.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory 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 and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to or necessary for our programs.

Even if we are able to commercialize ataluren or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations and practices that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. 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 might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and 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 to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize ataluren or any other product candidate successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the E.U. and U.S. healthcare industries and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for ataluren or any other product that we commercialize and, if coverage and reimbursement are available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining reimbursement for ataluren may be particularly difficult because of the higher prices typically associated with drugs directed at smaller populations of patients. In addition, third-party payors are likely to impose strict requirements for reimbursement of a higher priced drug. If reimbursement is not

available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the applicable regulatory authority. 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. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. In the European Union, reference pricing systems and other measures may lead to cost containment and reduced prices. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for any 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 the related litigation;
- increased insurance costs, or an ability to maintain appropriate insurance coverage;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We have product liability insurance that covers our clinical trials up to a $5.0 million annual aggregate limit and subject to a per claim deductible. The amount of insurance that we currently hold may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage when and if we begin commercializing ataluren or any other product candidate that receives marketing approval. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

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 have a material adverse effect on the success of 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. Our operations currently, and may in the future, involve the use of hazardous and flammable materials, including chemicals and medical and biological materials, and produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and wastes, we cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials or disposal of hazardous wastes, we could be held liable for any resulting damages, and any liability could exceed our resources.

Although 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, this insurance may not provide adequate coverage against potential liabilities. We also maintain liability insurance for some of these risks, but our policy excludes pollution and has a coverage limit of $5.0 million.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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 focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. For example, we initiated separate Phase 2 clinical trials of ataluren for the treatment of hemophilia in 2009 and the metabolic disorder methylmalomic acidemia in 2010, but then suspended these clinical trials to focus on the development of ataluren for nmDMD and nmCF when we found variability in the assays used in these trials and preliminary data from these trials did not indicate definitive evidence of activity. 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 products.

We have based our research and development efforts on small-molecule drugs that target post-transcriptional control processes. Notwithstanding our large investment to date and anticipated future expenditures in proprietary technologies, including GEMS and our alternative splicing technology, which we use in the discovery of these molecules, we have not yet developed, and may never successfully develop, any marketed drugs using this approach. As a result of pursuing the development of product candidates using our proprietary technologies, we may fail to develop product candidates or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development.

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 such product candidate.

Risks Related to our Dependence on Third Parties

Use of third parties to manufacture our product candidates may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities for the production of clinical or commercial supplies of our product candidates. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We currently rely on third parties for supply of the active pharmaceutical ingredients in our product candidates. Our strategy is to outsource all manufacturing of our product candidates and products to third parties.

We do not currently have any agreements with third-party manufacturers for the long-term commercial supply of any of our product candidates. We obtain our supply of the bulk drug substance for ataluren from two third-party manufacturers. We engage a separate manufacturer to provide fill and finish services for the finished product that we are using in our clinical trials of ataluren. We may be unable to conclude agreements for commercial supply with third-party manufacturers, or may be unable to do so on acceptable terms.

Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practice, or cGMP, regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

If the third parties that we engage to manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, we likely would experience delays in advancing these trials while we identify and qualify replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.

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 develop product candidates and commercialize any products that receive regulatory approval on a timely and competitive basis.

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We do not independently conduct clinical trials for our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to perform this function. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, 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 Good Clinical Practices, or GCP, 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. We also are required to register ongoing 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. Similar GCP and transparency requirements apply in the European Union. Failure to comply with such requirements, including with respect to clinical trials conducted outside the European Union, can also lead regulatory authorities to refuse to take into account clinical trial data submitted as part of an MAA.

For example, in the first half of 2013 inspectors acting at the request of the EMA conducted GCP inspections of selected clinical sites from our completed Phase 2b clinical trial of ataluren for the treatment of nmDMD and our clinical trial site relating to our pending MAA for conditional approval of ataluren for the treatment of nmDMD. Following these inspections, we received inspection reports containing a combination of critical and major findings. These findings relate to waivers we granted to admit patients to our Phase 2b clinical trial of ataluren for the treatment of nmDMD in advance of formal approval of protocol amendments that would have established their eligibility for the trial, as well as our oversight of our trial sites and the completeness or sufficiency of clinical trial documentation. In response to these findings, we described to the EMA the enhanced internal procedures and controls we have implemented, and the internal quality assurance department we have established, since the conclusion of our Phase 2b clinical trial of ataluren for the treatment of nmDMD. In addition, we proposed corrective action plans to address the inspectors' specific findings. If we do not meet our commitment to the corrective actions we proposed to the EMA, we may face additional consequences, including rejection of data or other direct action by national regulatory authorities, which could require us to conduct additional clinical trials or other supportive studies to obtain EMA approval of ataluren for the treatment of nmDMD.

Furthermore, third parties that we rely on for our clinical development activities may also have relationships with other entities, some of which may be our competitors. 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 will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Our product development costs will increase if we experience delays in testing or obtaining marketing approvals.

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 our products, producing additional losses and depriving us of potential product revenue.

We currently depend, and expect to continue to depend, on collaborations with third parties for the development and commercialization of some of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

For each of our product candidates, we plan to evaluate the merits of retaining commercialization rights for ourselves or entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies, such as our collaborations with Roche and the SMA Foundation, for our spinal muscular atrophy program. We generally plan to seek collaborators for the development and commercialization of product candidates that have high anticipated development costs, are directed at indications for which a potential collaborator has a particular expertise, or involve markets that require a large sales and marketing organization to serve effectively. Our likely collaborator(s) for any marketing, distribution, development, licensing or broader collaboration arrangements may include: large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and/or biotechnology companies.

We will have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' desire and abilities to successfully perform the functions assigned to them in these arrangements. In particular, the successful development of a product candidate from our spinal muscular atrophy program will initially depend on the success of our collaborations with the SMA Foundation and Roche, including whether Roche pursues clinical development of any compounds identified under the collaborations.

Collaborations involving our product candidates, including our collaborations with the SMA Foundation and Roche, pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- 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 diverts resources or creates 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;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- 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;
- 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;
- disputes may arise between the collaborator and us as to the ownership of intellectual property arising during the collaboration;

- we may grant exclusive rights to our collaborators, which would prevent us from collaborating with others;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; 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.

Collaborators have terminated collaborations with us in the past. For example, in 2008, we entered into a collaboration with Genzyme Corporation for the development and commercialization of ataluren under which we granted to Genzyme rights to commercialize ataluren in all countries other than the United States and Canada. In 2011, we restructured the collaboration and regained worldwide rights to ataluren, with Genzyme obtaining an option to commercialize ataluren in indications other than nmDMD outside the United States and Canada. In 2012, this option expired without being exercised by Genzyme and the collaboration terminated.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

If we are not able to establish additional collaborations, we may have to alter our development and commercialization plans.

Our product development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate further with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

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 design or results of clinical trials, the likelihood of approval by regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge; and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

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 a product candidate, 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 fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are a party to a number of license agreements and expect to enter into additional licenses in the future. Our existing licenses impose, and we expect that future licenses will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by these agreements, which could materially adversely affect the value of the product candidate being developed under such license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms, or cause us to lose rights in important intellectual property or technology.

We have also received grant funding for some of our development programs from philanthropic organizations and patient advocacy groups pursuant to agreements that impose development and commercialization diligence obligations on us. If we fail to comply with these obligations, the applicable organization could require us to grant to the organization exclusive rights under certain of our intellectual property, which could materially adversely affect the value to us of product candidates covered by that intellectual property even if we are entitled to a share of any consideration received by such organization in connection with any subsequent development or commercialization of the product candidates.

Some of our patented technology was developed with U.S. federal government funding. When new technologies are developed with U.S. government funding, the government obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise "march-in" rights to use or allow third parties to use our patented technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government and U.S. government funding must be disclosed in any resulting patent applications. Furthermore, our rights in such inventions are subject to government license rights and certain restrictions on manufacturing products outside the United States.

Risks Related to our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products 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 technology and products. We seek to protect our proprietary position by filing patent applications in the United States and in certain foreign jurisdictions related to our novel technologies and product candidates that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, if we license technology or product candidates from third parties in the future, these license agreements may not permit us to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering this intellectual property. These agreements could also give our licensors the right to enforce the licensed patents without our involvement, or to decide not to enforce the patents at all. Therefore, in these circumstances, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and 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 and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and 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.

The laws of foreign countries may not protect our rights to the same extent 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 U.S. law does. In addition, we may not pursue or obtain patent protection in all major markets. 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 know with certainty whether 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, we may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office or become involved in opposition, derivation, reexamination, inter partes review, post grant review, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

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 owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. In addition, other companies may attempt to circumvent any regulatory data protection or market exclusivity that we obtain under applicable legislation, which may require us to allocate significant resources to preventing such circumvention. Legal and regulatory developments in the European Union and elsewhere may also result in clinical trial data submitted as part of an MAA becoming publicly available. Such developments could enable other companies to circumvent our intellectual property rights and use our clinical trial data to obtain marketing authorizations in the European Union and in other jurisdictions. Such developments may also require us to allocate significant resources to prevent other companies from circumventing or violating our intellectual property rights. Our attempts to prevent third parties from circumventing our intellectual property and other rights may ultimately be unsuccessful. We may also fail to take the required actions or pay the necessary fees to maintain our patents.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate 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. 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. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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 claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the intellectual property and other proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, inter partes review or post-grant review proceedings before the U.S. Patent and Trademark Office. The risks of being involved in such litigation and proceedings may also increase as our product candidates approach commercialization, and as we gain greater visibility as a public company. Third parties may assert infringement claims against us based on existing or future intellectual property rights. We may not be aware of all such intellectual property rights potentially relating to our product candidates. For example, we have not conducted a recent freedom-to-operate search or analysis for ataluren. Any freedom-to-operate search or analysis previously conducted may not have uncovered all relevant patents and patent applications, and there may be pending or future patent applications that, if issued, would block us from commercializing ataluren. Thus, we do not know with certainty whether ataluren, any other product candidate, or our commercialization thereof, does not and will not infringe any third party's intellectual property.

If we are found to infringe a third party's intellectual property rights, or in order to avoid or settle litigation, we could be required to obtain a license to continue developing and marketing our products and technology. 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, and could require us to make substantial payments. We could be forced, including by court order, to cease commercializing the infringing technology or product. 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 or other intellectual property right. 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.

For example, it is possible that one or more third parties might bring a patent infringement or other legal proceeding against us regarding ataluren. We are aware of an issued U.S. patent and international patent applications that purport to disclose or contain claims to chemical scaffolds that are sufficiently broad that they could be read to encompass ataluren, even though neither the issued U.S. patent nor any of the international patent applications specifically discloses ataluren. In order to successfully challenge the validity of any issued U.S. patent, we would need to overcome a presumption of validity. This burden is a high one requiring us to present clear and convincing evidence as to the invalidity of these claims. There is no assurance that a court would find these claims to be invalid. In addition, we believe that our testing of ataluren in clinical trials for the purpose of seeking FDA approval would be a valid defense against any infringement claims in the United States based on the availability of a statutory exemption. However, there can be no assurance that our interpretation of the statutory exemption would be upheld, and the statutory exemption would only cover our preclinical research activities, and not the commercialization of ataluren.

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

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. 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 employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees 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. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our 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 or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and could distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could 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 substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. 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, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets or that the agreements we have executed will provide adequate protection. 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, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be obtained or independently developed by a competitor, our competitive position would be harmed.

We have not yet registered our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

Our trademark applications may not be allowed for registration, and our registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the U.S. Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would.

Risks Related to Regulatory Approval of our Product Candidates

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates, including ataluren, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market ataluren or any of our other product candidates from regulatory authorities in any jurisdiction. In 2011, we submitted a new drug application, or NDA, to the FDA for approval of ataluren for the treatment of nmDMD. The FDA refused to file this NDA on the grounds that the NDA did not contain substantial evidence of effectiveness based on the single placebo controlled Phase 2b clinical trial conducted to date.

We have only limited experience in filing and supporting the applications necessary to obtain marketing approvals for product candidates and expect to rely on third-party contract research

organizations to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Regulatory authorities may determine that ataluren or any of our other product candidates are not effective or only moderately effective, or have undesirable or unintended side effects, toxicities, safety profiles or other characteristics that preclude us from obtaining marketing approval or that prevent or limit commercial use.

The process of obtaining marketing approvals is expensive, 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. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, 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 ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

We may not be able to obtain orphan drug exclusivity for our product candidates. If our competitors are able to obtain orphan drug exclusivity for their products that are the same drug as our product candidates, or can be classified as a similar medicinal product within the meaning of E.U. law, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the European Union and the United States, may designate drugs for relatively small patient populations as orphan drugs. We have obtained orphan drug designations from the EMA and from the FDA for ataluren for the treatment of nmDMD and nmCF. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of market exclusivity, which, subject to certain exceptions, precludes the EMA from accepting another marketing application for a similar medicinal product or the FDA from approving another marketing application for the same drug for the same indication for that time period. The applicable market exclusivity period is ten years in the European Union and seven years in the United States. The E.U. exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation, including if the drug is sufficiently profitable so that market exclusivity is no longer justified.

In the European Union, a "similar medicinal product" is a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. For a drug such as ataluren, which is composed of small molecules, the FDA defines "same drug" as a drug that contains the same active moiety and is intended for the same use. Obtaining orphan drug exclusivity for ataluren for these indications, both in the European Union and in the United States, may be important to the product candidate's success. If a competitor obtains orphan drug exclusivity for and approval of a product with the same indication as ataluren before we do and if the competitor's product is the same drug or a similar medicinal product as ours, we could be excluded from the market. Even if we obtain orphan drug exclusivity for ataluren for these indications, we may not be able to maintain it. For example, if a competitive product that is the same drug or a similar medicinal product as our product candidate is shown to be clinically superior to our product candidate, any orphan drug exclusivity we have obtained will not block the

approval of such competitive product. In addition, orphan drug exclusivity will not prevent the approval of a product that is the same drug as our product candidate if the FDA finds that we cannot assure the availability of sufficient quantities of the drug to meet the needs of the persons with the disease or condition for which the drug was designated.

The fast track designation for ataluren may not actually lead to a faster development or regulatory review or approval process.

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. We have obtained a fast track designation from the FDA for ataluren for the treatment of nmDMD. However, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw our fast track designation if the FDA believes that the designation is no longer supported by data from our clinical development program. Our fast track designation does not guarantee that we will qualify for or be able to take advantage of the FDA's expedited review procedures.

Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. The FDA's requirements include submissions of safety and other post-marketing information and reports, registration requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and complaints and corresponding maintenance of records and documents, requirements regarding the distribution of samples to healthcare professionals 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 may be subject to significant conditions of approval, including the requirement of risk evaluation and mitigation strategy, or REMS. The FDA also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling and regulatory requirements. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not comply with the laws governing promotion of approved drugs, we may be subject to enforcement action for off-label promotion. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to civil and criminal penalties, investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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

- restrictions on such products, manufacturers or manufacturing processes;
- changes to or restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to implement a REMS;
- requirements to conduct post-marketing studies or clinical trials;

- warning 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;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions; or
- the imposition of civil or criminal penalties.

Non-compliance with E.U. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Failure to obtain or maintain regulatory approval in international jurisdictions would prevent us from marketing our products abroad.

In order to market and sell ataluren and our other products in the European Union and many other jurisdictions, we 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 from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, some countries outside the United States require approval of the sales price of a drug before it can be marketed. In many countries, separate procedures must be followed to obtain reimbursement. We may not obtain marketing, pricing or reimbursement approvals 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 may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. Regulatory approvals in countries outside the United States do not ensure pricing approvals in those countries or in any other countries, and regulatory approvals and pricing approvals do not ensure that reimbursement will be obtained.

Our ability to obtain and maintain conditional marketing authorizations in the European Union is limited to specific circumstances and subject to several conditions and obligations. Conditional marketing authorizations based on incomplete clinical data may be granted for a limited number of listed medicinal products for human use, including products designated as orphan medicinal products under E.U. law, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, including with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data, may be specified in the conditional marketing authorization. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional

or modified conditions. Even if we obtain conditional approval for ataluren for the treatment of either or both of nmDMD and nmCF, we may not be able to renew such conditional approval. A failure to renew any conditional approval that we obtain prior to full approval for the applicable indication would prevent us from continuing to market ataluren for such indication.

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

In some countries, particularly the member states 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. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various E.U. member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidate to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on prices or reimbursement levels within the country of publication and other countries. 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 adversely affected.

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

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates, including ataluren, for which we obtain marketing approval. Our future arrangements with customers, healthcare providers and professionals and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, and are not limited to, the following:

- The federal healthcare anti-kickback statute prohibits, among other things, persons 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 under federally funded healthcare programs such as Medicare and Medicaid. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others. Several other countries, including the United Kingdom, have enacted similar anti-kickback, fraud and abuse, and healthcare laws and regulations.

- The federal False Claims Act imposes civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for 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 government and qui tam relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be submitted to the government. There is also a separate false claims provision imposing criminal penalties.

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

- HIPAA also imposes criminal liability for 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 Physician Sunshine Act requirements under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, referred to together as the Affordable Care Act, require 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 made to or at the request of covered recipients, such as physicians and teaching hospitals, and physician ownership and investment interests in such manufacturers. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and 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.

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, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Exclusion, suspension and debarment from government funded healthcare programs would significantly impact our ability to commercialize, sell or distribute any drug. If any of the physicians or other providers or entities with whom we expect to do business are 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.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we 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 prevent or delay marketing approval of ataluren or any of our other product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates, including ataluren, for which we obtain marketing approval.

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.

In March 2010, President Obama signed into law the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Affordable Care Act revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with health care practitioners. We will not know the full effects of the Affordable Care Act until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the full effect of the Affordable Care Act, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

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 U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Dr. Stuart W. Peltz, our co-founder and Chief Executive Officer, and the other principal members of our executive and scientific teams. Although we have formal employment agreements with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain "key person" insurance on any of our executive officers. The loss of the services of any of these persons might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel 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. In addition, 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 employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We expect to expand our development, regulatory and sales and marketing capabilities, 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 development, regulatory affairs and sales and marketing. To manage our anticipated future growth, 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. 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 recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to our Common Stock

Our executive officers, directors and principal stockholders have the ability to control or significantly influence all matters submitted to stockholders for approval.

Our executive officers, directors and principal stockholders, in the aggregate, beneficially own shares representing approximately 56.0% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control or significantly influence 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 or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms 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 our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing 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:

- provide for a classified board of directors such that not all members of the board are 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 stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- 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 stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

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

Our shares of common stock began trading on The NASDAQ Global Select Market on June 20, 2013. Given the limited trading history of our common stock, there is a risk that an active trading market for our common stock will not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of our stockholders to sell their shares.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

Our stock price may be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased it. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of ataluren and any other product candidate that we develop;
- 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;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- 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.

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 until December 31, 2018, provided that, if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any June 30 before that time or if we have annual gross revenues of $1 billion or more in any fiscal year, we would cease to be an emerging growth company as of December 31 of the applicable year. We also would cease to be an emerging growth company if we issue more than $1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend 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 in the assessment of our internal control over financial reporting;
- 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 shareholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this Annual Report on Form 10-K.We cannot predict whether investors will find our common stock less attractive if we rely 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.

In addition, the JOBS Act also provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to delay such adoption of new or revised accounting standards, and as a result, we may not comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for public companies that are not emerging growth companies. As a result of such election, our financial statements may not be comparable to the financial statements of other public companies.

We are currently incurring and expect to continue to incur increased costs as a result of operating as a public company, and our management is and will continue to be required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an "emerging growth company," we incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, the Dodd-Frank Act, the listing requirements of The NASDAQ Global Select 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. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more

time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

However, for as long as we remain an emerging growth company, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies as described in the preceding risk factor. Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, as an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm until we are no longer an emerging growth company. To achieve compliance with 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, potentially 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 we will not be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our capital in the foreseeable future, capital appreciation, if any, will be our stockholders sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders sole source of gain for the foreseeable future.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop 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 intend to sell shares, could reduce the market price of our common stock. A significant number of our shares are currently restricted as a result of securities laws or lock-up agreements. Moreover, certain holders of our common stock have rights, subject to some 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. We also have registered on a Form S-8 registration statement all shares of common stock that we may issue under our equity compensation plans. As a result, these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. In addition, certain of our employees, executive officers and directors have entered into, or may enter into, Rule 10b5-1 plans providing for sales of shares of our Common Stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the employee, director or officer when entering into the plan, without further direction from the employee, officer or director. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers and directors may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information. Following our initial public offering in June 2013, certain of our employees, directors and executive officers entered

into Rule 10b5-1 plans in 2013 with respect to sales of shares of restricted common stock granted or otherwise acquired in 2013. As of February 27, 2014, an aggregate of 220,794 shares of our common stock held by 10 of our directors and executive officers were subject to these Rule 10b5-1 plans.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our principal facilities consist of approximately 82,798 square feet of research and office space located at 100, 200 and 250 Corporate Court, Middlesex Business Center, South Plainfield, New Jersey, that we occupy under a lease that expires in 2019, with two consecutive five-year renewal options to renew the lease after 2019. We have subleased 11,171 square feet of our space in 250 Corporate Court for a two-year term expiring in October 2014.

Item 3. Legal Proceedings

From time to time in the ordinary course of our business, we are subject to claims, legal proceedings and disputes as a result of patients seeking to participate in our clinical trials or otherwise gain access to our product candidates. These matters are subject to various uncertainties, and it is possible that some of these matters may be resolved unfavorably to us. However, we believe that the ultimate outcome of the matters that are currently pending will not have a material adverse impact on our business.

Item 4. Mine Safety Disclosures

None.

PART II

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

Market Information

Our common stock has been publicly traded on the NASDAQ Global Select Market under the symbol "PTCT" since June 20, 2013. Prior to that time, there was no public market for our common stock.

The following table sets forth, for the periods indicated, the high and low sales prices per share of our common stock as reported on the NASDAQ Global Select Market:

	High	Low
Second Quarter	17.92	13.03
(June 20, 2013 - June 30, 2013)		
Third Quarter	24.38	13.88
Fourth Quarter	22.42	13.15

Holders

As of March 4, 2014, there were 79 holders of record of our common stock. This number does not include beneficial owners whose shares are held in street name.

Dividends

We have never declared or paid cash dividends on our common stock, and we do not expect to pay any cash dividends on our common stock in the foreseeable future.

Recent Sales of Unregistered Securities

Set forth below is information regarding securities sold by us during 2013 that were not registered under the Securities Act of 1933, as amended, or the Securities Act. Also included is the consideration, if any, received by us for the securities and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

Issuances of securities

In May 2013, we issued and sold 375,000 shares of our series four senior preferred stock, at a price per share of $12.00, for an aggregate purchase price of $4,500,000.

In March 2013, we issued and sold an aggregate of 4,497,035 shares of our series four senior preferred stock, at a price per share of $12.00, for an aggregate purchase price of $53,964,420. In addition, we issued an aggregate of 502,919 shares of our series four senior preferred stock upon conversion of the convertible promissory notes described below that we originally issued in January and February 2013. All outstanding shares of our series four senior preferred stock automatically converted into an aggregate of 4,999,954 shares of common stock at the closing of our initial public offering in June 2013. In connection with the series four senior preferred stock financing, we also effected a reclassification of all of the outstanding shares of our series one preferred stock, series two preferred stock and series three preferred stock into an aggregate of 6,700,487 shares of series five junior preferred stock. In addition, we issued an aggregate of 2,095,515 shares of our series five junior preferred stock upon the automatic exercise of the preferred stock warrants described below that we originally issued in January 2013. All outstanding shares of our series five junior preferred stock automatically converted into an aggregate of 8,796,002 shares of our common stock at the closing of our initial public offering in June 2013.

In January and February 2013, we issued convertible promissory notes in an aggregate principal amount of $6,000,000. These promissory notes converted into an aggregate of 502,919 shares of series four senior preferred stock in connection with the series four senior preferred stock financing in March 2013. In connection with this financing, in January 2013, we issued to holders of the convertible promissory notes described above warrants to purchase an aggregate of 515,186 shares of series one preferred stock, at an exercise price of $0.01 per share, and warrants to purchase an aggregate of 2,012,489 shares of series two preferred stock, at an exercise price of $0.01 per share. In connection with our series four senior preferred stock financing, in March 2013, all outstanding warrants to purchase series one preferred stock and series two preferred stock that were issued in January 2013 were automatically exercised for shares of series five junior preferred stock.

No underwriters were involved in the foregoing issuances of securities. The securities described in this section were issued to accredited investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The recipients of securities in the transactions described above represented that they were accredited investors and were acquiring the securities for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time and appropriate legends were affixed to the instruments representing such securities issued in such transactions The purchasers received written disclosures that the securities had not been

registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

Stock option and other equity awards

During the year ended December 31, 2013, we issued to certain employees, directors and consultants options to purchase an aggregate of 2,117,113 shares of common stock at a weighted-average exercise price of $11.29 per share.

In May 2013, we issued an aggregate of 396,200 shares of our common stock to our executive officers, directors, advisors and certain other employees in consideration of services provided or to be provided.

In March 2013, we issued an aggregate of 735,324 shares of our common stock to our executive officers, directors, advisors and certain other employees and options to purchase 4,613 shares of our common stock to certain of our directors, in each case in consideration for services provided or to be provided.

These equity awards were issued prior to the closing of our initial public offering pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption from the registration requirements of the Securities Act provided by Rule 701 promulgated under the Securities Act or pursuant to Section 4(2) under the Securities Act relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

Purchase 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 Registered Securities

On June 25, 2013, we closed our initial public offering of 9,627,800 shares of our common stock, including 1,255,800 shares of our common stock pursuant to the exercise by the underwriters of an over-allotment option, at a public offering price of $15.00 per share for an aggregate offering price of approximately $144.4 million. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-188657), which was declared effective by the SEC on June 19, 2013.

We received aggregate net proceeds from the offering of approximately $131.6 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. None of the underwriting discounts and commissions or other offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10 percent or more of our common stock or to any affiliates of ours.

We have invested the net proceeds from the offering in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities. There has been no material change in our planned use of the net proceeds from the offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act.

Item 6. Selected Financial Data

The following table sets forth certain financial data with respect to our business. The selected consolidated financial data is derived from, and should be read in conjunction with, our Consolidated Financial Statements and related Notes and Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations," and other information contained elsewhere in this Annual Report on Form 10-K.

Statement of operations data
(in thousands, except share and per share data)

	Year ended December 31,		
	2013	2012	2011
Revenues:			
Collaboration revenue	$ 31,326	$ 28,779	$ 98,961
Grant revenue	3,370	5,167	6,451
Total revenues	34,696	33,946	105,412
Operating expenses:			
Research and development	54,875	46,139	58,677
General and administrative	25,219	14,615	16,153
Total operating expenses	80,094	60,754	74,830
(Loss) income from operations	(45,398)	(26,808)	30,582
Interest expense, net	(6,084)	(1,210)	(2,444)
Loss on extinguishment of debt	(130)	—	—
Other income, net	38	1,783	461
(Loss) income from operations before tax benefit	(51,574)	(26,235)	28,599
Tax benefit	—	—	2,306
Net (loss) income	(51,574)	(26,235)	30,905
Deemed dividend	(18,249)	—	—
Gain on exchange of convertible preferred stock in connection with recapitalization	3,391	159,954	—
Less beneficial conversion charge	—	(378)	—
Net (loss) income attributable to common stockholders	$ (66,432)	$ 133,341	$ 30,905
Net (loss) income attributable to common stockholders per share:			
Basic	$ (5.18)	$ 219.76	$ 23.95
Diluted	$ (5.18)	$ 42.50	$ 4.55
Weighted-average shares outstanding:			
Basic	12,829,411	3,328	1,089
Diluted	12,829,411	17,205	5,729

(1) See Note 8 to our audited financial statements appearing at the end of this prospectus regarding the calculation of net income (loss) per share.

Balance sheet data
(in thousands)

	As of December 31,		
	2013	2012	2011
Cash, cash equivalents and marketable securities	$ 142,468	$ 2,726	$ 28,431
Working capital	131,891	(23,564)	(10,091)
Total assets	151,903	13,072	44,148
Long-term debt, including current portion	49	4,883	11,689
Convertible preferred stock	—	80,824	214,380
Accumulated deficit	(328,798)	(277,225)	(250,612)
Total stockholders' equity (deficit)	136,542	(99,641)	(238,605)

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

The following discussion of our financial condition and results of operations should be read in conjunction with our financial statements and the notes to those financial statements appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth in Part I, Item 1A. Risk Factors, of this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a biopharmaceutical company focused on the discovery and development of orally administered, proprietary small molecule drugs that target post-transcriptional control processes. Our lead product candidate is ataluren for the treatment of patients with genetic disorders that arise from a type of genetic mutation known as a nonsense mutation. In addition to ataluren, we have a pipeline of product candidates that are in preclinical development. Our preclinical and discovery programs are focused on the development of new treatments for multiple therapeutic areas, including neuromuscular disease, oncology and infectious disease.

We have initiated a confirmatory Phase 3 clinical trial of ataluren for the treatment of Duchenne muscular dystrophy caused by nonsense mutations, or nmDMD. We refer to this trial as the Ataluren Confirmatory Trial in DMD, or ACT DMD. We dosed the first patient in this trial in April 2013. In October 2012, we submitted a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for conditional approval of ataluren for the treatment of nmDMD. In January 2014, EMA's Committee for Medicinal Products for Human Use, or CHMP, adopted a negative opinion recommending the refusal of the granting of the conditional marketing authorization for ataluren for the treatment of nmDMD. We have requested a re-examination of the CHMP opinion and currently expect a final outcome in the second quarter of 2014. We plan to complete our confirmatory Phase 3 ACT DMD clinical trial before applying for marketing approval from the U.S. Food and Drug Administration, or FDA. We are also planning a Phase 3 clinical trial of ataluren for the treatment of cystic fibrosis caused by nonsense mutations, or nmCF. We plan to begin dosing patients in this trial in the first half of 2014. In addition, we are pursuing early access programs for ataluren for nmDMD patients in selected territories that support reimbursement for such programs. We also plan to pursue additional indications for ataluren beyond nmDMD and nmCF and expect to initiate a proof-of-concept study for a third indication in 2014.

To date, we have financed our operations primarily through our public offering in February 2014, our initial public offering in June 2013, private placements of our preferred stock, collaborations, bank debt and convertible debt financings and grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product

candidates. As of December 31, 2013, we had an accumulated deficit of $328.8 million. We had a net loss of $51.6 million for the year ended December 31, 2013 and a net loss of $26.2 million for the year ended December 31, 2012.

We anticipate that our expenses will increase substantially in connection with initiating and continuing confirmatory Phase 3 clinical trials for ataluren for the treatment of nmDMD and nmCF, commencing early access programs for ataluren for nmDMD patients in selected territories and seeking marketing approval for ataluren for these indications in the European Union and the United States. If we obtain marketing approval of ataluren for either nmDMD or nmCF, we also expect to incur significant sales, marketing, distribution and manufacturing expenses, as well as ongoing research and development expenses for our other product candidates. The timing of commercialization expenses for ataluren depends in part on whether we receive conditional approval for ataluren for either or both of nmDMD and nmCF. Furthermore, as a result of our initial public offering in June 2013, we have incurred and expect to continue to incur additional costs associated with operating as a public company. Although we cannot reasonably estimate the amount of these additional public company costs, we expect that these costs will include significant legal, accounting, investor relations and other expenses that we did not incur as a private company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts. We will need to generate significant revenues to achieve and sustain profitability, and we may never do so.

Financial Operations Overview

Revenues

To date, we have not generated any product sale revenues. Based on our current plans, we do not expect to generate significant product revenues unless and until we obtain marketing approval for, and commercialize, ataluren for the treatment of nmDMD or nmCF. The timing of any product revenues depends in part on whether we receive conditional approval for ataluren for either or both of nmDMD and nmCF. Our revenues to date have consisted of collaborative agreements revenues and grant revenues.

We have ongoing collaborations with F. Hoffman La Roche Ltd and Hoffman La Roche Inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or SMA Foundation, for our spinal muscular atrophy program and early stage discovery arrangements with other institutions.

Genzyme. In July 2008, we entered into an exclusive global collaboration with Genzyme to develop and commercialize ataluren for the treatment of genetic disorders due to nonsense mutations. Under the terms of this agreement, we granted Genzyme rights to commercialize ataluren in all countries except the United States and Canada, which rights we retained. Genzyme made a nonrefundable, upfront payment to us of $100.0 million in July 2008, which we then began recognizing over the estimated period of performance under the arrangement.

In August 2011, we announced a restructuring of the agreement with Genzyme. Under the terms of the restructuring, we regained worldwide rights to ataluren and Genzyme made an additional payment of $7.5 million to us in exchange for an option to commercialize ataluren in indications other than nmDMD outside the United States and Canada. In March 2012, Genzyme declined to exercise the option, the option expired and the collaboration terminated.

We evaluated the August 2011 restructuring of the agreement and determined it to be a material modification to the original agreement for financial reporting purposes pursuant to the revised multiple

element revenue recognition guidance. We reevaluated the collaboration arrangement under this revised guidance and recorded a one-time adjustment to our deferred revenue balance to reflect the value of the remaining performance obligations under the restructured agreement as represented by the best estimate of selling price. As a result of this reevaluation, we recognized approximately $79.0 million of existing deferred revenue as of the modification date.

Roche and the SMA Foundation. In November 2011, we entered into a license and collaboration agreement with Roche and the SMA Foundation pursuant to which we are collaborating with Roche and the SMA Foundation to further develop and commercialize compounds identified under our spinal muscular atrophy sponsored research program with the SMA Foundation, as described below, and to research, develop and commercialize other small molecule compounds with potential for therapeutic use in patients with spinal muscular atrophy. Pursuant to the license and collaboration agreement, Roche paid us an upfront non-refundable payment of $30.0 million.

In August 2013, we announced the selection of a development candidate. The achievement of this milestone triggered a $10.0 million payment to us from Roche, which we recorded as collaboration revenue for the year ended December 31, 2013.

In January 2014, we initiated a Phase 1 clinical program, which triggered a $7.5 million milestone payment to us from Roche. Roche is responsible for pursuing clinical development of compounds from the program, consistent with a governance structure that includes representation from us and the SMA Foundation, and then commercialization of these compounds.

Grant revenue. We receive grant funding from various institutions and governmental bodies. The grants are typically for early discovery research, and generally the grant program lasts from two to five years.

Research and development expenses

Research and development expenses consist of the costs associated with our research activities, as well as the costs associated with our drug discovery efforts, conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings. Our research and development expenses consist of:

- external research and development expenses incurred under agreements with third party contract research organizations and investigative sites, third party manufacturing organizations and consultants;
- employee related expenses, which include salaries and benefits, including stock based compensation, for the personnel involved in our drug discovery and development activities; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment, and laboratory and other supplies.

We use our employee and infrastructure resources across multiple research projects, including our drug development programs. We track expenses related to our clinical programs and certain preclinical programs on a per project basis.

We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we initiate and continue confirmatory Phase 3 clinical trials of ataluren for the treatment of nmDMD and nmCF, continue our research activities in our preclinical programs and initiate clinical development of other product candidates. The timing and amount of these expenses will depend upon the outcome of our ongoing clinical trials and the costs associated with our planned clinical trials. The timing and amount of these expenses will also depend on the costs associated with potential future clinical trials of our product candidates and the related expansion of our research and

development organization, regulatory requirements, advancement of our preclinical programs and product candidate manufacturing costs.

The following table provides research and development expense for our most advanced principal product development programs.

	Year ended December 31,		
	2013	2012	2011
Ataluren	$ 30,270	$ 21,470	$ 30,231
Antibacterial	5,906	4,806	1,944
BMI1	1,172	4,413	5,084
Spinal muscular atrophy	2,776	3,029	7,444
Other research and preclinical	14,751	12,421	13,974
Total research and development	$ 54,875	$ 46,139	$ 58,677

The successful development of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our clinical trials and other research and development activities;
- the potential benefits of our product candidate over other therapies;
- our ability to market, commercialize and achieve market acceptance for any of our product candidates that we are developing or may develop in the future;
- clinical trial results;
- the terms and timing of regulatory approvals; and
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of ataluren or any other product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the EMA or FDA or other regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate will be required for the completion of clinical development of ataluren or any other product candidate or if we experience significant delays in enrollment in any our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and administrative expense

General and administrative expense consists primarily of salaries and other related costs for personnel, including stock based compensation expenses, in our executive, legal, business development, finance, accounting, information technology and human resource functions. Other general and administrative expenses include facility related costs not otherwise included in research and development expense; advertising and promotional expenses; costs associated with industry and trade shows; and professional fees for legal services, including patent related expenses, and accounting services.

We expect that general and administrative expense will increase in future periods as a result of increased payroll, expanded infrastructure, commercial operations, increased consulting, legal, accounting and investor relations expenses associated with being a public company and costs incurred to seek collaborations with respect to any of our product candidates, among other factors.

Interest expense, net

Interest expense, net consists of interest related to our secured debt facility and interest income earned on investments. In July 2013, we paid in full the outstanding principal and interest related to our secured debt facility.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in the notes to our financial statements appearing at the end of this prospectus, 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.

As an emerging growth company under the Jumpstart Our Business Startups Act of 2012, we have elected to delay the adoption of new or revised accounting standards until those standards would otherwise apply to private companies. As a result of this election, our financial statements may not be comparable to the financial statements of other public companies.

Revenue recognition

We recognize revenue when amounts are realized or realizable and earned. Revenue is considered realizable and earned when the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the price is fixed or determinable; and (4) collection of the amounts due are reasonably assured.

Our revenue is generated primarily through collaborative research and development and licensing agreements and grants.

The terms of these agreements typically include payments of one or more of the following: nonrefundable, upfront license fees; milestone payments; research funding; and royalties on future product sales. In addition, we generate service revenue through agreements that generally provide for fees for research and development services and may include additional payments upon achievement of specified events.

For existing collaborations entered into prior to the adoption in 2011 of the revised multiple element revenue recognition guidance described below, we recognize revenue consistent with the approach established at the inception of each arrangement. For these existing collaborations, where we have continued involvement, we recorded nonrefundable, upfront fees as deferred revenue and recognize revenue on a straight line basis as collaboration revenue over the expected performance period.

For new collaborations or for material modifications made to existing collaborations, in 2011, we adopted the updated multiple element revenue recognition guidance. Under this new guidance, all non-contingent arrangement consideration is allocated to the identified units of accounting based on their relative selling price at inception of the collaboration arrangement. We derive the selling price using a combination of internal subjective and available external objective information, such as comparable transactions. We recognize revenue commensurate with delivery, such as in the case with

delivery of a license, or ratably over the course of a service period, as appropriate, such as in the case of ongoing research and development activities.

We evaluate all contingent consideration earned, such as a milestone payment, using the criteria as provided by the Financial Accounting Standards Board, or FASB, guidance on the milestone method of revenue recognition. At the inception of a collaboration arrangement, we evaluate if milestone payments are substantive. The criteria requires that (1) we determine if the milestone is commensurate with either its performance to achieve the milestone or the enhancement of value resulting from our activities to achieve the milestone; (2) the milestone be related to past performance; and (3) the milestone be reasonable relative to all deliverable and payment terms of the collaboration arrangement. If these criteria are met then the contingent milestones can be considered as substantive milestones and will be recognized as revenue in the period that the milestone is achieved. We recognize royalties as earned in accordance with the terms of various research and collaboration agreements. If not substantive, the contingent consideration is allocated to the existing units of accounting based on relative selling price and recognized following the same basis previously established for the associated unit of accounting.

We recognize reimbursements for research and development costs under collaboration agreements as revenue as the services are performed. We record these reimbursements as revenue and not as a reduction of research and development expenses as we have the risks and rewards as the principal in the research and development activities.

Our principal obligation under our grant agreements is to conduct the internal or external research in the specific field funded by the grant. We determine, through the grant's normal research process, which research and development projects to pursue. We recognize grant revenues as the research activities are performed. If the grant includes an upfront payment, we defer the amount and recognize it as revenue as the expenditures are incurred.

Accrued expenses

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves communicating with our applicable personnel to identify 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 actual cost. The majority of our service providers invoice us monthly in arrears for services performed. 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. Examples of estimated accrued expenses include:

- fees paid to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of clinical trial materials; and
- professional service fees.

Share-based compensation

We expect to grant additional stock options that will result in additional share based compensation expense. Accordingly, we describe below the methodology we have employed to date in measuring such expenses. Following our initial public offering, which was completed in June 2013, stock option values have been determined based on the market price of our common stock.

Prior to becoming a public company, we used various valuation methodologies in accordance with the framework of the 2004 American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, or the AICPA Practice Aid, to estimate the fair value of our common stock. The methodologies included an option pricing method to estimate our underlying equity value, and a methodology that determined an estimated value under an initial public offering, or IPO, scenario and a sale scenario based upon an assessment of the probability of occurrence of each scenario. Each valuation methodology includes estimates and assumptions that require judgment. These estimates include assumptions regarding future performance, including the completion of clinical trials and the time to complete an IPO or sale of the company. As with any valuation, significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date. Factors that we considered in determining the fair value of our common stock include:

- pricing of private sales of our preferred stock;
- prior valuations of stock grants and preferred stock sales and the effect of events, including the progression of our product candidates, that have occurred between the time of the grants or sales;
- comparative rights and preferences of the security being granted compared to the rights and preferences of our other outstanding equity;
- comparative values of public companies discounted for the risk and limited liquidity provided for in the shares we are issuing;
- estimates and analysis provided by management and contemporaneous valuations;
- perspective provided by investment banks, including the likelihood of an initial public offering and our potential value in an initial public offering; and
- general economic trends and external market conditions affecting the biopharmaceutical industry.

We measure the cost of employee services received in exchange for an award of equity instruments based on the grant date fair value of the award. For service type awards, share-based compensation expenses is recognized on a straight-line basis over the period during which the employee is required to provide service in exchange for the entire award. For awards that vest or begin vesting upon achievement of a performance condition, we estimate the likelihood of satisfaction of the performance condition and recognize compensation expense when achievement of the performance condition is deemed probable using an accelerated attribution model.

The fair value of options is calculated using the Black Scholes option pricing model to determine the fair value of stock options on the date of grant based on key assumptions such expected volatility and expected term. As a new public company, we do not have sufficient history to estimate the volatility of our common stock price or the expected life of the options. We calculate expected volatility based on reported data for similar publicly traded companies for which historical information is available and will continue to do so until the historical volatility of our common stock is sufficient to measure expected volatility for future option grants.

Restricted stock awards are granted subject to certain restrictions, including service conditions. The grant date fair value of restricted stock awards, which is determined based upon the market value of our common stock on the grant date, is expensed over the vesting period.

The fair value of grants made in the years ended December 31, 2013, 2012 and 2011 was contemporaneously estimated on the date of grant using the following assumptions:

	Year ended December 31,		
	2013	2012	2011
Risk-free interest rate	0.85 - 1.90%	1.14%	2.40%
Expected volatility	87 - 89%	87%	87%
Expected term	6.00 - 6.25 years	6.00 - 6.25 years	6.00 - 6.25 years

We assumed no expected dividends for all grants. The weighted average grant date fair value per share was $8.23 for options granted during the year ended December 31, 2013, $160.65 for options granted during the year ended December 31, 2012 and $364.80 for options granted during the year ended December 31, 2011.

We use the "simplified method" to determine the expected term of options. Under this method, the expected term represents the average of the vesting period and the contractual term. The expected volatility of share options was estimated based on a historical volatility analysis of peers that were similar to us with respect to industry, stage of life cycle, size and financial leverage. The risk-free rate of the options is based on U.S. Government Securities Treasury Constant Maturities yields at the date of grant for a term similar to the expected term of the option.

We recognized share based compensation expense of approximately $8.4 million during the year ended December 31, 2013, $2.3 million during the year ended December 31, 2012 and $2.8 million during the year ended December 31, 2011.

We had total unrecognized compensation cost related to unvested share based compensation arrangements of $21.6 million as of December 31, 2013, $2.2 million as of December 31, 2012 and $4.0 million as of December 31, 2011. We expect to recognize this cost as compensation expense over the weighted average remaining service period of approximately 2.49 years.

Warrant liability

We classify as liabilities warrants to purchase our common stock with nonstandard antidilution provisions and warrants to purchase our preferred stock that include a put feature, regardless of the probability or likelihood that may conditionally obligate us to ultimately transfer assets, and record the estimated fair value of these warrants at each reporting period. We record as gain or loss any change in fair value of these warrants each reporting period in other income on our statement of operations.

Income taxes

As part of the process of preparing our financial statements, we are required to estimate our income taxes in each of the jurisdictions in which we operate. This process involves estimating our actual current tax expense together with assessing temporary differences resulting from differing treatments of items for tax and accounting purposes. These differences result in deferred tax assets and liabilities. As of December 31, 2013, we had federal net operating loss carryforwards of $259.4 million, which expire starting in 2021, and federal research and development credit carryforwards of $6.0 million, which expire starting in 2019. We also had state net operating loss carryforwards of $176.0 million, which expire starting in 2029, and state research and development credit carryforwards of $2.3 million, which expire starting in 2022. The Internal Revenue Code contains provisions that may limit the net operating loss and credit carryforwards available to be used in any given year given certain historical changes in the ownership interests of significant stockholders. At December 31, 2013, we recorded a full valuation allowance against our net deferred tax asset of approximately $132.5 million, as our management believes it cannot at this time conclude that it is more likely than not they will be realized. If we determine in the future that we will be able to realize all or a portion of our net

deferred tax asset, an adjustment to the deferred tax valuation allowance would increase net income in the period in which we make such a determination.

Results of Operations

Year ended December 31, 2013 compared to year ended December 31, 2012

(in thousands)	2013	2012	Change 2013 vs. 2012
Revenue	$ 34,696	$ 33,946	$ 750
Research and development expenses	54,875	46,139	8,736
General and administrative expenses	25,219	14,615	10,604
Interest expense, net	6,084	1,210	4,874
Loss on extinguishment of debt	130	—	130
Other income, net	38	1,783	(1,745)

Revenues. Revenues were $34.7 million for the year ended December 31, 2013, an increase of $0.8 million from revenues of $33.9 million for the year ended December 31, 2012. Collaboration revenue was $31.3 million for the year ended December 31, 2013, an increase of $2.5 million from collaboration revenues of $28.8 million for the year ended December 31, 2012. The increase primarily resulted from the achievement of a $10.0 million milestone related to the Roche agreement in July 2013, partially offset by a decrease in the recognition of the deferred revenue balance related to the value of the remaining performance obligations under our restructured agreement with Genzyme in 2012. Grant revenue was $3.4 million for the year ended December 31, 2013, a decrease of $1.8 million from grant revenue of $5.2 million for the year ended December 31, 2012.

Research and development expense. Research and development expense was $54.9 million for the year ended December 31, 2013, an increase of $8.8 million, or 19%, from $46.1 million for the year ended December 31, 2012. The increase resulted primarily from increased costs for clinical trials of $8.5 million related to the initiation of the Phase 3 clinical trial of ataluren for the treatment of nmDMD and an increase in share-based compensation of $1.2 million partially offset by a decrease in personnel costs of $2.1 million as a result of a reduction in force that we implemented in the second quarter of 2012.

General and administrative expense. General and administrative expense was $25.2 million for the year ended December 31, 2013, an increase of $10.6 million, or 72.6%, from $14.6 million for the year ended December 31, 2012. The increase resulted primarily from an increase in share-based compensation of $4.9 million and increases in public company related expenses and pre-commercial activities.

Interest expense, net. Interest expense was $6.1 million for the year ended December 31, 2013, an increase of $4.9 million from $1.2 million for the year ended December 31, 2012. The increase was due to interest expense related to the amortization of the debt discount associated with the convertible debt that we issued in 2013 partially offset by interest income related to investments.

Loss on extinguishment of debt. In July 2013, we paid in full the outstanding principal and interest of $2.6 million due under promissory notes issued related to a $25 million secured debt facility with a syndicate of two lenders. In connection with the repayment, we incurred a loss on extinguishment of debt of $0.1 million, primarily related to the write off of deferred financing costs, the acceleration of recognition of debt extinguishment fees and the prepayment premium payable. The notes were secured by substantially all our assets except for intellectual property and carried a fixed interest rate of 13.65%.

Other income, net. Other income, net was $38 for the year ended December 31, 2013, a decrease of $1.8 million as compared to the year ended December 31, 2012. The decrease was due to the change in fair value related to our warrant liability.

Year ended December 31, 2012 compared to year ended December 31, 2011

(in thousands)	2012	2011	Change 2012 vs. 2011
Revenue	$ 33,946	$ 105,412	$ (71,466)
Research and development expenses	46,139	58,677	(12,538)
General and administrative expenses	14,615	16,153	(1,538)
Interest expense	1,210	2,444	(1,234)
Other income, net	1,783	461	1,322
Tax benefit	—	2,306	(2,306)

Revenues. Revenues were $33.9 million for the year ended December 31, 2012, a decrease of $71.5 million from revenues of $105.4 million for the year ended December 31, 2011. Collaboration revenue was $28.8 million for the year ended December 31, 2012, a decrease of $70.2 million from collaboration revenues of $99.0 million for the year ended December 31, 2011. The decrease resulted primarily from a one-time non cash adjustment in 2011 to our deferred revenue balance to reflect the value of the remaining performance obligations under our restructured agreement with Genzyme. We recognized approximately $79 million of existing deferred revenue under our agreement with Genzyme as of the modification date. Grant revenue was $5.2 million for the year ended December 31, 2012, a decrease of $1.3 million from grant revenue of $6.5 million for the year ended December 31, 2011.

Research and development expense. Research and development expense was $46.1 million for the year ended December 31, 2012, a decrease of $12.6 million, or 21%, from $58.7 million for the year ended December 31, 2011. The decrease resulted primarily from decreased costs for clinical trials of $5.8 million, decrease in manufacturing of clinical trial supplies of $2.3 million and a decrease in personnel costs of $2.3 million as a result of a reduction in force that we implemented in the second quarter of 2012. Clinical trial expense for 2011 reflected costs associated with our Phase 3 clinical trial of ataluren for the treatment of nmCF, which concluded in November 2011, and a related extension trial and a Phase 3 continuation trial for ataluren for the treatment of nmDMD. Clinical trial expense for 2012 reflected costs associated with the ongoing extension trial for patients who had participated in our Phase 3 clinical trial of ataluren for the treatment of nmCF, the ongoing continuation trial for ataluren for the treatment of nmDMD and a second Phase 3 continuation trial that we initiated in 2012 for ataluren for the treatment of nmDMD.

General and administrative expense. General and administrative expense was $14.6 million for the year ended December 31, 2012, a decrease of $1.6 million, or 9.5%, from $16.2 million for the year ended December 31, 2011. The decrease was due principally to decreased personnel costs of $1.6 million as a result of a reduction in force that we implemented in the second quarter of 2012.

Interest expense. Interest expense was $1.2 million for the year ended December 31, 2012, a decrease of $1.2 million from $2.4 million for the year ended December 31, 2011. The increase was due to a smaller loan balance in 2012 as we continued to repay outstanding debt.

Other income, net. Other Income, net was $1.8 million for the year ended December 31, 2012, an increase of $1.3 million from $0.5 million for the year ended December 31, 2011. The increase was due to the change in fair value related to our warrant liability.

Tax benefit. We recognized a tax benefit related to our sale of net operating losses in the New Jersey Technology Business Tax Certificate Transfer Program. For the year ended December 31, 2011, our benefit was $2.3 million. We did not qualify for this program in 2012.

Liquidity and Capital Resources

Since inception, we have incurred significant operating losses. To date, we have not generated any product sale revenues. We have financed our operations primarily through the issuance and sale of our common stock in our public offering in February 2014 and our initial public offering in June 2013, private placements of our preferred stock, collaborations, bank debt and convertible debt financings and grant funding and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates.

In February 2014, we closed a public offering of 5,163,265 shares of common stock at a public offering price of $24.50 per share, including 673,469 shares pursuant to the exercise by the underwriters of an over-allotment option. We received net proceeds from the public offering of approximately $118.4 million after deducting underwriting discounts and commissions and other offering expenses payable by us.

In June 2013, we closed the initial public offering of our common stock, pursuant to which we issued and sold an aggregate of 9,627,800 shares of common stock at a public offering price of $15.00 per share, including 1,255,800 shares pursuant to the exercise by the underwriters of an over-allotment option. We received net proceeds from the initial public offering of approximately $131.6 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

We have engaged in the following preferred stock and convertible debt financings since January 1, 2011.

Series One preferred stock financing. In May and July 2012, we issued and sold an aggregate of 1,483,337 shares of our series One preferred stock, at a price per share of $20.00, for an aggregate purchase price of $29.7 million. In connection with the series One preferred stock financing, we also effected a recapitalization of our previously outstanding preferred stock into an aggregate of 10,701,405 shares of series Two preferred stock and 2,853,517 shares of series Three preferred stock. Stockholders who participated in the series One preferred stock financing received series Two preferred stock following the recapitalization of our outstanding preferred stock.

Bridge financing. In January and February 2013, we issued convertible promissory notes in an aggregate principal amount of $6 million. In connection with this bridge financing, we also issued to the holders of the promissory notes warrants to purchase an aggregate of 515,186 shares of our series One preferred stock, at an exercise price of $0.01 per share, and warrants to purchase an aggregate of 2,012,489 shares of our series Two preferred stock, at an exercise price of $0.01 per share.

Series Four preferred stock financing. In March 2013, we issued and sold an aggregate of 4,497,035 shares of our series Four senior preferred stock, at a price per share of $12.00, for an aggregate purchase price of $54 million. In addition, we issued an aggregate of 502,919 shares of our series Four senior preferred stock upon conversion of the convertible promissory notes described above that we originally issued in January and February 2013. In connection with the series Four senior preferred stock financing, we effected a one-for-120 reverse stock split of our common stock and a recapitalization of our previously outstanding preferred stock into an aggregate of 6,700,487 shares of series Five junior preferred stock. In addition, we issued an aggregate of 2,095,515 shares of our series Five junior preferred stock upon the automatic exercise of the preferred stock warrants that we originally issued in January 2013. In May 2013, we issued and sold an additional 375,000 shares of our series Four preferred stock, at a price per share of $12.00, for an aggregate purchase price of $4.5 million.

Upon closing our initial public offering, all outstanding shares of the Series Four and Series Five were converted into 14,170,956 shares of common stock.

Discussion of Cash flows

As of December 31, 2013, we had cash, cash equivalents and marketable securities of $142.5 million. In addition, we received approximately $118.4 million net proceeds in February 2014 from our public offering.

The following table provides information regarding our cash flows and our capital expenditures for the periods indicated.

	Year ended December 31,		
(in thousands)	**2013**	**2012**	**2011**
Cash provided by (used in):			
Operating activities	$ (46,922)	$ (47,928)	$ (20,767)
Investing activities	(127,828)	(189)	27,703
Financing activities	187,439	22,411	(7,180)

Year ended December 31, 2013, compared to the Year ended December 31, 2012

Net cash used in operating activities was $46.9 million for the year ended December 31, 2013 and $47.9 million for the year ended December 31, 2012. The change in net cash used in operating activities primarily related to supporting clinical development, pre-commercial activities and public company readiness.

Net cash used in investing activities was $127.8 million for the year ended December 31, 2013. Net cash used in investing activities was $0.2 million for the year ended December 31, 2012. Cash used in investing activities in 2013 primarily related to purchases of investments of approximately $156.0 million and purchases of fixed assets of $0.8 million partially offset by maturities of investments of $29.1 million. Cash used in investing activities in 2012 was related to purchases of fixed assets.

Net cash provided by financing activities was $187.4 million for the year ended December 31, 2013. Net cash provided by financing activities was $22.4 million for the year ended December 31, 2012. Net cash provided by financing activities in 2013 was primarily attributable to the $131.6 million in net proceeds received from the initial public offering and $60.8 million in net proceeds that we received from the sale of Series Four preferred stock. Partially offsetting these proceeds were payments on debt obligations of $5.0 million in 2013. Net cash provided by financing activities in 2012 was primarily attributable to the $29.3 million in proceeds that we received from a preferred stock financing. Partially offsetting these proceeds were payments on debt obligations of $6.9 million in 2012.

Year ended December 31, 2012, compared to the Year ended December 31, 2011

Net cash used in operating activities was $47.9 million for the year ended December 31, 2012 and $20.8 million for the year ended December 31, 2011. The net cash used in 2012 and 2011 primarily reflects changes in deferred revenue, including an upfront cash payment of $30 million in 2011 related to the collaboration agreement with Roche for a spinal muscular atrophy program, which is being amortized over the research term, and decreased spending in 2012 on research and development costs due to the completion of our Phase 2b clinical trial of ataluren for nmDMD and our Phase 3 clinical trial of ataluren for nmCF.

Net cash used in investing activities was $0.2 million for the year ended December 31, 2012. Net cash provided by investing activities was $27.7 million for the year ended December 31, 2011. Cash provided by investing activities in 2011 was primarily related to net maturities of investments.

Net cash provided by financing activities was $22.4 million for the year ended December 31, 2012. Net cash provided by financing activities in 2012 was primarily attributable to the $29.3 million in proceeds that we received from a preferred stock financing. Partially offsetting these proceeds were payments on debt obligations of $6.9 million in 2012. Net cash used in financing activities was $7.2 million for the year ended December 31, 2011. Net cash used in financing activities in 2011 was attributable to payments on debt obligations.

Funding requirements

We anticipate that our expenses will increase substantially in connection with initiating and continuing confirmatory Phase 3 clinical trials for ataluren for the treatment of nmDMD and nmCF, commencing early access programs for ataluren for nmDMD patients in selected territories and seeking marketing approval for ataluren for these indications in the European Union and the United States. If we obtain marketing approval of ataluren for either nmDMD or nmCF, we also expect to incur significant selling, marketing, distribution and manufacturing expenses. The timing of commercialization expenses for ataluren depends in part on whether we receive conditional approval for ataluren for either or both of nmDMD and nmCF.

In addition, our expenses will increase if and as we:

- initiate or continue the research and development of ataluren for additional indications and of our other product candidates;
- seek to discover and develop additional product candidates;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

We believe that the net proceeds from our public offering, together with our existing cash and cash equivalents, marketable securities and research funding that we expect to receive under our collaborations, will be sufficient to enable us to fund our operating expenses, debt service obligations and capital expenditure requirements through the fourth quarter of 2016. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate assumes, among other things, that we do not receive conditional approval to market ataluren for nmDMD or nmCF in the European Union prior to completing a confirmatory Phase 3 clinical trial for the applicable indication and, as a result, that we do not incur significant related commercialization expenses prior to such time. Our future capital requirements will depend on many factors, including:

- the progress and results of confirmatory Phase 3 clinical trials of ataluren for nmDMD and nmCF;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for ataluren for additional indications and for our other product candidates;
- the number and development requirements of other product candidates that we pursue;
- the costs, timing and outcome of regulatory review of ataluren and our other product candidates;
- the costs and timing of commercialization activities, including product sales, marketing, distribution and manufacturing, for any of our product candidates that receive marketing approval;
- subject to receipt of marketing approval, revenue received from commercial sales of ataluren or any of our other product candidates;

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

- the extent to which we acquire or invest in other businesses, products and technologies; and

- our ability to establish and maintain collaborations.

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, grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution 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.

Contractual Obligations

The following table summarizes our significant contractual obligations and commercial commitments as of December 31, 2013.

(in thousands)	Total	Less than 1 year	1 - 3 years	4 - 5 years	More than 5 years
Debt obligations	$ 49	$ 49	$ —	$ —	$ —
Operating and equipment lease obligations(1)	4,551	890	2,547	$ 1,114	—
Total fixed contractual obligations	$ 4,600	$ 939	$ 2,547	$ 1,114	$ —

(1) We lease office space under a noncancelable operating lease with a term that extends through February 2019.

The preceding table excludes contingent contractual payments that we may become obligated to make. Under various agreements, we will be required to pay royalties and milestone payments upon the successful development and commercialization of products, including the following agreements with The Wellcome Trust Limited, or Wellcome Trust, and SMA Foundation.

We have entered into funding agreements with Wellcome Trust for the research and development of small molecule compounds in connection with our BMI1 and antibacterial programs. To the extent that we develop and commercialize program intellectual property on a for-profit basis, we may become obligated to pay to Wellcome Trust development and regulatory milestone payments of up to an aggregate of $68.9 million and single digit royalties on sales of any research program product. Our obligation to pay such royalties would continue on a country-by-country basis until the longer of the expiration of the last patent in the program intellectual property in such country covering the research program product and the expiration of market exclusivity of such product in such country.

We have also entered into a sponsored research agreement with the SMA Foundation in connection with our spinal muscular atrophy program. We may become obligated to pay the SMA Foundation single digit royalties on worldwide net product sales of any collaboration product that we successfully develop and subsequently commercialize or, with respect to collaboration products we outlicense, a specified percentage of certain payments we receive from our licensee. We are not obligated to make such payments unless and until annual sales of a collaboration product exceed a designated threshold. Our obligation to make such payments would end upon our payment to the SMA Foundation of a specified amount.

We have employment agreements with certain employees which require the funding of a specific level of payments, if certain events, such as a change in control or termination without cause, occur.

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 Securities and Exchange Commission rules.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase.

Item 8. Financial Statements and Supplementary Data.

Index to financial statements

Report of independent registered accounting firm

The Board of Directors and Stockholders
PTC Therapeutics, Inc.

We have audited the accompanying balance sheets of PTC Therapeutics, Inc. (the Company) as of December 31, 2013 and 2012, and the related statements of operations, comprehensive income (loss), statements of convertible preferred stock and stockholders' deficit, and cash flows for each of the three years in the period ended December 31, 2013. 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 audit 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 financial position of PTC Therapeutics, Inc. at December 31, 2013 and 2012 and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2013, in conformity with U.S. generally accepted accounting principles.

/s/ ERNST & YOUNG LLP

MetroPark, New Jersey
March 6, 2014

PTC Therapeutics, Inc.

Balance sheets

	December 31, 2013	December 31, 2012
Assets		
Current assets:		
Cash and cash equivalents	$ 15,414,403	$ 2,725,702
Marketable securities	127,053,124	—
Prepaid expenses and other current assets	1,599,200	855,750
Grant and collaboration receivables, net	957,722	1,013,813
Total current assets	145,024,449	4,595,265
Fixed assets, net	6,729,364	8,280,037
Deposits and other assets	149,008	197,050
Total assets	$ 151,902,821	$ 13,072,352
Liabilities, convertible preferred stocks and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable and accrued expenses	$ 12,207,383	$ 7,023,971
Current portion of long-term debt	48,622	4,444,171
Deferred revenue	877,434	16,690,747
Total current liabilities	13,133,439	28,158,889
Deferred revenue, less current portion	—	741,667
Long-term debt, less current portion	—	438,810
Other long-term liabilities	2,226,970	2,549,719
Total liabilities	15,360,409	31,889,085
Commitments and contingencies *(Note 13)*		
Series One convertible preferred stock, designated 2,000,000 shares; issued and outstanding 1,483,337 shares at December 31, 2012	—	62,263,852
Series Two convertible preferred stock, designated 13,750,000 shares; issued and outstanding 10,701,405 shares at December 31, 2012	—	18,182,129
Series Three convertible preferred stock, designated 13,750,000 shares; issued and outstanding 2,853,517 shares at December 31, 2012	—	377,787
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value. Undesignated 5,000,000 shares; issued and outstanding 0 shares at December 31, 2013	—	—
Common stock, $0.001 par value. Authorized 125,000,000 shares; issued and outstanding 23,803,282 shares at December 31, 2013. Authorized 17,000,000 shares; issued and outstanding 4,526 shares at December 31, 2012	24,344	545
Additional paid-in capital	465,245,968	177,583,672
Accumulated other comprehensive income	70,393	—
Accumulated deficit	(328,798,293)	(277,224,718)
Total stockholders' equity (deficit)	136,542,412	(99,640,501)
Total liabilities, convertible preferred stocks and stockholders' equity (deficit)	$ 151,902,821	$ 13,072,352

See accompanying notes.

PTC Therapeutics, Inc.

Statements of operations

	Year ended December 31,		
	2013	2012	2011
Revenues:			
Collaboration revenue	$ 31,326,117	$ 28,779,078	$ 98,960,851
Grant revenue	3,370,210	5,166,985	6,451,296
Total revenues	34,696,327	33,946,063	105,412,147
Operating expenses:			
Research and development	54,875,144	46,138,868	58,677,081
General and administrative	25,218,652	14,615,376	16,153,069
Total operating expenses	80,093,796	60,754,244	74,830,150
(Loss) income from operations	(45,397,469)	(26,808,181)	30,581,997
Interest expense, net	(6,083,655)	(1,209,577)	(2,444,417)
Loss on extinguishment of debt	(129,963)	—	—
Other income, net	37,512	1,782,656	461,358
(Loss) income from operations before tax benefit	(51,573,575)	(26,235,102)	28,598,938
Tax benefit	—	—	2,305,576
Net (loss) income	(51,573,575)	(26,235,102)	30,904,514
Deemed dividend	(18,248,768)	—	—
Gain on exchange of convertible preferred stock in connection with recapitalization	3,390,750	159,954,069	—
Less beneficial conversion charge	—	(377,787)	—
Net (loss) income attributable to common stockholders	$ (66,431,593)	$ 133,341,180	$ 30,904,514
Net (loss) income attributable to common stockholders per share:			
Basic	$ (5.18)	$ 219.76	$ 23.95
Diluted	$ (5.18)	$ 42.50	$ 4.55
Weighted-average shares outstanding:			
Basic	12,829,411	3,328	1,089
Diluted	12,829,411	17,205	5,729

See accompanying notes.

PTC Therapeutics, Inc.

Statements of comprehensive (loss) income

	Year ended December 31,		
	2013	2012	2011
Net (loss) income	$ (51,573,575)	$ (26,235,102)	$ 30,904,514
Other comprehensive (loss) income:			
Unrealized (loss) gain on marketable securities	70,393	—	(3,606)
Comprehensive (loss) income	$ (51,503,182)	$ (26,235,102)	$ 30,900,908

See accompanying notes.

PTC Therapeutics, Inc.

Statements of convertible preferred stock and changes in stockholders' equity (deficit)
period from January 1, 2011 through December 31, 2013

	Series A - G convertible preferred stock		Series One - Three convertible preferred stock		Series Four convertible preferred stock		Series Five convertible preferred stock		Common stock		Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance, January 1, 2011	154,728,267	$ 214,379,914	—	$ —	—	$ —	—	$ —	130,586	$ 131	$ 9,184,483	$ 3,606	$(281,516,343)	$(272,328,123)
Exercise of stock options	—	—	—	—	—	—	—	—	1,536	2	5,887	—	—	5,889
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	2,816,637	—	—	2,816,637
Net income	—	—	—	—	—	—	—	—	—	—	—	—	30,904,514	30,904,514
Unrealized loss on investments	—	—	—	—	—	—	—	—	—	—	—	(3,606)	—	(3,606)
Balance, December 31, 2011	154,728,267	$ 214,379,914	—	$ —	—	$ —	—	$ —	132,122	$ 133	$ 12,007,007	$ —	$(250,611,829)	$(238,604,689)
Conversion of Series E and E-2 convertible preferred stock to common stock	(5,167,365)	(2,956,829)	—	—	—	—	—	—	413,223	412	2,956,417	—	—	2,956,829
Issuance of Series One convertible preferred stock, exchange of Series A - G convertible preferred stock for Series Two and Series Three convertible preferred stock	(149,560,902)	(211,423,085)	15,038,259	80,823,768	—	—	—	—	—	—	159,954,069	—	—	159,954,069
Beneficial conversion charge	—	—	—	—	—	—	—	—	—	—	377,787	—	(377,787)	—
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	2,288,392	—	—	2,288,392
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(26,235,102)	(26,235,102)
Balance, December 31, 2012	—	$ —	15,038,259	$ 80,823,768	—	$ —	—	$ —	545,345	$ 545	$177,583,672	$ —	$(277,224,718)	$ (99,640,501)
Reverse stock split	—	—	—	—	—	—	—	—	(540,819)	—	—	—	—	—
Issuance of Series Four convertible preferred stock, exchange of Series One, Two, and Three convertible preferred stock for Series Five convertible preferred stock	—	—	(15,038,259)	(80,823,768)	5,374,954	60,785,363	8,796,002	101,681,783	—	—	(14,857,927)	—	—	(14,857,927)
Issuance of common stock from IPO and exercise of over allotment, net of offering costs	—	—	—	—	—	—	—	—	9,627,800	9,628	131,640,060	—	—	131,649,688
Conversion of Series Four and Series Five convertible preferred stock	—	—	—	—	(5,374,954)	(60,785,363)	(8,796,002)	(101,681,783)	14,170,956	14,171	162,452,975	—	—	162,467,146
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	8,427,188	—	—	8,427,188
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(51,573,575)	(51,573,575)
Unrealized gain on investments	—	—	—	—	—	—	—	—	—	—	—	70,393	—	70,393
Balance, December 31, 2013	—	$ —	—	$ —	—	$ —	—	$ —	23,803,282	$ 24,344	$465,245,968	$ 70,393	$(328,798,293)	$ 136,542,412

See accompanying notes.

PTC Therapeutics, Inc.

Statements of cash flows

Year ended December 31, 2013 , 2012, and 2011

	Year ended December 31,		
	2013	2012	2011
Cash flows from operating activities			
Net (loss) income	$ (51,573,575)	$ (26,235,102)	$ 30,904,514
Adjustments to reconcile net (loss) income to net cash used in operating activities:			
Depreciation	2,396,405	2,704,151	2,871,200
Change in valuation of warrant liability	(37,507)	(1,782,655)	(461,947)
Noncash interest expense	6,048,580	225,730	416,612
Loss on extinguishment of debt	129,963	—	—
Share-based compensation expense	8,427,188	2,288,392	2,816,637
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(760,501)	2,452,430	(1,355,123)
Grant and collaboration receivables	56,091	230,315	2,052,550
Deposits and other assets	48,042	83,817	214,345
Accounts payable and accrued expenses	5,183,412	(6,025,483)	(3,159,711)
Other long-term liabilities	(285,242)	102,757	(67,151)
Deferred revenue	(16,554,980)	(21,972,143)	(54,998,713)
Net cash used in operating activities	(46,922,124)	(47,927,791)	(20,766,787)
Cash flows from investing activities			
Purchases of fixed assets	(845,732)	(188,681)	(165,116)
Purchases of marketable securities	(156,044,515)	—	(2,019,163)
Maturities of marketable securities	29,061,784	—	29,887,327
Net cash (used in) provided by investing activities	(127,828,463)	(188,681)	27,703,048
Cash flows from financing activities			
Payments on long-term debt	(4,995,763)	(6,943,988)	(7,185,610)
Net proceeds from sale of Series One preferred stock	—	29,354,752	—
Net proceeds from sale of Series Four preferred stock	60,785,363	—	—
Net proceeds from IPO	131,649,688	—	—
Proceeds from issuance of common stock	—	—	5,889
Net cash provided by (used in) financing activities	187,439,288	22,410,764	(7,179,721)
Net increase (decrease) in cash and cash equivalents	12,688,701	(25,705,708)	(243,460)
Cash and cash equivalents, beginning of period	2,725,702	28,431,410	28,674,870
Cash and cash equivalents, end of period	$ 15,414,403	$ 2,725,702	$ 28,431,410
Supplemental disclosure of cash information			
Cash paid for interest	$ 367,065	$ 1,211,764	$ 2,486,682
Cash paid for income taxes	$ 2,077	$ 2,000	$ 2,077
Supplemental disclosures of noncash information related to investing and financing activities			
Change in unrealized gain (loss) on marketable securities	$ 70,393	$ —	$ (3,606)
Change in carry value of preferred securities resulting from recapitalization	$ 3,390,750	$ 159,954,069	$ —

See accompanying notes.

PTC Therapeutics, Inc.

Notes to financial statements

December 31, 2013

1. The Company

PTC Therapeutics, Inc. (the Company or PTC) was incorporated as a Delaware corporation on March 31, 1998. The Company is a biopharmaceutical company focused on the discovery and development of orally administered, proprietary small-molecule drugs that target post-transcriptional control processes.

The Company has devoted substantially all of its efforts to research and development, including clinical trials. The Company has not completed development of any drugs. The Company has not generated product revenue to date and is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals, the difficulties inherent in the development of commercially usable products, the potential need to obtain additional capital necessary to fund the development of its products, and competition from other companies. As of December 31, 2013, the Company had an accumulated deficit of approximately $328.8 million. The Company has financed its operations to date primarily through a public offering in February 2014, its initial public offering in June 2013 (see note 7 below), private placements of its convertible preferred stock, collaborations, bank debt, convertible debt financings, grant funding and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease area addressed by the Company's product candidates. The Company believes that its existing cash, cash equivalents, and marketable securities provide for sufficient resources to fund its currently planned operations through 2016.

2. Summary of significant accounting policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles (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 financial statements in conformity with U.S. generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Segment and geographic information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment.

Cash equivalents

The Company considers all highly liquid investments with a maturity of 90 days or less at the time of purchase to be cash equivalents. Cash equivalents are carried at cost which approximates fair value due to their short-term nature.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

2. Summary of significant accounting policies (Continued)

Marketable securities

Management determines the classification of marketable securities at the time of purchase and reevaluates such designation as of each balance sheet date. Marketable securities are classified as available-for-sale and carried at fair value, with any unrealized gain or loss recorded as a separate component of stockholders' equity (deficit).

Fixed assets

Fixed assets are stated at cost. Depreciation is computed starting when the asset is placed into service on a straight-line basis over the estimated useful life of the related asset as follows:

Leasehold improvements	Lesser of useful life or lease term
Computer equipment and software	3 years
Furniture, fixtures, and lab equipment	3 to 7 years

Grant and collaboration receivables

The Company records receivables in conjunction with grant and collaboration agreements when the services have been performed. The Company will record an allowance for bad debt if receivables are anticipated to be uncollectible. There is no indication that any receivables are uncollectible as of December 31, 2013 and 2012. Write-offs of receivables have historically been insignificant.

Concentration of risks

The Company has no significant off-balance sheet risk or credit risk concentrations. The Company maintains its cash and cash equivalents with various financial institutions. The Company maintains cash accounts that may at times exceed the federally insured limit; however, it has not experienced and does not anticipate experiencing any credit losses from maintaining cash accounts in excess of such limits.

The Company's revenues from its two largest collaboration partners and its largest grant as a percentage of total revenues were 80%, 10%, and 8%; 67%, 11%, and 9%; 85%, 8%, and 3%, for 2013, 2012, and 2011, respectively.

Reverse stock split

As a result of the one-for-120 reverse stock split that was effected on March 7, 2013, each 120 shares of the Company's outstanding common stock were reclassified and combined into one share of common stock. All references to common stock have been restated to reflect the reverse stock split on a retroactive basis.

Deferred rent

The Company has an operating lease for office space. Rent expense is recorded on a straight-line basis over the initial lease term. The difference between the actual cash paid and the straight-line rent expense is recorded as deferred rent. Leasehold improvements made related to this lease, subsequent to its inception, are amortized over the remaining lease term.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

2. Summary of significant accounting policies (Continued)

Revenue recognition

The Company recognizes revenue when amounts are realized or realizable and earned. Revenue is considered realizable and earned when the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the price is fixed or determinable; and (4) collection of the amounts due are reasonably assured.

The Company's revenue is generated primarily through collaborative research and development and licensing agreements and grants.

The terms of these agreements typically include payments to the Company of one or more of the following: nonrefundable, upfront license fees; milestone payments; research funding and royalties on future product sales. In addition, the Company generates service revenue through agreements that generally provide for fees for research and development services and may include additional payments upon achievement of specified events.

For existing collaborations entered into prior to the adoption in 2011 of the revised multiple element revenue recognition guidance described below, the Company recognized revenue consistent with the approach established at the inception of each arrangement. For these existing collaborations, where the Company has continuing involvement, the Company recorded nonrefundable, upfront fees as deferred revenue and recognizes revenue on a straight-line basis as collaboration revenue over the expected performance period.

For new collaborations or for material modifications made to existing collaborations, in 2011 and thereafter, the Company adopted the updated multiple element revenue recognition guidance. Under this new guidance, all non-contingent arrangement consideration is allocated to the identified units of accounting based on their relative selling price at inception of the collaboration arrangement. The Company derives the selling price using a combination of internal subjective and available external objective information, such as comparable transactions. The Company recognizes revenue commensurate with delivery, such as in the case with delivery of a license, or ratably over the course of a service period, as appropriate, such as in the case of ongoing research and development activities.

The Company evaluates all contingent consideration earned, such as a milestone payment, using the criteria as provided by the Financial Accounting Standards Board (FASB), guidance on the milestone method of revenue recognition. At the inception of a collaboration arrangement, the Company evaluates if milestone payments are substantive. The criteria requires that (1) the Company determines if the milestone is commensurate with either its performance to achieve the milestone or the enhancement of value resulting from our activities to achieve the milestone; (2) the milestone be related to past performance; and (3) the milestone be reasonable relative to all deliverable and payment terms of the collaboration arrangement. If these criteria are met then the contingent milestones can be considered as substantive milestones and will be recognized as revenue in the period that the milestone is achieved. The Company recognizes royalties as earned in accordance with the terms of various research and collaboration agreements. If not substantive, the contingent consideration is allocated to the existing units of accounting based on relative selling price and recognized following the same basis previously established for the associated unit of accounting.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

2. Summary of significant accounting policies (Continued)

The Company recognizes revenue for reimbursements of research and development costs under collaboration agreements as the services are performed. The Company records these reimbursements as revenue and not as a reduction of research and development expenses as the Company has the risks and rewards as the principal in the research and development activities.

Research and development costs

Research and development expenses include the clinical development costs associated with the Company's product development programs and research and development costs associated with the Company's discovery programs. These expenses include internal research and development costs and the costs of research and development conducted on behalf of the Company by third parties, including sponsored university-based research agreements and clinical study vendors. All research and development costs are expensed as incurred. Costs incurred in obtaining technology licenses are charged immediately to research and development expense if the technology licensed has not reached technological feasibility and has no alternative future uses.

Nonrefundable advance payments made for goods and services that will be used in future research and development activities are deferred if the contracted party has not yet performed the related activities. The amount deferred is then recognized as expense when the research and development activities are performed. The Company had deferred research and development advance payments of approximately $0.2 million as of December 31, 2012. The deferred research and development advance payments were not significant as of December 31, 2013.

Fair value of financial instruments

The Company follows the fair value measurement rules, which provides guidance on the use of fair value in accounting and disclosure for assets and liabilities when such accounting and disclosure is called for by other accounting literature. These rules establish a fair value hierarchy for inputs to be used to measure fair value of financial assets and liabilities. This hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three levels: Level 1 (highest priority), Level 2, and Level 3 (lowest priority).

- Level 1—Unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the balance sheet date.

- Level 2—Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly. Level 2 inputs include quoted prices for similar assets and liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, inputs other than quoted prices that are observable for the asset or liability (i.e., interest rates, yield curves, etc.), and inputs that are derived principally from or corroborated by observable market data by correlation or other means (market corroborated inputs).

- Level 3—Inputs are unobservable and reflect the Company's assumptions as to what market participants would use in pricing the asset or liability. The Company develops these inputs based on the best information available.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

2. Summary of significant accounting policies (Continued)

Cash equivalents and investments are reflected in the accompanying financial statements at fair value. The carrying amount of grant and collaboration receivables and accounts payable and accrued expenses approximates fair value due to the short-term nature of those instruments.

Beneficial conversion

When the Company issues a debt or an equity security that is convertible into common stock at a discount from the fair value of the common stock at the date the debt or equity security counterparty is legally committed to purchase such a security (Commitment Date), a beneficial conversion charge is measured and recorded on the Commitment Date for the difference between the fair value of the Company's common stock and the effective conversion price of the convertible debt or equity security. If the intrinsic value of the beneficial conversion feature is greater than the proceeds allocated to the convertible debt or equity security, the amount of the discount assigned to the beneficial conversion feature is limited to the amount of the proceeds allocated to the convertible debt or equity security.

The amount allocated to the beneficial conversion feature is presented as a discount or reduction to the related debt security or as an immediate charge to earnings available to common shareholders for convertible preferred stock instruments that are convertible by the shareholders at any time. In connection with the Company's recapitalization of its outstanding convertible preferred stock in 2012, the Company recorded a beneficial conversion charge representing the difference between the effective conversion price and the fair value of the Company's common stock as of the Commitment Date. Because the intrinsic value was in excess of the proceeds allocated to the Company's new Series Three convertible preferred stock; the beneficial conversion charge was limited to the allocated proceeds of approximately $0.4 million.

Warrant liability

Warrants to purchase the Company's common stock with nonstandard antidilution provisions and preferred stock that include a put feature, regardless of the probability or likelihood that may conditionally obligate the issuer to ultimately transfer assets, are classified as liabilities and are recorded at their estimated fair value at each reporting period. Any change in fair value of these warrants is recorded as gain/(loss) on warrant valuation each reporting period in Other income on the Company's statement of operations.

Impairment of long-lived assets

The Company monitors its long-lived assets for indicators of impairment. If such indicators are present, the Company assesses the recoverability of affected assets by determining whether the carrying value of such assets is less than the sum of the undiscounted future cash flows of the assets. If such assets are found not to be recoverable, the Company measures the amount of such impairment by comparing the carrying value of the assets to the fair value of the assets, with the fair value generally determined based on the present value of the expected future cash flows associated with the assets. Although current and historical negative cash flows are indicators of impairment, management believes the future cash flows to be received from the long-lived assets and the potential success of the Company's research programs will exceed the assets' carrying value, and accordingly, the Company believes that no impairment of long-lived assets exists as of December 31, 2013.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

2. Summary of significant accounting policies (Continued)

Share-based compensation

The Company measures the cost of employee services received in exchange for an award of equity instruments based on the grant date fair value of the award. Restricted stock awards are measured based on the fair market values of the underlying stock on the dates of grant. For service type awards, share-based compensation expense is recognized on a straight-line basis over the period during which the employee is required to provide service in exchange for the entire award. For awards that vest or begin vesting upon achievement of a performance condition, the Company estimates the likelihood of satisfaction of the performance condition and recognizes compensation expense when achievement of the performance condition is deemed probable using an accelerated attribution model.

The fair value of options is calculated using the Black-Scholes option pricing model to determine the fair value of stock options on the date of grant based on key assumptions such as expected volatility and expected term. As a new public company, the Company does not have sufficient history to estimate the volatility of its common stock price or the expected life of the options. The Company calculates expected volatility based on reported data for similar publicly traded companies for which historical information is available and will continue to do so until the historical volatility of its common stock is sufficient to measure expected volatility for future option grants.

Prior to becoming a public company, the Company utilized various valuation methodologies in accordance with the framework of the 2004 American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its stock. The methodologies included an option pricing method to estimate the Company's underlying equity value, and a methodology that determined an estimated value under an initial public offering (IPO) scenario and a sale scenario based upon an assessment of the probability of occurrence of each scenario. Each valuation methodology included estimates and assumptions that required the Company's judgment. These estimates included assumptions regarding future performance, including the completion of clinical trials and the time to complete an IPO or sale of the Company. As with any valuation, significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

Income taxes

Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and net operating loss and credit carryforwards. Deferred tax assets and liabilities are measured at rates expected to apply to taxable income in the years in which those temporary differences and carryforwards are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the statement of operations in the period that includes the enactment date. A valuation allowance is recorded when it is not more likely than not that all or a portion of the net deferred tax assets will be realized.

Net (loss) income per share

Basic net income per share is calculated by dividing the net income attributable to common stockholders by the weighted average number of common shares outstanding for the period, without

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

2. Summary of significant accounting policies (Continued)

consideration for common stock equivalents. Diluted net income per share is calculated by dividing the net income attributable to common stockholders by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method and the if-converted method. During periods in which the Company incurs net losses, both basic and diluted loss per share is calculated by dividing the net loss by the weighted average shares outstanding —potentially dilutive securities are excluded from the calculation because their effect would be anti-dilutive. Dilutive common stock equivalents are comprised of convertible preferred stock and options outstanding under the Company's stock option plans.

3. Fair value of financial instruments and investments

Fair value of certain investments is based upon market prices using quoted prices in active markets for identical assets quoted on the last day of the year. In establishing the estimated fair value of the remaining investments, the Company used the fair value as determined by its investment advisors using observable inputs other than quoted prices.

The Company reviews its investments on a periodic basis for other-than-temporary impairments. This review is subjective, as it requires management to evaluate whether an event or change in circumstances has occurred in that period that may have a significant adverse effect on the fair value of the investment.

The following represents the fair value using the hierarchy described in Note 2 for the Company's financial assets and liabilities that are required to be measured at fair value on a recurring basis as of December 31, 2013 and 2012:

	December 31, 2013			
	Total	Quoted prices in active markets for identical assets (level 1)	Significant other observable inputs (level 2)	Significant unobservable inputs (level 3)
Marketable securities	$ 127,053,124	$ —	$ 127,053,124	$ —
Warrant liability	$ 58,154	$ —	$ —	$ 58,154

	December 31, 2012			
	Total	Quoted prices in active markets for identical assets (level 1)	Significant other observable inputs (level 2)	Significant unobservable inputs (level 3)
Warrant liability	$ 95,661	$ —	$ —	$ 95,661

The Company uses the market approach to measure fair value for its financial assets. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets. The Company's marketable securities investments classified as Level 2 primarily utilize broker to value these securities. No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the year ended December 31, 2013.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

3. Fair value of financial instruments and investments (Continued)

The following is a summary of marketable securities accounted for as available-for-sale securities at December 31, 2013:

	December 31, 2013			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 14,993,309	$ 5,151	$ —	$ 14,998,460
U.S. corporate debt securities	111,989,422	96,737	(31,495)	112,054,664
	$ 126,982,731	$ 101,888	$ (31,495)	$ 127,053,124

Unrealized gains and losses are reported as a component of accumulated other comprehensive (loss) income in stockholders' equity (deficit). During the year ended December 31, 2013, the proceeds from the sale of marketable securities and realized gains/losses were immaterial. The cost of securities sold is based on the specific identification method. The Company evaluates investments with unrealized losses to determine if the losses are other than temporary. At December 31, 2013, the Company held securities with an unrealized loss position that were not considered to be other-than-temporarily impaired as the Company has the ability to hold such investments until recovery of their fair value. In addition, the Company considered the financial condition, credit ratings and near-term prospects of the issuers, and the magnitude of the losses as compared to the cost and the length of time the investments have been in an unrealized loss position when determining if the losses are other than temporary.

Marketable securities on the balance sheet at December 31, 2013 mature as follows:

	December 31, 2013	
	Less Than 12 Months	More Than 12 Months
Commercial paper	$ 14,998,460	$ —
U.S. corporate debt securities	54,158,359	57,896,305
Total Marketable securities	$ 69,156,819	$ 57,896,305

There were no marketable securities as of December 31, 2012.

Level 3 valuation

The warrant liability is classified in Other long-term liabilities on the Company's balance sheet. The warrant liability is marked-to-market each reporting period with the change in fair value recorded as a gain or loss within Other income on the Company's statement of operations until the warrants are exercised, expire or other facts and circumstances lead the warrant liability to be reclassified as an equity instrument. The fair value of the warrant liability is determined at each reporting period by utilizing the Black-Scholes option pricing model.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

3. Fair value of financial instruments and investments (Continued)

The table presented below is a summary of changes in the fair value of the Company's Level 3 valuation for warrant liability for the years ended December 31, 2013 and 2012:

	Level 3 assets
Beginning balance January 1, 2012	$ 1,878,316
Change in fair value of warrant liability	(1,782,655)
Ending balance as of December 31, 2012	$ 95,661
Change in fair value of warrant liability	(37,507)
Ending balance as of December 31, 2013	$ 58,154

Fair value of the warrant liability is estimated using an option-pricing model, which includes variables such as the expected volatility based on guideline public companies, the preferred stock value, and the estimated time to a liquidity event. The significant assumptions used in preparing the option pricing model for valuing the Company's warrants as of December 31, 2013 include (i) volatility (61-89%), (ii) risk free interest rate (0.07%-2.1%), (iii) strike price ($128.00-$2,520.00), (iv) fair value of common stock($16.97) and (v) expected life (0.3-5.7 years). The significant assumptions used in preparing the option pricing model for valuing the Company's warrants as of December 31, 2012 include (i) volatility (87%), (ii) risk free interest rate (0.16%-1.18%), (iii) strike price ($16.00), (iv) fair value of preferred shares ($2.35) and (v) expected life (1.0-7.0 years). The fair value of the preferred shares declined significantly due to the recapitalization of the Company's outstanding convertible preferred stock in June 2012 as described in Note 7.

4. Fixed assets

Fixed assets, net were as follows at December 31, 2013 and 2012:

	December 31,	
	2013	2012
Leasehold improvements	$ 12,473,836	$ 12,473,836
Computer equipment and software	2,284,836	2,118,713
Furniture, fixtures, and lab equipment	14,283,875	13,969,758
Assets not yet placed in service	369,644	4,152
	29,412,191	28,566,459
Less accumulated depreciation and amortization	(22,682,827)	(20,286,422)
	$ 6,729,364	$ 8,280,037

Depreciation expense was approximately $2.4 million, $2.7 million, and $2.9 million for the years ended December 31, 2013, 2012 and 2011, respectively.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

5. Accounts payable and accrued expenses

Accounts payable and accrued expenses at December 31, 2013 and 2012 consist of the following:

	December 31,	
	2013	2012
Employee compensation, benefits, and related accruals	$ 5,102,795	$ 3,096,475
Consulting and contracted research	4,006,336	2,515,678
Professional fees	1,294,637	559,228
Accounts payable	1,123,895	621,591
Other	679,720	230,999
	$ 12,207,383	$ 7,023,971

6. Long-term debt

In May 2009, the Company entered into a capital lease for a laboratory instrument. This lease carries an implied interest rate of 8.2% and is payable in fixed monthly installments. As of December 31, 2013 and 2012, the Company had approximately $0.1 million and $0.2 million of remaining principal, respectively, which approximates the fair value.

In September 2009, the Company entered into a $25.0 million secured debt facility with a syndicate of two lenders. In conjunction with entering into the debt facility, the Company issued warrants to purchase 62,500 shares of Series F-2 convertible preferred stock at an exercise price of $16.00 per share to the lenders. The warrants became exercisable in proportion to the amount of the facility borrowed. The fair value of the warrants was reflected as a discount to debt, and this discount is accreted to interest expense over the term of the debt facility.

The Company borrowed $12.5 million under the facility in September 2009 and an additional $10.0 million under the facility in December 2010 and issued the lenders promissory notes. The notes are secured by substantially all of the Company's assets except for intellectual property. The notes carry a fixed interest rate of 13.65% and required interest-only payments for the first five months, with principal repayment beginning in month six and continuing for 30 months. As of December 31, 2011 warrants to acquire 56,250 shares of Series F-2 were exercisable. In connection with the recapitalization of the Company's outstanding convertible preferred stock in 2012, these warrants were amended to be warrants to purchase Series Two convertible preferred stock. As of December 31, 2012, the outstanding balance on the notes was $4.8 million.

In July 2013, the Company paid in full the outstanding principal and interest of $2.6 million due under the promissory notes issued in connection with the secured debt facility. As a result of this transaction, the Company recorded a loss on extinguishment of debt of $0.1 million on the Company's statement of operations for the year ended December 31, 2013. The loss on extinguishment of debt primarily represented the write off of related deferred financing costs, the acceleration of recognition of debt extinguishment fees and the prepayment premium payable.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

7. Capital structure

Convertible preferred stock prior to 2012 recapitalization

As of December 31, 2011, the Company had authorized for issuance up to 156,995,095 shares of preferred stock, $0.001 par value. The authorized shares as of December 31, 2011 were designated as follows: 750,000 shares of Series A convertible preferred stock (Series A), 187,500 shares of Series B convertible preferred stock (Series B), 6,295,000 shares of Series C convertible preferred stock (Series C), 13,769,935 shares of Series D convertible preferred stock (Series D), 126,735,022 shares of Series E convertible preferred stock (Series E), 3,670,138 shares of Series E-2 convertible preferred stock (Series E-2), 675,000 shares of Series F convertible preferred stock (Series F), 1,612,500 shares of Series F-2 convertible preferred stock (Series F-2) and 3,300,000 shares of Series G convertible preferred stock (Series G).

The rights and preferences of the shares of Series A, Series B, Series C, Series D, Series E, Series E-2, Series F, Series F-2 and Series G were as follows:

Conversion—Each share of Series A, Series B, Series C, Series D, Series E, Series E-2, Series F, Series F-2 and Series G was convertible at any time at the option of the holder into such number of shares of common stock as determined by applying a conversion factor to the outstanding shares of approximately 0.0833, 0.1333, 0.1389, 0.1548, 0.0548, 1.0000, 1.0000, 1.0000 and 1.0000 for the Series A, Series B, Series C, Series D, Series E, Series E-2, Series F, Series F-2, and Series G respectively. These conversion factors were calculated based on the then-applicable conversion price with respect to each respective series of preferred stock. These conversion factors were subject to adjustment in the event the Company issued additional equity securities at prices below the then-applicable conversion price, or if the Company engaged in specified changes to its capitalization, such as stock splits or stock dividends. The conversion of each series of preferred stock would be automatic upon the closing of a qualified initial public offering or any other public offering upon the written election of the Company and holders of both (1) at least two thirds of the outstanding preferred shares on an as-converted to common stock basis and (2) at least two thirds of the Series F, F-2 and G shares voting together as a single class on an as-converted to common stock basis.

Voting—Each preferred shareholder was entitled to the number of votes per share as if the preferred shares were converted to common stock. Additionally, the holders of the preferred stock, voting as a single class, were entitled to elect six members of the Board of Directors.

Liquidation—Upon the liquidation, dissolution, reorganization or winding-up of the Company, holders of preferred stock were entitled to receive, before any distribution or payment on the common stock, an amount equal to $1.00 per share for Series A, $2.00 per share for Series B, $2.50 per share for Series C, $3.25 per share for Series D, $0.397644 per share for Series E, $7.26 per share for Series E-2, $16.00 per share for Series F, $16.00 per share for Series F-2, and $16.00 per share for Series G, plus all declared, but unpaid, dividends. As of December 31, 2011, the aggregate liquidation preference was $0.8 million, $0.4 million, $15.0 million, $42.6 million, $50.0 million, $26.6 million, $10.0 million, $24.2 million, and $50.3 million for the Series A, Series B, Series C, Series D, Series E, Series E-2, Series F, Series F-2, and Series G, respectively. In cases where the liquidation preference applied, if there were insufficient funds to pay the full preference value to all holders, then, as a group, the holders of the Series E, Series E-2, Series F, Series F-2, and Series G would have been paid together first, ratably, in proportion to their respective liquidation preferences. To the extent there were

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

7. Capital structure (Continued)

excess assets to distribute, the holders of the Series D would have been paid second. Finally, as a group, the holders of the Series A, Series B, and Series C would have been paid last, ratably, in proportion to their respective liquidation preferences. Dividends were payable only if and when declared. The Company has not declared any dividends through December 31, 2012.

2012 Recapitalization

In July 2012, the Company completed a recapitalization pursuant to which all outstanding shares of Series A, B, C, D, E, E-2, F, F-2, and G convertible preferred stock (Prior Series Preferred) were exchanged into Series Three convertible preferred stock (Series Three). Warrants to acquire Prior Series Preferred became warrants to acquire Series Two convertible preferred stock (Series Two). In addition, those investors that elected to participate in the sale of Series One convertible preferred stock (Series One) were entitled to exchange their Series Three shares for Series Two shares.

In connection with the recapitalization, the Company sold 1,483,337 shares of Series One for aggregate gross proceeds of approximately $29.7 million.

The Company accounted for the recapitalization as an extinguishment of its Prior Series Preferred and recorded the Series One, Series Two and Series Three shares at their fair value as of the recapitalization date. In accordance with authoritative accounting guidance, the Company recorded a gain attributable to the common stockholders on the extinguishment of the Prior Series Preferred. The gain of approximately $160.0 million represents the excess of the carrying amount of Prior Series Preferred stock immediately prior to the recapitalization over the fair value of the Series One, Two and Three stock issued in connection with the recapitalization.

Valuation—The value of the Company was estimated using the probability weighted expected return method (PWERM). The PWERM considered the most significant near-term driver of value for the Company as the ability to file a marketing authorization application (MAA) with The European Medicines Agency (EMA) for conditional approval of ataluren. The Company has initiated a confirmatory Phase 3 clinical trial of ataluren for the treatment of nmDMD. If favorable, the results of the confirmatory Phase 3 clinical trial could serve as the basis for full approval by the EMA and the FDA of ataluren for the treatment of nmDMD in the European Union and the United States. The remaining scenarios in the PWERM related to funding the completion of the confirmatory Phase 3 clinical trial of ataluren for the treatment of nmDMD.

After identifying the various potential liquidity scenarios and their likely timing, a pre-money enterprise value was assigned to each scenario based on a combination of management's guidance and recent trends in the capital markets. The resulting enterprise value for each liquidity event was divided by the total shares that would be outstanding under each scenario to arrive at a price per share for the common and preferred classes of stock. Each scenario was then assigned an outcome probability based on management's estimates. The resulting probability weighted share values were then discounted to present value at a rate that reflects general industry risks (but not Company specific risks).

The rights and preferences of the shares of Series One, Two and Three are as follows:

Dividends—The holders of Series One and Series Two, in preference to the holders of common stock, are entitled to noncumulative dividends when and if declared by the Board of Directors. The

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

7. Capital structure (Continued)

holders of Series Three are not entitled to dividends. The Company has not declared any dividends through December 31, 2012.

Liquidation—Upon the liquidation, dissolution, reorganization or winding-up of the Company, the holders of Series One will be entitled to receive, before any distribution or payment is made to any other class of security, an amount equal to two times the original issuance price, plus all declared, but unpaid, dividends. To the extent there are excess assets to distribute, the holders of Series Two will be entitled to receive 76.47% of such excess assets, and the holders of Series One will be entitled to receive 23.53% of such excess assets, until the holders of Series Two receive an amount equal to one times the stated liquidation preference amount for the Series Two, plus all declared, but unpaid, dividends. In the event there are remaining assets after Series Two distributions, the holders of Series Three are entitled to receive 8.82% of such remaining assets, and the holders of Series One and Series Two will be entitled to receive 23.53% and 67.65%, respectively, of such remaining assets, until the holders of Series Three receive an amount equal to one times the stated liquidation preference amount for the Series Three, plus all declared, but unpaid, dividends. To the extent there are remaining assets to distribute, the holders of Series One, Series Two, and Series Three will be entitled to receive 20%, 55%, and 25% of such remaining assets, respectively.

Voting—Each holder of Series One is entitled to cast the number of votes equal to five times the number of common shares into which such holder's shares of Series One would convert. Except as required by law, holders of Series Two and Series Three have limited voting rights. Additionally, the holders of Series One, voting as a single class, are entitled to elect twelve members of the Board of Directors.

Conversion—Each share of Series One is convertible at any time at the option of the holder into two shares of common stock. Each share of Series Two and Series Three is convertible at any time at the option of the holder into one share of common stock. These conversion ratios are subject to adjustment for certain dilutive events, including certain types of stock splits or stock dividends or future recapitalizations.

2013 Recapitalization

During January and February of 2013, the Company entered into a "bridge" financing arrangement with certain existing investors providing for the issuance by the Company of an aggregate of $6.0 million of convertible promissory notes and warrants to purchase 2,527,675 shares of Series One and Series Two convertible preferred stock. The warrants have a per share exercise price of $0.01, and as such, they are referred to as "penny warrants". This bridge financing was closed in anticipation of the March 2013 Series Four financing event, which the Company refers to as the "2013 recapitalization".

The Company allocated the proceeds of the convertible promissory notes between debt and warrant liability. Since the value of the warrants exceeded the proceeds from the convertible notes issued to existing investors, the value of the warrant in excess of the proceeds is considered a deemed dividend and reflected as an equity transaction in the financial statements. The Company recorded $6.0 million to interest expense related to the debt discount associated with the convertible debt during the quarter ended March 31, 2013.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

7. Capital structure (Continued)

On March 7, 2013, the Company closed a private placement of a new series of convertible preferred stock that resulted in another recapitalization event (the 2013 recapitalization). In this private placement, the Company issued and sold an aggregate of 4,497,035 shares of its Series Four senior preferred stock (Series Four) for an aggregate purchase price of approximately $54.0 million. Including the $6.0 million raised with the bridge financing, total gross proceeds raised during the quarter ended March 31, 2013 was approximately $60.0 million. In addition, the Company issued an aggregate of 502,919 shares of Series Four upon the share settlement of the convertible promissory notes described above that were issued in January and February 2013.

In connection with this private placement, the Company effected a one-for-120 reverse stock split of its common stock and an exchange of outstanding shares of Series One, Series Two and Series Three convertible preferred stock into an aggregate of 6,700,487 shares of a new series of Series Five junior preferred stock (Series Five). In addition, the Company issued an aggregate of 2,527,675 shares of Series One and Series Two convertible preferred stock upon the exercise of the warrants issued in connection with the bridge loan that were immediately exchanged for 2,095,515 shares of Series Five during the 2013 recapitalization.

The Company accounted for the 2013 recapitalization as an extinguishment of its Series One, Series Two and Series Three convertible preferred stock and recorded the Series Five shares at their fair value as of the recapitalization date. In accordance with authoritative accounting guidance, the Company recorded a gain attributable to the common stockholders on the extinguishment of the Series One, Series Two and Series Three convertible preferred stock. The gain of approximately $3.4 million represents the excess of the Series One, Series Two and Series Three convertible preferred stock over the fair value of the shares Series Five issued in connection with the recapitalization.

Valuation—The value of the Company was estimated using the PWERM. The PWERM considered the most significant near-term driver of value for the Company as the Company's ability to complete a Phase 3 clinical trial of ataluren for the treatment of Duchenne muscular dystrophy caused by nonsense mutations (nmDMD). The remaining scenarios in the PWERM related to funding the completion of the Phase 3 clinical trial for nmDMD. The path to raising this money made up the remaining nodes in the PWERM.

After identifying the various potential liquidity scenarios and their likely timing, a pre-money enterprise value was assigned to each scenario based on a combination of management's guidance and recent trends in the capital markets. The resulting enterprise value for each liquidity event was divided by the total shares that would be outstanding under each scenario to arrive at a price per share for the common and preferred classes of stock. Each scenario was then assigned an outcome probability based on management's estimates. The resulting probability weighted share values were then discounted to present value at a rate that reflects general industry risks (but not Company specific risks).

The rights and preferences of the shares of Series Four and Series Five are as follows:

Dividends—The holders of Series Four and Series Five, in preference to the holders of common stock, are entitled to noncumulative dividends when and if declared by the Board of Directors.

Liquidation—Upon the liquidation, dissolution, reorganization or winding-up of the Company, the holders of Series Four will be entitled to receive, before any distribution or payment is made to any

7. Capital structure (Continued)

other class of security, an amount equal to the original issuance price, plus all declared, but unpaid, dividends. To the extent there are excess assets to distribute, the holders of Series Five will be entitled to receive, before any distribution or payment is made to the holders of the common stock, an amount equal to the stated liquidation preference, plus all declared, but unpaid, dividends. To the extent there are remaining assets to distribute, the holders of common stock will be entitled to receive such remaining assets.

Voting—Each holder of Series Four and Series Five are entitled to cast the number of votes into which such holder's shares would convert. Except as required by law, holders of common stock have limited voting rights. Additionally, except as required by law, and except in certain enumerated circumstances, holders of Series Four and Series Five shall vote together with the holders of common stock as a single class.

Conversion—Each share of Series Four and Series Five is convertible at any time at the option of the holder into one share of common stock. These conversion ratios are subject to adjustment for certain dilutive events, including certain types of stock splits or stock dividends or future recapitalizations.

In May 2013, the Company issued and sold an additional 375,000 shares of Series Four, at a price per share of $12.00, for an aggregate purchase price of $4.5 million.

Common Stock

In May 2013, the Company's Board of Directors and stockholders approved an amendment to the Company's certificate of incorporation increasing the number of authorized shares of common stock to 125,000,000.

Initial Public Offering

In June 2013, the Company closed the initial public offering of its common stock pursuant to a registration statement on Form S-1, as amended. The Company issued and sold an aggregate of 9,627,800 shares of common stock under the registration statement at a public offering price of $15.00 per share, including 1,255,800 shares pursuant to the exercise by the underwriters of an over-allotment option. The Company received net proceeds from the initial public offering of approximately $131.6 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

Upon closing the initial public offering, all outstanding shares of the Series Four and Series Five were converted into 14,170,956 shares of common stock.

Warrants

All of the Company's outstanding warrants are classified as liabilities as of December 31, 2013 and 2012 because they contain either non-standard antidilution provisions or they were exercisable into preferred shares that include a put feature.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

7. Capital structure (Continued)

The following is a summary of the Company's outstanding warrants as of December 31, 2013:

	Warrant shares	Exercise price	Expiration
Common stock	1,428	$ 128.00	2014
Common stock	6,250	$ 128.00	2017
Common stock	7,030	$ 128.00	2019 and 2020
Common stock	452	$ 2,520.00	2014

The following is a summary of the Company's outstanding warrants as of December 31, 2012:

	Warrant shares	Exercise price	Expiration
Series Two	24,712	$ 16.00	2014
Series Two	50,000	$ 16.00	2017
Series Two	56,250	$ 16.00	2019 and 2020
Common stock	645	$ 2,520	2013 and 2014

In connection with the 2013 recapitalization, all of the Series Two outstanding warrants became warrants to purchase Series Five. In connection with the Company's initial public offering all of the Series Five outstanding warrants became warrants to purchase common stock.

8. Earnings per share

Basic earnings per share is computed by dividing net income (loss) available to common stockholders by the weighted-average number of common shares outstanding. Diluted earnings per share is computed by dividing net income (loss) available to common stockholders by the weighted-average number of common shares plus the effect of dilutive potential common shares outstanding during the period.

The Prior Series Preferred outstanding in 2011 and 2012 (through the date of the recapitalization) as well as the Series One, Series Two and Series Three outstanding during 2012 (subsequent to the recapitalization) participated in earnings of the Company through dividend rights. Accordingly, the Company measured earnings per share based upon the two-class method. Net income attributable to common stockholders excludes $132.6 million and $30.9 million for the years ended 2012 and 2011, respectively, for net income attributable to participating securities.

The diluted earnings per share for the years ended December 31, 2012 and 2011 exclude the impact of approximately 0.6 million and 1.3 million common stock equivalents, respectively, since the effect of including these securities would be anti-dilutive.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

8. Earnings per share (Continued)

The following table sets forth the computation of basic and diluted earnings per share for common stockholders:

Net (loss) income per share

	Year ended December 31		
	2013	2012	2011
Numerator			
Net (loss) income	$ (51,573,575)	$ (26,235,102)	$ 30,904,514
Deemed dividend	(18,248,768)	—	—
Gain on exchange of convertible preferred stock in connection with recapitalization	3,390,750	159,954,069	—
Less beneficial conversion charge	—	(377,787)	—
Less net income attributable to participating preferred stock	—	(132,609,918)	(30,878,445)
Net (loss) income attributable to common stockholders	$ (66,431,593)	$ 731,262	$ 26,069
Denominator			
Denominator for basic earnings per share	12,829,411	3,328	1,089
Effect of dilutive securities:			
Employee stock options	—	—	4,640
Series 3 convertible preferred stock	—	13,877	—
Denominator for diluted earnings per share	12,829,411	17,205	5,729
Net (loss) income per share:			
Basic	(5.18)	219.76	23.95
Diluted	(5.18)	42.50	4.55

9. Stock option plan

In 2009, the Company's shareholders approved the 2009 Equity and Long-Term Incentive Plan, which provides for the granting of stock option awards, restricted stock awards, and other stock-based and cash-based awards, subject to certain adjustments and annual increases.

On March 5, 2013, the Company's Board of Directors approved the 2013 Stock Incentive Plan, which provides for the granting of stock option awards, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards in the aggregate of 739,937 shares of common stock. On March 5, 2013, the Board approved a grant of 735,324 shares of restricted stock and 4,613 stock options. There are no additional shares available for issuance under this plan.

In May 2013, the Company's Board of Directors and stockholders increased by 2,500,000 the number of shares authorized under the 2009 Stock Incentive Plan, which provides for the granting of stock option awards, restricted stock awards, and other stock-based and cash-based awards.

In May 2013, the Company's Board of Directors and stockholders approved the 2013 Long Term Incentive Plan, which became effective upon the closing of the Company's IPO. The 2013 Long Term

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

9. Stock option plan (Continued)

Incentive Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards and other stock-based awards. The number of shares of common stock reserved for issuance under the 2013 Long Term Incentive Plan is the sum of (1) 122,296 shares of common stock available for issuance under the Company's 2009 Equity and Long Term Incentive Plan and 2013 Stock Incentive Plan, (2) the number of shares (up to 3,040,444 shares) equal to the sum of the number of shares of common stock subject to outstanding awards under the Company's 1998 Employee, Director and Consultant Stock Option Plan and 2013 Stock Incentive Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right plus (3) an annual increase, to be added on the first day of each fiscal year until the expiration of the 2013 Long Term Incentive Plan, equal to the lowest of 2,500,000 shares of common stock, 4% of the number of shares of common stock outstanding on the first day of the fiscal year and an amount determined by the Company's Board of Directors. As of December 31, 2013, awards for 96,917 shares of common stock are available for issuance.

The Board of Directors has the authority to select the individuals to whom options are granted and determine the terms of each option, including (i) the number of shares of common stock subject to the option; (ii) the date on which the option becomes exercisable; (iii) the option exercise price, which, in the case of incentive stock options, must be at least 100% (110% in the case of incentive stock options granted to a stockholder owning in excess of 10% of the Company's stock) of the fair market value of the common stock as of the date of grant; and (iv) the duration of the option (which, in the case of incentive stock options, may not exceed ten years). Options typically vest over a three- or four-year period.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

9. Stock option plan (Continued)

A summary of stock option activity is as follows:

	Number of options	Exercise price	Weighted-average exercise price	Weighted-average remaining contractual term	Aggregate intrinsic value
Outstanding at December 31, 2010	39,557	$ 226.80 - $1,149.60	$ 547.20		
Granted	8,123	$ 490.80	$ 490.80		
Exercised	(11)	$ 451.20 - $508.80	$ 459.60		
Forfeited	(875)	$ 226.80 - $1,149.60	$ 757.20		
Outstanding at December 31, 2011	46,794	$ 226.80 - $1,149.60	$ 532.80	5.74 years	
Granted	5,715	$ 218.40	$ 218.40		
Exercised	—				
Forfeited	(10,115)	$ 218.40 - $1,149.60	$ 604.80		
Outstanding at December 31, 2012	42,394	$ 218.40 - $1,149.60	$ 474.00	5.02 years	
Granted	2,117,113	$ 10.59 - $20.76	$ 11.29		
Exercised	—				
Forfeited	(63,915)	$ 10.85 - $1,149.60	$ 12.57		
Outstanding at December 31, 2013	2,095,592	$ 10.59 - $1,149.60	$ 20.24	9.29 years	$ 11,905,903
Vested or expected to vest at December 31, 2013	1,971,286		$ 20.78	9.28 years	$ 11,209,761
Exercisable at December 31, 2013	146,340		$ 129.81	7.90 years	$ 688,971

The total intrinsic value (the excess of the market price over the exercise price) for stock options exercised in 2011 was immaterial. There were no stock option exercises in 2013 or 2012.

The fair value of grants made in the years ended December 31, 2013, 2012 and 2011 was contemporaneously estimated on the date of grant using the following assumptions:

	2013	2012	2011
Risk-free interest rate	0.85 - 1.90%	1.14%	2.40%
Expected volatility	87 - 89%	87%	87%
Expected term	6.00 - 6.25 years	6.00 - 6.25 years	6.00 - 6.25 years

The Company assumed no expected dividends for all grants. The weighted average grant date fair value of options granted during the years ended December 31, 2013, 2012 and 2011 was $8.23, $160.65 and $364.80, respectively.

The Company uses the "simplified method" to determine the expected term of options. Under this method, the expected term represents the average of the vesting period and the contractual term. The expected volatility of share options was estimated based on a historical volatility analysis of peers that were similar to the Company with respect to industry, stage of life cycle, size, and financial leverage.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

9. Stock option plan (Continued)

The risk-free rate of the option is based on U.S. Government Securities Treasury Constant Maturities yields at the date of grant for a term similar to the expected term of the option.

The following table summarizes stock options outstanding and exercisable at December 31, 2013:

	Outstanding			Exercisable	
Range of Exercise Price	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Number of Options	Weighted Average Exercise Price
$10.59 - $10.85	1,945,213	$ 10.85	9.37	109,113	$ 10.84
$10.85 - $20.76	109,400	$ 19.43	9.87	—	$ —
$20.76 - $490.80	28,226	$ 311.28	3.75	24,676	$ 309.97
$490.80 - 735.60	8,964	$ 673.95	3.87	8,966	$ 673.95
$1,149.60	3,789	$ 1,149.60	6.01	3,585	$ 1,149.60
	2,095,592			146,340	

In December 2013, the Compensation Committee of the Board of Directors modified the terms of certain performance based stock options granted to executive management. Under the modified terms, the Committee waived all remaining performance conditions associated with the initial vesting of the options such that the options vest with service only conditions. The Company accounted for the modification to the option grants pursuant to ASC Topic 718-20-35 and recognized approximately $0.6 million as additional compensation that was charged to operations during the period ended December 31, 2013.

Restricted Stock Awards—Restricted stock awards are granted subject to certain restrictions, including in some cases service conditions (restricted stock). The grant-date fair value of restricted stock awards, which has been determined based upon the market value of the Company's shares on the grant date, is expensed over the vesting period.

The following table summarizes information on the Company's restricted stock:

	Restricted Stock	
	Number of Shares	Weighted Average Grant Date Fair Value
January 1, 2013	—	—
Granted	1,131,524	$ 10.68
Vested	—	$ —
Forfeited	(21,298)	$ 10.65
Unvested at December 31, 2013	1,110,226	$ 10.68

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

9. Stock option plan (Continued)

The Company recorded share-based compensation expense in the statement of operations as follows:

	Year ended December 31,		
	2013	2012	2011
Research and development	$ 2,039,880	$ 804,576	$ 916,495
General and administrative	6,387,308	1,483,816	1,900,142
Total	$ 8,427,188	$ 2,288,392	$ 2,816,637

The Company utilizes newly issued shares to satisfy stock option exercises.

As of December 31, 2013, there was approximately $21.6 million of total unrecognized compensation cost related to unvested share-based compensation arrangements granted under the Company's Plans. This cost is expected to be recognized as compensation expense over the weighted average remaining service period of approximately 2.49 years.

10. Other comprehensive income (loss) and accumulated other comprehensive items

Other comprehensive income (loss) includes changes in equity that are excluded from net loss, such as unrealized gains and losses on marketable securities.

The following table summarizes other comprehensive income (loss) and the changes in accumulated other comprehensive items, by component, for the years ended December 31, 2013, 2012, and 2011, respectively.

	Unrealized Gains On Marketable Securities	Total Accumulated Other Comprehensive Items
Balance at January 1, 2011	$ 3,606	$ 3,606
Other comprehensive loss before reclassifications	(3,606)	(3,606)
Amounts reclassified from other comprehensive items	—	—
Other comprehensive income/(loss)	—	—
Balance at December 31, 2011	$ —	$ —
Other comprehensive income/(loss) before reclassifications	—	—
Amounts reclassified from other comprehensive items	—	—
Other comprehensive income/(loss)	—	—
Balance at December 31, 2012	$ —	$ —
Other comprehensive income before reclassifications	70,393	70,393
Amounts reclassified from other comprehensive items	—	—
Other comprehensive income	70,393	70,393
Balance at December 31, 2013	$ 70,393	$ 70,393

11. Collaborations and grants

The Company has ongoing collaborations with the Spinal Muscular Atrophy Foundation (SMA Foundation) and F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc. (collectively, Roche) and early

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

11. Collaborations and grants (Continued)

stage discovery arrangements with other institutions. During 2011, the Genzyme collaboration was modified and later terminated. The following are the key terms to the Company's (i) terminated collaboration with Genzyme, (ii) ongoing collaborations and (iii) early stage discovery and development arrangements.

Terminated collaboration

Genzyme

In July 2008, Genzyme Corporation (now a Sanofi company) and the Company entered into an exclusive global collaboration to develop and commercialize ataluren, the Company's novel oral therapy in late-stage development for the treatment of genetic disorders due to nonsense mutations. Under the terms of this agreement, the Company granted Genzyme rights to commercialize ataluren in all countries except the United States and Canada, which rights the Company retained. Genzyme made a nonrefundable upfront payment to the Company of $100.0 million in July 2008, which was being recognized over the Company's estimated period of performance under the arrangement.

In August 2011, the Company and Genzyme announced a restructuring of the agreement. Under the terms of the restructuring, the Company regained worldwide rights to ataluren and Genzyme made an additional payment of $7.5 million to the Company in exchange for an option to commercialize ataluren in indications other than nonsense mutation Duchenne muscular dystrophy (nmDMD) outside the United States and Canada. On March 27, 2012, the Company received notification that Genzyme declined to exercise the option, at which time the option expired. As a result, the collaboration was terminated.

The Company evaluated the August 2011 restructuring of the Genzyme collaboration agreement and determined it to be a material modification to the original agreement for financial reporting purposes pursuant to the revised multiple element revenue recognition guidance. The Company determined that given the significance of the changes in relation to the initial arrangement, including the decrease in the total consideration that could be paid to the Company, the significant removal of existing deliverables, the significant changes in the intellectual property rights and the significant change in the performance period, the initial arrangement had been effectively terminated. The Company elected to reevaluate the amended agreement and performed an analysis to calculate the estimated selling price of the undelivered elements of the arrangement. Based on this analysis, the Company determined that the undelivered element had an estimated selling price of $8.8 million, and as such, adjusted the Company's deferred revenue balance to reflect this amount as of the contract amendment date. The Company amortized the balance through the option period. The effect of this reevaluation was to recognize approximately $79.0 million as of the restructuring date. For the years ended December 31, 2011 and 2012, the Company recognized approximately $90.0 million and $3.8 million respectively, in collaboration revenue from Genzyme.

Current collaboration

Roche and SMA Foundation

In November 2011, the Company and the SMA Foundation entered into a licensing and collaboration agreement with Roche for a spinal muscular atrophy program. Under the terms of the agreement, Roche acquired an exclusive worldwide license to the Company's spinal muscular atrophy

11. Collaborations and grants (Continued)

program, which includes three compounds currently in preclinical development, as well as potential back-up compounds. The Company received a nonrefundable upfront cash payment of $30.0 million and Roche agreed to provide funding for research activities performed on its behalf.

The Company applied the revised multiple element revenue recognition guidance in evaluating the accounting treatment of this collaboration agreement. The Company identified two possible significant deliverables in the collaboration agreement, the license and the research activities. The Company evaluated whether these significant deliverables have stand-alone value and determined that the license does not have standalone value without the ongoing research and development services given the unique nature of the technology. As such, both of these elements were combined as a single unit for accounting purposes. As a result, the Company deferred the $30.0 million upfront payment which is being recognized over the estimated performance period of two years, which is the contracted research period. For the year ended December 31, 2013 and 2012, the Company recognized approximately $26.6 million and $18.4 million respectively, in collaboration revenue. The balance of the remaining deferred upfront payment was $0 at December 31, 2013.

Under the agreement, the Company is eligible to receive additional payments from Roche if specified events are achieved with respect to each licensed product, including up to $135.0 million in research and development event milestones, up to $325.0 million in sales milestones upon achievement of sales events, and up to double digit royalties on worldwide annual net sales of a commercial product.

The Company considers that each of the potential milestone events under the agreement would be substantive because the applicable criteria of its revenue recognition policy (see Note 2) would be satisfied.

Early stage collaboration and discovery agreements

The Company has arrangements with several organizations pursuant to which the Company uses its discovery technologies to help identify potential drug candidates. The Company does not take ownership of the potential compounds, but rather provides research services to the collaborator using its specialized technology platform.

Generally, these arrangements are structured such that the collaborator and the Company work together to jointly select targets from which to apply its discovery technologies. The research period for the Company to apply its technology is generally three to four years. The Company will typically receive a nonrefundable, upfront cash payment and the collaborator agrees to provide funding for research activities performed on its behalf.

For those arrangements entered into or significantly modified after January 1, 2011, the Company applies the revised multiple element revenue recognition guidance in evaluating the accounting treatment for these arrangements. Generally, the two significant deliverables in these arrangements are the license and the research activities. The Company evaluates whether the deliverables have standalone value. However, since the Company's discovery technologies are highly specialized, the Company has determined that the license does not have standalone value without the ongoing research and development services and accounts for these arrangements as a single unit of accounting.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

11. Collaborations and grants (Continued)

As a result, the Company has deferred revenue of $0.9 million and $3.0 million as of December 31, 2013 and 2012, respectively, related to these arrangements. For the years ended December 31, 2013 and 2012, the Company recognized approximately $4.8 million and $6.6 million in collaboration revenue, respectively.

The Company is eligible to receive additional payments from its early stage discovery research arrangements if the discovery compounds are ultimately developed and commercialized. The aggregate potential payments the Company is eligible for if all products are developed is $143.0 million and up to $252.0 million in sales milestones upon achievement of specified sales events and up to double digit royalties on worldwide annual net sales of the licensed product.

The Company considers that each of the potential milestone events under the agreement would be substantive because the applicable criteria of its revenue recognition policy (see Note 2) would be satisfied.

Grant revenue

The company receives grant funding from various institutions and governmental bodies. The grants are typically for early discovery research, and typically the grant program lasts from two to five years. The Company records revenue as the research activities are performed. If the granting agency provides for an upfront payment, the amount is deferred and recognized as revenue as the expenditures are incurred.

12. Income taxes

A reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows:

	December 31,		
	2013	2012	2011
Federal income tax (benefit) at statutory rate	34.00%	34.00%	34.00%
State income tax benefit, net of federal benefit	5.65	3.80	4.20
Permanent differences	(5.90)	—	—
Research and development	15.88	—	—
Increase to valuation allowance	(49.63)	(35.80)	(45.90)
Other	—	(2.00)	(1.60)
Effective income tax rate	0.00%	0.00%	(9.30)%

The Company recognized a tax benefit of $2.3 million in connection with the sale of net operating losses and research and development credits in the New Jersey Transfer Program for the year ended

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

12. Income taxes (Continued)

December 31, 2011. The significant components of the Company's deferred tax assets and liabilities at December 31, 2013 and 2012 are as follows:

	2013	2012
Deferred tax assets:		
Amortization	$ 80,387	$ 91,871
Depreciation	1,922,332	1,535,952
Accrued expense	332,539	1,208,846
Deferred revenue	350,447	6,962,506
Federal tax credits	14,081,615	5,383,092
State tax credits	1,587,217	1,094,833
Federal net operating losses	88,187,475	71,752,278
State net operating losses	10,456,688	7,619,606
Capitalized research and development costs	12,254,381	10,479,055
Other	3,211,720	742,341
Total gross deferred tax assets	132,464,801	106,870,380
Less valuation allowance	(132,464,801)	(106,870,380)
Net deferred tax assets	$ —	$ —

At December 31, 2013 and 2012, the Company recorded a full valuation allowance against its net deferred tax assets of approximately $132.5 million and $106.9 million, respectively. The change in the valuation allowance during the years ended December 31, 2013 and 2012 was approximately $25.6 million and $9.4 million, respectively. A full valuation allowance has been recorded since, in the judgment of management, these assets are not more likely than not to be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during periods in which those temporary differences and carryforwards become deductible or are utilized.

As of December 31, 2013, the Company has approximately $259.4 million and $176.0 million of federal and state net operating loss carryforwards, respectively. As of December 31, 2013, credit carryforwards for federal and state purposes are approximately $6.0 million and $2.3 million, respectively. The federal net operating loss carryforwards begin to expire in 2021, while the federal credit carryforwards begin to expire in 2019. State net operating loss carryforwards begin to expire in 2029, and the state credit carryforwards begin to expire in 2022. Sections 382 and 383 of the Internal Revenue Code of 1986 subject the future utilization of net operating losses and certain other tax attributes, such as research and experimental tax credits, to an annual limitation in the event of certain ownership changes, as defined. The Company has had a number of equity transactions since inception, and several of these have created ownership changes that could create such a limitation. The Company has not recently performed an analysis to determine the Company's ability to utilize such carryforwards prior to expiration. An analysis will be performed in the future, as necessary.

The State of New Jersey provides the Technology Business Tax Certificate Transfer Program enabling approved unprofitable biotechnology businesses to sell their unused net operating loss carryforwards to unaffiliated, profitable corporate taxpayers in the State of New Jersey for cash. The Company has participated in this program and sold state net operating losses totaling $28.5 million

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

12. Income taxes (Continued)

during 2011. The New Jersey net operating losses sold during 2011 were generated during 2009. For 2011, the Company established a receivable for the $2.3 million, which was received in 2012. The Company did not participate in this program in 2012 or 2013.

The income tax benefit for the years ended December 31, 2013 and 2012 differed from the amounts computed by applying the U.S. federal income tax rate of 34% to loss before tax benefit as a result of non-deductible expenses, tax credits generated, utilization of net operating loss carryforwards and increases in the Company's valuation allowance. At December 31, 2013 the Company had no unrecognized income tax benefits. The Company applies the accounting guidance for uncertain income tax provisions. This guidance clarifies the accounting for uncertainty in income taxes recognized in financial statements and requires the impact of a tax position to be recognized in the financial statements if that position is more likely than not of being sustained by the taxing authority. As of December 31, 2013, the Company did not have any unrecognized tax benefits and has not accrued any interest or penalties through 2013. The Company does not expect to have any unrecognized tax benefits within the next twelve months. The Company's policy is to recognize interest and penalties related to tax matters within the income tax provision. Tax years beginning in 2010 are generally subject to examination by taxing authorities, although net operating losses from all years are subject to examinations and adjustments for at least three years following the year in which the attributes are used.

In July 2013, the FASB issued amended guidance for the presentation of an unrecognized tax benefit when a net operating loss carry forward exits, which is effective for the Company January 1, 2014. This amended guidance requires an entity to present an unrecognized tax benefit as a reduction of a deferred tax asset for a net operating carry forward, a similar tax loss or a tax credit carry forward. If an applicable deferred tax asset is not available or a company does not expect to use the applicable deferred tax asset, the unrecognized tax benefit should be presented as a liability in the financial statements and should not be combined with an unrelated deferred tax asset. The Company does not expect the adoption of this amended guidance to have a significant impact on the consolidated financial statements.

13. Commitments and contingencies

Operating leases

The Company leases office space under a noncancelable operating lease through February 2019. Rent expense was approximately $0.7 million for each of the years ended December 31, 2013, 2012 and

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

13. Commitments and contingencies (Continued)

2011. The Company also leases certain office equipment under operating leases. Future minimum lease payments as of December 31, 2013 are as follows:

2014	$ 890,000
2015	849,000
2016	849,000
2017	849,000
2018	952,000
Thereafter	162,000
	$ 4,551,000

Other contingencies

Under various agreements, the Company will be required to pay royalties and milestone payments upon the successful development and commercialization of products. The Company has entered into funding agreements with The Wellcome Trust Limited (Wellcome Trust) for the research and development of small molecule compounds. To the extent that the Company develops and commercializes program intellectual property on a for-profit basis, it may become obligated to pay to Wellcome Trust development and regulatory milestone payments of up to an aggregate of $68.9 million and single-digit royalties on sales of any research program product. The Company's obligation to pay such royalties would continue on a country-by-country basis until the longer of the expiration of the last patent in the program intellectual property in such country covering the research program product and the expiration of market exclusivity of such product in such country.

The Company has also entered into a collaboration agreement with the SMA Foundation. The Company may become obligated to pay the SMA Foundation single-digit royalties on worldwide net product sales of any collaboration product that we successfully develop and subsequently commercialize or, if we outlicense rights to a collaboration product, a specified percentage of certain payments we receive from our licensee. The Company is not obligated to make such payments unless and until annual sales of a collaboration product exceed a designated threshold. The Company's obligation to make such payments would end upon our payment to the SMA Foundation of a specified amount.

The Company has employment agreements with certain employees which require the funding of a specific level of payments, if certain events, such as a change in control or termination without cause, occur.

14. 401(k) plan

The Company maintains a 401(k) plan for its employees. Employee contributions are voluntary. The Company may match employee contributions in amounts to be determined at the Company's sole discretion. The Company provides a 20% matching contribution for up to the first 5% of each contributing employee's base salary contributions. The Company made matching contributions to the 401(k) plan and recorded expense of approximately $0.1 million, $0.2 million and $0.2 million for the years ended December 31, 2013, 2012 and 2011, respectively.

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

15. Selected quarterly financial data

The following financial information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for 2013 and 2012 are as follows:

	For the quarters ending			
	March 31	June 30	September 30	December 31
2013:				
Collaboration and grant revenue	$ 7,141,664	$ 6,854,212	$ 16,289,573	$ 4,410,878
Operating expenses	15,718,073	21,307,148	20,565,188	22,503,387
Loss from operations	(8,576,409)	(14,452,936)	(4,275,615)	(18,092,509)
Net loss	(14,684,535)	(14,586,578)	(4,416,499)	(17,885,963)
Deemed dividend	(18,248,768)	—	—	—
Gain on exchange of convertible preferred stock in connection with recapitalization	3,390,750	—	—	—
Net loss attributable to common stockholders	(29,542,553)	(14,586,578)	(4,416,499)	(17,885,963)
Basic net loss per common share(1)	$ (6,527.30)	$ (5.51)	$ (0.19)	$ (0.75)
Diluted net loss per common share(1)	$ (6,527.30)	$ (5.51)	$ (0.19)	$ (0.75)
2012:				
Collaboration and grant revenue	$ 12,525,720	$ 7,585,177	$ 7,195,076	$ 6,640,090
Operating expenses	18,745,957	15,083,384	14,250,383	12,674,520
Loss from operations	(6,220,237)	(7,498,207)	(7,055,307)	(6,034,430)
Net loss	(6,597,861)	(6,068,072)	(7,297,125)	(6,272,044)
Gain on exchange of convertible preferred stock in connection with recapitalization	—	159,954,069	—	—
Less beneficial conversion charge	—	(377,787)	—	—
Net income (loss) attributable to common stockholders	(6,597,861)	153,508,210	(7,297,125)	(6,272,044)
Basic net income (loss) per common share(1)	$ (5,992.61)	$ 168.00	$ (1,605.53)	$ (1,380.13)
Diluted net income (loss) per common share(1)	$ (5,992.61)	$ 48.29	$ (1,605.53)	$ (1,380.13)

(1) The amounts were computed independently for each quarter and the sum of the quarters may not total the annual amounts.

16. Subsequent events

The Company continues to advance the development of its spinal muscular atrophy (SMA) collaboration with Roche and the SMA Foundation. The collaboration was initially funded in part by the SMA Foundation. In December 2011, the Company announced a partnership with Roche in the collaboration which provided an upfront payment of $30.0 million, up to $460.0 million in milestone payments and royalties on future sales. In August 2013, a development candidate for the program was announced which triggered a $10.0 million milestone payment from Roche. In January 2014, a

PTC Therapeutics, Inc.

Notes to financial statements (Continued)

December 31, 2013

16. Subsequent events (Continued)

Phase 1 clinical program was initiated which triggered a $7.5 million milestone payment from Roche. Roche is responsible for pursuing clinical development of compounds from the program consistent with a governance structure that includes representation from the Company and the SMA Foundation and then commercialization of these compounds.

In February 2014, the Company initiated an underwritten public offering of 4,489,796 million shares of common stock at a public offering price of $24.50 per share, before underwriting discounts. All of the shares in the offering were offered and sold by PTC. In addition, PTC granted the underwriters an option for a period of 30 days to purchase up to 673,469 additional shares of common stock at the public offering price, less the underwriting discount, which the underwriters exercised in full. J.P. Morgan and Credit Suisse acted as joint lead book-running managers for the offering. A registration statement relating to these securities was declared effective by the Securities and Exchange Commission on February 12, 2014. The Company received net proceeds of approximately $118.4 million upon the close of the offering.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2013. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. 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. Based on the evaluation of our disclosure controls and procedures as of December 31, 2013, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting occurred during the quarter ended December 31, 2013 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item as set forth under the captions "Proposal 1—Election of Directors," "Executive Officers," "Section 16(a) Beneficial Ownership Reporting Compliance," "Corporate Governance—Audit Committee," and "Stockholder Proposals and Nominations for Director"in our Proxy Statement for the 2014 Annual Meeting of Shareholders is incorporated in this Annual Report on Form 10-K by reference.

Code of Ethics

We have adopted a code of business conduct and ethics that applies to our directors and officers (including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions) as well as our other employees. A copy of our code of business conduct and ethics is available on our website, www.ptcbio.com, under "Investor Relations," and is available in print to any person who requests it. We intend to post on our website all disclosures that are required by applicable law, the rules of the Securities and Exchange Commission or the NASDAQ Global Select Market concerning any amendment to, or waiver of, our code of business conduct and ethics.

Item 11. Executive Compensation

The information required by this item as set forth in under the captions "Executive Compensation," "Director Compensation," and "Corporate Governance—Compensation Committee Interlocks and Insider Participation" in our Proxy Statement for the 2014 Annual Meeting of Shareholders is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item as set forth under the captions"Equity Compensation Plan Information" and "Principal Stockholders"in our Proxy Statement for the 2014 Annual Meeting of Shareholders is incorporated in 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 as set forth under the caption ""Corporate Governance—Transactions with Related Person," and "Corporate Governance - Director Independence"in our Proxy Statement for the 2014 Annual Meeting of Shareholders is incorporated in this Annual Report on Form 10-K by reference.

Item 14. Principal Accountant Fees and Services

The information required by this item as set forth under the caption "Proposal 2—Ratification of Election of Independent Registered Public Accounting Firm"in our Proxy Statement for the 2014 Annual Meeting of Shareholders is incorporated in this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

Financial Statements

The following statements and supplementary data are included in Part II Item 8 of the Annual Report on Form 10-K.

- Report of Independent Registered Public Accounting Firm
- Consolidated Balance Sheets as of December 31, 2013 and 2012
- Consolidated Statements of Operations for the years ended December 31, 2013, 2012 and 2011
- Consolidated Statements of Comprehensive Income (Loss) for the years ended December 31, 2013, 2012 and 2011
- Consolidated Statements of Cash Flows for the years ended December 31, 2013, 2012 and 2011
- Consolidated Statements of Stockholders' Equity for the years ended December 31, 2013, 2012and 2011
- Notes to Consolidated Financial Statements

Exhibits

Those exhibits required to be filed by Item 601 of Regulation S-K are listed in the Exhibit Index immediately preceding the exhibits hereto and such listing is incorporated herein by reference.

Exhibit Index

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.3 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.4 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
4.1	Specimen Stock Certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
4.2	Second Amended and Restated Investor Rights Agreement dated as of March 7, 2013 (incorporated by reference to Exhibit 4.2 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.1+	1998 Employee, Director and Consultant Stock Option Plan, as amended (incorporated by reference to Exhibit 10.1 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.2+	Form of Incentive Stock Option Certificate under 1998 Employee, Director and Consultant Stock Option Plan (incorporated by reference to Exhibit 10.2 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.3+	Form of Non-Qualified Stock Option Certificate under 1998 Employee, Director and Consultant Stock Option Plan (incorporated by reference to Exhibit 10.3 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.4+	2009 Equity and Long Term Incentive Plan, as amended (incorporated by reference to Exhibit 10.4 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.5+	Form of Notice of Award for Incentive Stock Option under 2009 Equity and Long Term Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.6+	Form of Notice of Award for Nonstatutory Stock Option under 2009 Equity and Long Term Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.7+	2013 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.8+	Form of Restricted Stock Agreement under 2013 Stock Incentive Plan (incorporated by reference to Exhibit 10.8 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.9+	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.10+	2013 Long Term Incentive Plan (incorporated by reference to Exhibit 10.10 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)

Exhibit Number	Description of Exhibit
10.11+	Form of Incentive Stock Option Agreement under 2013 Long Term Incentive Plan (incorporated by reference to Exhibit 10.11 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.12+	Form of Nonstatutory Stock Option Agreement under 2013 Long Term Incentive Plan (incorporated by reference to Exhibit 10.12 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.13	Lease Agreement, dated as of July 11, 2000, as amended, between the Registrant and 46.24 Associates L.P. (incorporated by reference to Exhibit 10.13 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.14†	License and Collaboration Agreement, dated as of November 23, 2011, as amended, by and among the Registrant, F. Hoffmann-La Roche Ltd and Hoffmann-La Roche, Inc. and Spinal Muscular Atrophy Foundation (incorporated by reference to Exhibit 10.14 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.15†	Sponsored Research Agreement, as amended dated as of June 1, 2006, by and between the Registrant and Spinal Muscular Atrophy Foundation (incorporated by reference to Exhibit 10.15 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.16†	Funding Agreement, dated as of May 26, 2010, by and between the Registrant and The Wellcome Trust Limited (incorporated by reference to Exhibit 10.16 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.17†	Funding Agreement, dated as of December 21, 2011, by and between the Registrant and The Wellcome Trust Limited (incorporated by reference to Exhibit 10.17 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.19+	Form of Restricted Stock Agreement under 2009 Equity and Long Term Incentive Plan (incorporated by reference to Exhibit 10.19 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.20+	Amended and Restated Employment Agreement between the Registrant and Stuart W. Peltz (incorporated by reference to Exhibit 10.20 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.21+	Amended and Restated Employment Agreement between the Registrant and Claudia Hirawat (incorporated by reference to Exhibit 10.21 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.22+	Amended and Restated Employment Agreement between the Registrant and Mark E. Boulding (incorporated by reference to Exhibit 10.22 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.23+	Employment Agreement between the Registrant and Mark A. Rothera (incorporated by reference to Exhibit 10.23 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.24+	Amended and Restated Employment Agreement between the Registrant and Neil Almstead (incorporated by reference to Exhibit 10.24 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)

Exhibit Number	Description of Exhibit
10.25+	Employment Agreement between the Registrant and Shane Kovacs (incorporated by reference to Exhibit 10.26 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
21.1	Subsidiaries of the Registrant
24.1	Power of attorney (included on the signature page to this Form 10-K)
23.1	Consent of Independent Registered Public Accounting Firm
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Database
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document

† Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

+ Management contract, compensatory plan or arrangement.

* In accordance with Rule 406T of Regulation S-T, the XBRL related information in Exhibit 101 to this Annual Report on Form 10-K is deemed not filed or part of a registration statement or prospectus for purposes of Sections 11 or 12 of the Securities Act, is deemed not filed for purposes of Section 18 of the Exchange Act, and otherwise is not subject to liability under these sections.

Stockholders may obtain (without charge) a copy of this Annual Report on Form 10-K (including the financial statements and financials statement schedules) and a copy of any exhibit thereto (upon payment of a fee limited to our reasonable expenses in furnishing such exhibit) by writing to PTC Therapeutics, Inc., 100 Corporate Court, South Plainfield, New Jersey 07080.

Signatures and power of attorney

We, the undersigned officers and directors of PTC Therapeutics, Inc., hereby severally constitute and appoint Stuart W. Peltz and Mark E. Boulding, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

PTC THERAPEUTICS, INC.

Date: March 6, 2014

By: /s/ STUART W. PELTZ

Stuart W. Peltz, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

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

Dated: March 6, 2014

By: /s/ STUART W. PELTZ

Stuart W. Peltz
Chief Executive Officer
Director

Dated: March 6, 2014

By: /s/ SHANE KOVACS

Shane Kovacs
Chief Financial Officer
(Principal Financial and Accounting Officer)

Dated: March 6, 2014

By: /s/ MICHAEL SCHMERTZLER

Michael Schmertzler
Director

Dated: March 6, 2014

By: /s/ RICHARD ALDRICH

Richard Aldrich
Director

Dated: March 6, 2014	By:	/s/ AXEL BOLTE
		Axel Bolte *Director*
Dated: March 6, 2014	By:	/s/ ALLAN JACOBSON
		Allan Jacobson *Director*
Dated: March 6, 2014	By:	/s/ ADAM KOPPEL
		Adam Koppel *Director*
Dated: March 6, 2014	By:	/s/ MICHAEL KRANDA
		Michael Kranda *Director*
Dated: March 6, 2014	By:	/s/ GEOFFREY MCDONOUGH
		Geoffrey McDonough *Director*
Dated: March 6, 2014	By:	/s/ DAVID P. SOUTHWELL
		David P. Southwell *Director*
Dated: March 6, 2014	By:	/s/ JEROME B. ZELDIS
		Jerome B. Zeldis *Director*

Exhibit 21.1

LIST OF SUBSIDIARIES OF
PTC THERAPEUTICS, INC.

	Jurisdiction of Incorporation or Organization
PTC Therapeutics, Limited	England and Wales

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LIST OF SUBSIDIARIES OF PTC THERAPEUTICS, INC.

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Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-194323) pertaining to the 2013 Long Term Incentive Plan, and the Inducement Stock Option Award and in the Registration Statement (Form S-8 No. 333-189962) pertaining to the 2013 Long Term Incentive Plan, the 2013 Stock Incentive Plan, the 2009 Equity and Long Term Incentive Plan, as amended, and the1998 Employee, Director and Consultant Stock Option Plan, as amended of PTC Therapeutics, Inc. of our report dated March 6, 2014, with respect to the financial statements of PTC Therapeutics, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2013.

/s/ Ernst & Young LLP

MetroPark, New Jersey
March 6, 2014

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Exhibit 31.1

CERTIFICATIONS

I, Stuart W. Peltz, certify that:

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

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

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

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

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

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

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

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

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

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

Date: March 6, 2014

By: /s/ STUART W. PELTZ

Stuart W. Peltz
Chief Executive Officer
(Principal Executive Officer)

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Exhibit 31.2

CERTIFICATIONS

I, Shane Kovacs, certify that:

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

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

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

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

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

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

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

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

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

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

Date: March 6, 2014

By: /s/ SHANE KOVACS

Shane Kovacs
Chief Financial Officer
(Principal Financial and Accounting Officer)

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Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of PTC Therapeutics, Inc. (the "Company") for the period ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Stuart W. Peltz, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

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

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

Date: March 6, 2014

By: /s/ STUART W. PELTZ

Stuart W. Peltz
Chief Executive Officer
(Principal Executive Officer)

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Exhibit 32.2

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

In connection with the Annual Report on Form 10-K of PTC Therapeutics, Inc. (the "Company") for the period ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Shane Kovacs, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

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

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

Date: March 6, 2014

By: /s/ SHANE KOVACS

Shane Kovacs
Chief Financial Officer
(Principal Financial and Accounting Officer)

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