

Sarepta Therapeutics, Inc.
Form 424B5
October 05, 2015
Table of Contents

**Filed pursuant to Rule 424(b)(5)
Registration No. 333-184807**

The information in this preliminary prospectus supplement and the accompanying prospectus, relating to an effective registration statement under the Securities Act of 1933, as amended, is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated October 5, 2015

Preliminary Prospectus Supplement

(To Prospectus dated May 5, 2015)

\$125,000,000

Sarepta Therapeutics, Inc.

Common Stock

We are offering up to \$125,000,000 of our common stock in this offering.

Our common stock is listed on The NASDAQ Global Select Market under the symbol SRPT. On October 2, 2015, the last reported sale price of our common stock on The NASDAQ Global Select Market was \$39.59 per share.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions	\$	\$
Proceeds, before expenses, to us	\$	\$

We have granted the underwriters an option to purchase up to \$18,750,000 of additional shares from us at the public offering price, less underwriting discounts and commissions, within 30 days of the date of this prospectus supplement. If the underwriters exercise this option in full, the total underwriting discounts and commissions will be \$7,187,500 and the total proceeds, before expenses, to us will be \$136,562,500.

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider all of the information set forth in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein. See Risk Factors beginning on page S-5 of this prospectus supplement, page 3 of the accompanying prospectus and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters are offering the shares of our common stock as set forth under Underwriting. Delivery of the shares of common stock will be made on or about October , 2015.

Credit Suisse

The date of this prospectus supplement is October , 2015.

Morgan Stanley

Table of Contents

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

	Page
<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	S-ii
<u>PROSPECTUS SUPPLEMENT SUMMARY</u>	S-1
<u>THE OFFERING</u>	S-4
<u>RISK FACTORS</u>	S-5
<u>FORWARD-LOOKING STATEMENTS</u>	S-26
<u>USE OF PROCEEDS</u>	S-29
<u>MATERIAL U.S. FEDERAL TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK</u>	S-30
<u>DILUTION</u>	S-34
<u>UNDERWRITING</u>	S-36
<u>LEGAL MATTERS</u>	S-41
<u>EXPERTS</u>	S-41
<u>WHERE YOU CAN FIND ADDITIONAL INFORMATION</u>	S-41
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	S-42
ACCOMPANYING PROSPECTUS	

	Page
<u>ABOUT THIS PROSPECTUS</u>	1
<u>THE COMPANY</u>	2
<u>RISK FACTORS</u>	3
<u>FORWARD-LOOKING STATEMENTS</u>	4
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	6
<u>USE OF PROCEEDS</u>	7
<u>SELLING SECURITY HOLDERS</u>	8
<u>GENERAL DESCRIPTION OF SECURITIES WE MAY SELL</u>	9
<u>PLAN OF DISTRIBUTION</u>	23
<u>LEGAL MATTERS</u>	26
<u>EXPERTS</u>	26
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	26
<u>INFORMATION INCORPORATED BY REFERENCE</u>	27

DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT
LIABILITIES

S-i

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is the prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under **Where You Can Find Additional Information** on page S-41 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference therein.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. We have not, and the underwriters have not, authorized any other person to provide any information other than that contained or incorporated by reference in this prospectus supplement or in any free writing prospectus prepared by or on behalf of us. Neither we nor the underwriters take any responsibility for, and can provide no assurance as to the reliability of, any information that others may give you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation. You should not assume that the information contained in this prospectus supplement, the accompanying prospectus or the documents incorporated herein or therein by reference is accurate as of any date other than their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates.

In this prospectus supplement and the accompanying prospectus, unless the context specifies or implies otherwise, the terms the Company, Sarepta, we, us, and our refer to Sarepta Therapeutics, Inc. and its subsidiaries.

Table of Contents**PROSPECTUS SUPPLEMENT SUMMARY**

This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all the information you should consider before investing in our common stock pursuant to this prospectus supplement and the accompanying prospectus. Before making an investment decision, to fully understand this offering and its consequences to you, you should carefully read this entire prospectus supplement and the accompanying prospectus, including Risk Factors beginning on page S-5 of this prospectus supplement, the financial statements, and related notes, and the other information that we incorporated by reference herein.

Sarepta Therapeutics, Inc.**Overview**

We are a biopharmaceutical company focused on the discovery and development of unique RNA-targeted therapeutics for the treatment of rare, infectious and other diseases. Applying our proprietary, highly-differentiated and innovative platform technologies, we are able to target a broad range of diseases and disorders through distinct RNA-targeted mechanisms of action. We are primarily focused on rapidly advancing the development of our potentially disease-modifying Duchenne muscular dystrophy (DMD) product candidates, including our lead DMD product candidate, eteplirsen, designed to skip exon 51. On August 25, 2015, we announced the FDA's acceptance of our New Drug Application (NDA) for eteplirsen for the treatment of DMD amenable to exon 51 skipping. We are also developing therapeutics using our technology for the treatment of drug resistant bacteria and infectious, rare and other human diseases.

Our RNA-targeted technologies work at the most fundamental level of biology and potentially could have a meaningful impact across a broad range of human diseases and disorders. Our lead program focuses on the development of disease-modifying therapeutic candidates for DMD, a rare genetic muscle-wasting disease caused by the absence of dystrophin, a protein necessary for muscle function. Currently, there are no approved disease-modifying therapies for DMD in the U.S.; the FDA, however, has accepted NDAs for eteplirsen, our lead product candidate for DMD, and for drisapersen, which is being developed by BioMarin Pharmaceuticals, Inc., each for patients amenable to exon 51 skipping. Approximately 13 percent of people with DMD are estimated to have the mutation amenable to exon 51 skipping. If we are successful in our development efforts, eteplirsen will address a severe and currently unmet medical need. We are in the process of conducting or initiating several studies for product candidates designed to skip exons 45, 51 and 53 in the U.S. and the European Union (the E.U.). These include (i) studies to further evaluate eteplirsen that include our open label study that began after completion of our Phase IIb eteplirsen study, a confirmatory trial in ambulatory patients, a study on participants with advanced stage DMD and a study with participants with early stage DMD, (ii) a dose-ranging study for our product candidate designed to skip exon 45 and (iii) a placebo-controlled confirmatory study with product candidates designed to skip exons 45 and 53. We have also leveraged the capabilities of our RNA-targeted technology platforms to develop investigational therapeutics for the treatment of infectious diseases such as influenza, Marburg and Ebola. We began developing treatments for Marburg and Ebola under prior contracts with the Department of Defense; further development of these product candidates, however, would be conditioned, in part, on obtaining additional funding or collaborations. Our discovery and research programs include collaborations with various third parties and focus on developing therapeutics in rare, genetic, anti-infective, neuromuscular and central nervous system diseases among other diseases. We are exploring the application of our proprietary phosphorodiamidate morpholino oligomer (PMO) platform technology in various diseases including drug resistant bacteria, DMD, Becker muscular dystrophy, progeria, adult onset Pompe disease and lupus.

S-1

Table of Contents

The basis of our novel RNA-targeted therapeutics is the PMO chemistries. Our next generation PMO-based chemistries include PMO-X[®], PMOplus[®] and PPMO. PMOs are highly resistant to degradation by enzymes, potentially enabling robust and sustained biological activity. In contrast to other RNA-targeted therapeutics, which are usually designed to down-regulate protein expression, our technologies are designed to selectively up-regulate or down-regulate protein expression, and more importantly, create novel proteins. PMOs have demonstrated inhibition of messenger RNA (mRNA) translation and alteration of pre-mRNA splicing. The chemistry of PMO-based molecules has the potential to reduce off-target effects, such as the immune stimulation often observed with ribose-based RNA technologies. We believe that our highly-differentiated, novel, proprietary and innovative RNA-targeted PMO-based platforms may represent a significant improvement over other RNA-targeted technologies. In addition, PMOs are highly adaptable molecules: with minor structural modifications, they can potentially be rapidly designed to target specific tissues, genetic sequences, or pathogens, and therefore, we believe they could potentially be applied to treat a broad spectrum of diseases.

We believe we have developed proprietary state-of-the-art manufacturing and scale-up techniques that will allow synthesis and purification of our product candidates to support clinical development as well as potential commercialization. We have entered into certain manufacturing and supply arrangements with third-party suppliers which will in part utilize these techniques to support production of certain of our product candidates and their components. We currently do not have any of our own internal mid-to-large scale manufacturing capabilities to support our product candidates.

Recent Developments

On October 1, 2015, we announced additional clinical efficacy and safety data from the Company's Phase IIb program of eteplirsen in patients with Duchenne muscular dystrophy (DMD). The data demonstrated that eteplirsen provided a statistically significant advantage of 151 meters in the ability of study participants to walk at three years, compared with external controls. Further, the fourth biopsy data confirmed the mechanism of action of eteplirsen, demonstrating exon skipping in all patients and dystrophin production in nearly all patients. New results from Sarepta's safety database, which includes approximately 100 patients exposed to eteplirsen, showed that the eteplirsen safety profile remained consistent with prior results. Common adverse drug reactions included flushing, erythema, and mild temperature elevation. No pulmonary embolisms, hospitalizations, injection site reactions or thrombocytopenia have been observed.

The primary clinical endpoint in the NDA was the comparison of the 6MWT ITT analysis of the eteplirsen-treated group compared to an external control with similar inclusion criteria. The FDA granted eteplirsen Priority Review status and assigned a Prescription Drug User Fee Act (PDUFA) action date of February 26, 2016. On September 4, 2015, the FDA informed us that, as of that date, it planned to hold an advisory committee meeting to discuss our NDA submission. An advisory committee meeting could be held at any time prior to an FDA decision on our eteplirsen NDA and may be held in the near future. Previously, the FDA granted Rare Pediatric Disease Designation to eteplirsen, as well Orphan Drug Designation and Fast Track Status.

Preliminary Financial Information

We have not yet closed our books for our third quarter ended September 30, 2015, and our independent registered public accounting firm has not completed its review of our results for the third quarter. Set forth below are certain preliminary estimates that we expect to report for our third quarter. Our actual results may differ materially from these estimates due to the completion of our financial closing procedures, final adjustments and other developments that may arise between now and the time the financial results for our third quarter are finalized.

In light of the above, we estimate that our cash, cash equivalents and invested cash as of September 30, 2015 was approximately \$111.4 million, consisting of approximately \$55.8 million of cash and cash equivalents, approximately \$44.1 million of short term investments and approximately \$11.5 million of restricted

S-2

Table of Contents

investments. We expect that our quarterly and annual operating expenses will continue to accelerate for the remainder of 2015, and further accelerate in 2016, as we manufacture increasing amounts of eteplirsen and make other preparations for its commercial launch, if FDA approval is received.

Corporate Information

We were incorporated in the State of Oregon on July 22, 1980 and reincorporated into the State of Delaware on June 6, 2013. Our executive office is located at 215 First Street, Suite 415, Cambridge, MA 02142 and our telephone number is (617) 274-4000. We maintain an Internet website at www.sarepta.com. We have not incorporated the information on our website by reference into this prospectus supplement, and you should not consider it to be a part of this prospectus supplement.

Edgar Filing: Sarepta Therapeutics, Inc. - Form 424B5

2,006,202 shares of our common stock available for future issuance under our 2011 Equity Incentive Plan;
and

421,025 shares of common stock issuable upon the exercise of stock options outstanding under our 2014
Employment Commencement Incentive Plan.

S-4

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. Investors should carefully consider the risks described in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, as well as other information in this prospectus supplement and the documents incorporated by reference herein before deciding whether to invest in our securities. The risks described below are not the only ones we face. If any of the following risks actually occurs, our business, financial condition or results of operations could be adversely affected. In such case, the trading price of our common stock could decline and you could lose all or part of your investment. Our actual results could differ materially from those anticipated in the forward-looking statements made throughout this prospectus supplement as a result of different factors, including the risks we face described below.

Risks Related to this Offering

Management will have broad discretion over the use of the net proceeds to us from this offering and may apply it to uses that do not improve our operating results or the value of your securities.

Our management will have broad discretion to use the net proceeds to us from this offering, and investors will be relying solely on the judgment of our board of directors and management regarding the application of these proceeds. Although we expect to use the net proceeds from this offering for product and commercial development, manufacturing, any business development activities and other general corporate purposes, we have not allocated these net proceeds for specific purposes. Investors will not have the opportunity, as part of their investment decision, to assess whether the proceeds are being used appropriately. Our use of the proceeds may not improve our operating results or increase the value of the securities being offered hereby.

A substantial number of shares of common stock may be sold in the market following this offering, which may depress the market price for our common stock.

Sales of a substantial number of shares of our common stock in the public market following this offering could cause the market price of our common stock to decline. A substantial majority of the outstanding shares of our common stock are, and the shares of common stock sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act of 1933, as amended (the Securities Act).

Investors in this offering will experience immediate and substantial dilution.

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on a net tangible book value of our common stock of \$3.84 per share as of June 30, 2015, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$ per share in the net tangible book value of common stock. See the section entitled Dilution below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

Our ability to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments is limited by provisions of the Internal Revenue Code, and it is possible that certain transactions or a combination of certain transactions may result in material additional limitations on our ability to use our net operating loss and tax credit carryforwards.

As of December 31, 2014, the Company had U.S. federal and state net operating loss carryforwards of \$324.0 million and \$220.9 million, respectively, available to reduce future taxable income, which expire 2015 through 2034. These

net operating losses have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize these tax benefits. In general, if we experience a greater than 50 percent

S-5

Table of Contents

aggregate change in ownership of certain significant stockholders over a three-year period, or a Section 382 ownership change, utilization of our pre-change NOL carryforwards will be subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, and similar state laws. Such limitations may result in expiration of a portion of the NOL carryforwards before utilization and may be substantial. If we experience a Section 382 ownership change in connection with this offering or as a result of future changes in our stock ownership, some of which changes are outside our control, the tax benefits related to the NOL carryforwards may be limited or lost.

Risks Related to Our Business

Most of our product candidates are at an early stage of development and may never receive regulatory approval.

With the exception of eteplirsen, which is subject to a pending NDA review and is still being evaluated in several studies, including a confirmatory clinical trial, and the exon 53 skipping product candidate for which we have completed Part I and are progressing into Part II of a Phase I/IIa clinical trial in the E.U. with the Skip-NMD consortium, our product candidates are in relatively early stages of development. These product candidates will require significant further development, financial resources and personnel to develop into commercially viable products and obtain regulatory approval, if at all. Currently, eteplirsen in DMD, the exon 53 skipping product candidate we are developing with the SKIP-NMD consortium, and AVI-7100 in influenza are in active clinical development. We have an open IND for our exon 45 skipping product candidate for which we plan to begin a dose-ranging study later this year and are working on initiating a clinical trial in the U.S. and the E.U. for exon 45 and 53 skipping product candidates. AVI-7537 in Ebola and AVI-7288 in Marburg were being developed through a program with the U.S. Department of Defense (the DoD) and further development is conditioned in part on obtaining additional funding, collaborations or emergency use. Our other product candidates are in preclinical development or inactive. We expect that much of our effort and many of our expenditures over the next several years will be devoted to clinical development and regulatory activities associated with eteplirsen and other exon-skipping candidates as part of our larger pan-exon strategy in DMD, our infectious disease candidates, our proprietary chemistry, and other potential therapeutic areas that provide long-term market opportunities. We may be delayed, restricted, or unable to further develop our active and other product candidates or successfully obtain approvals needed to market them.

Our RNA-targeted antisense technology has not been incorporated into a therapeutic commercial product and is still at a relatively early stage of development.

Our RNA-targeted platforms, utilizing proprietary PMO-based technology, have not been incorporated into a therapeutic commercial product and are still at a relatively early stage of development. This technology is used in all of our product candidates, including eteplirsen. Although we have conducted clinical studies with eteplirsen and an exon 53 skipping product candidate and preclinical studies with our other product candidates that use our PMO-based antisense technology, additional studies may be needed to determine the safety and efficacy of our PMO-based antisense technology. In addition, nonclinical models used to evaluate the activity and toxicity of product candidate compounds are not necessarily predictive of toxicity or efficacy of these compounds in the treatment of human disease. As such, there may be substantially different results observed in clinical trials from those observed in preclinical studies. Any failures or setbacks in developing or utilizing our PMO-based technology, including adverse effects in humans, could have a detrimental impact on our product candidate pipeline and our ability to maintain and/or enter into new corporate collaborations regarding these technologies, which would negatively affect our business and financial position.

Table of Contents

We have been granted orphan designations in the U.S. and in the E.U. for certain of our product candidates, however, there can be no guarantee that we will maintain orphan status for these product candidates nor that we will receive orphan drug approval and hence prevent third parties from developing and commercializing products that are competitive to these product candidates in the absence of other barriers to entry.

To date we have been granted orphan drug designation under the Orphan Drug Act by the FDA for two of our product candidates in DMD (including eteplirsen), AVI-7537 for the treatment of Ebola virus and AVI-7288 for the treatment of the Marburg virus. Upon approval from the FDA of an NDA, products granted orphan drug status are generally provided with seven years of marketing exclusivity in the United States, meaning the FDA will generally not approve applications for other product candidates for the same orphan indication that contain the same active ingredient. Even if we are the first to obtain approval of an orphan product and are granted exclusivity in the United States, there are limited circumstances under which a later competitor product may be approved for the same indication during the seven-year period of marketing exclusivity, such as if the later product is shown to be clinically superior to our product or due to an inability to assure a sufficient quantity of the orphan drug.

We also have been granted orphan medicinal product designations in the E.U. for two of our product candidates in DMD (including eteplirsen). Product candidates granted orphan status in Europe can be provided with up to 10 years of marketing exclusivity, meaning that another application for marketing authorization of a later similar medicinal product for the same therapeutic indication will generally not be approved in Europe during that time period. Although we may have product candidates that may obtain orphan drug exclusivity in Europe, the orphan status and associated exclusivity period may be modified for several reasons, including a significant change to the orphan medicinal product designations or status criteria after market authorization of the orphan product (e.g., product profitability exceeds the criteria for orphan drug designation), problems with the production or supply of the orphan drug or a competitor drug, although similar, is safer, more effective or otherwise clinically superior than the initial orphan drug.

We are not guaranteed to receive or maintain orphan status for our current or future product candidates, and if our product candidates that are granted orphan status were to lose their status as orphan drugs or the marketing exclusivity provided for them in the United States or the E.U., our business and results of operations could be materially adversely affected. While orphan status for any of our products, if granted or maintained, would provide market exclusivity in the United States and the E.U. for the time periods specified above, we would not be able to exclude other companies from manufacturing and/or selling products using the same active ingredient for the same indication beyond the exclusivity period applicable to our product on the basis of orphan drug status. In addition, we cannot guarantee that another company will not receive approval to market a product candidate that is granted orphan drug status in the United States or the E.U. for a product candidate that has the same active ingredient or is a similar medicinal product for the same indication as any of our product candidates for which we plan to file an NDA or marketing authorization application (MAA). If that were to happen, any pending new drug application or marketing authorization application for our product candidate for that indication may not be approved until the competing company's period of exclusivity has expired in the United States or the E.U., as applicable. Further, application of the orphan drug regulations in the United States and Europe is uncertain, and we cannot predict how the respective regulatory bodies will interpret and apply the regulations to our or our competitors' product candidates.

Even if we receive regulatory approvals for any of our product candidates it is possible that they may not become commercially viable products.

Even if a product candidate receives regulatory approval, the product may not gain market acceptance among physicians, patients, healthcare or third-party payers and the medical community which could limit commercialization of the product. Assuming that any of our product candidates receives the required regulatory approvals, commercial

success will depend on a number of factors, including but not limited to the following:

demonstration and/or confirmation of clinical efficacy and safety and acceptance of the same by the medical community;

S-7

Table of Contents

cost-effectiveness of the product;

the availability of adequate reimbursement by third parties, including government payers such as the Medicare and Medicaid programs, managed care organizations and private health insurers;

the product's potential advantage over alternative or competitive treatment methods;

whether the product can be manufactured in commercial quantities and at acceptable costs;

marketing and distribution support for the product;

any exclusivities or patent rights applicable to the product;

the market-size for the product which may be different than expected; and

our ability to achieve and sustain profitability, which may not occur if we are unable to develop and commercialize any of our product candidates, development is delayed or sales revenue from any product candidate that receives marketing approval is insufficient.

If there are significant delays in obtaining or we are unable to obtain or maintain required regulatory approvals, we will not be able to commercialize our product candidates in a timely manner or at all, which would materially impair our ability to generate revenue and have a successful business.

The research, testing, manufacturing, labeling, approval, commercialization, marketing, selling and distribution of drug products are subject to extensive regulation by applicable local, regional and national regulatory authorities and regulations may differ from jurisdiction to jurisdiction. In the United States, approvals and oversight from federal (e.g., FDA), state and other regulatory authorities are required for these activities. Sale and marketing of our product candidates in the United States or other countries is not permitted until we obtain the required approvals from the applicable regulatory authorities. Our ability to obtain the government or regulatory approvals required to commercialize any of our product candidates, including eteplirsén, on an accelerated approval (e.g., under the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA)) or any other basis, in any jurisdiction, including in the United States, cannot be assured, may be significantly delayed or may never be achieved for various reasons including the following:

Our preclinical, clinical, Chemistry, Manufacturing and Controls (CMC) and other data and analyses from past, current and future studies for any of our product candidates may not be sufficient to meet regulatory requirements for submissions, advisory committee panels, filings or approvals. The FDA or an advisory committee could disagree with our beliefs, interpretations and conclusions regarding data we submit in connection with an NDA submission, including any of the additional information and data we collect for the eteplirsén NDA, or other product candidates, and may delay, reject or refuse to file our NDA submission

until we meet their additional requirements, if ever. Even if we meet such requirements and our NDA is accepted for review or an advisory committee votes in favor of approving eteplirsen, the FDA could still deny approval of our product candidates, including eteplirsen, based on their review of the data or other factors.

The regulatory approval process for product candidates targeting orphan diseases, such as DMD, that use new technologies and processes, such as antisense oligonucleotide therapies, and novel endpoints, such as dystrophin measures, and natural history data, is uncertain due to the broad discretion of regulatory authorities, lack of precedent, varying levels of applicable expertise of regulators or their advisory committees, scientific developments, changes in the competitor landscape, shifting political priorities and changes in applicable laws, rules or regulations and interpretations of the same. We cannot be sure that any of our product candidates, including eteplirsen, will qualify for accelerated approval under FDASIA or any other expedited development, review and approval programs, or that, if a drug does qualify, that the product candidates will be approved, will be accepted as part of any such program or that the review time will be shorter than a standard review. As a result of uncertainty in the approval process, we may not be able to anticipate, prepare for or satisfy requests or requirements from regulatory authorities, including completing and submitting planned INDs and NDAs for our product

Table of Contents

candidates, in a timely manner, or at all. Examples of such requests or requirements could include, but are not limited to, conducting additional or redesigned trials and procedures (e.g., additional patient muscle biopsies and dystrophin analysis), repeating or completing additional analysis of our data, or providing additional supportive data. In addition, even if initially accepted, regulators may disagree with our data analysis, interpretations and conclusions at any point in the approval process, which could result in a decision by the Company to not proceed with development of a product candidate including a decision to not submit an NDA for a product based on feedback from regulators. Furthermore, we have or are currently in the process of collecting additional eteplirsen data and analysis, some in direct response to FDA requests. For example, the FDA has previously expressed concerns with dystrophin as a surrogate endpoint and has requested an independent assessment of dystrophin positive fibers measured in our eteplirsen Phase IIb study. The FDA has also requested matched natural history to better evaluate the ongoing clinical results of our eteplirsen 201/202 study. Any material inconsistencies between our existing data and analysis and the new and additional data we have or are collecting, including the independent assessment of dystrophin positive fibers, safety data, matched natural history and data from a fourth biopsy, could negatively impact review of our eteplirsen NDA submission. While our studies show a statistically significant increase, to the extent the FDA considers dystrophin a relevant biomarker, it may not consider the dystrophin production observed in our studies as confirming a clinical benefit. Additionally, the FDA may determine, after evaluating the totality of our data and analysis package or receiving the vote of an advisory committee that such package does not support an NDA approval.

We may not have the resources required to meet regulatory requirements and successfully navigate what is generally a lengthy, expensive and extensive approval process for commercialization of drug product candidates. For example, we received FDA requests relating to safety data at the highest dose in preclinical studies with an exon 53 skipping product candidate. Any failure on our part to respond to these requests in a timely and satisfactory manner could significantly delay or negatively impact our placebo-controlled confirmatory study timelines and/or the development plans we have for the exon 53 skipping product candidate. Responding to requests from regulators and meeting requirements for clinical studies, submissions, filings, advisory committees and approvals may require substantial personnel, financial or other resources, which, as a small pre-commercial biopharmaceutical company, we may not be able to obtain in a timely manner or at all. In addition, our ability to respond to requests from regulatory authorities that involve our agents, third-party vendors and associates may be complicated by our own limitations and those of the parties we work with. For example, changes to CMC processes for the production of eteplirsen may require coordination with our third-party manufacturers, which may or may not be limited in their abilities to execute such regulatory requests. It may be difficult or impossible for us to conform to regulatory guidance or successfully execute our product development plans in response to regulatory guidance, including related to clinical trial design and the timing of regulatory decisions with respect to our NDA submissions.

Due to the above factors, among others, our product candidates could take a significantly longer time to gain regulatory approval than we expect, or may never gain regulatory approval, which could delay or eliminate any potential commercialization or product revenue for us. Even if we are able to comply with all regulatory requests and requirements, the delays resulting from satisfying such requests and requirements, the cost of compliance, or the effect of regulatory decisions (e.g., limiting labeling and indications requested by us for a product candidate) may no longer make commercialization of a product candidate desirable for us from a business perspective, which could lead us to decide not to commercialize a product candidate.

Even after approval and commercialization of a product candidate, we would remain subject to ongoing regulatory compliance and oversight to maintain our approval. If we are not able to maintain regulatory compliance, we may be subject to civil and criminal penalties or we may not be permitted to continue marketing our products, which could

have a material adverse effect on our financial condition and harm our competitive position in the market place.

S-9

Table of Contents

Our preclinical and clinical trials may fail to demonstrate acceptable levels of safety, efficacy, and quality of our product candidates, which could prevent or significantly delay their regulatory approval.

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate, through extensive preclinical and clinical studies that the product candidate is safe and effective in humans. Ongoing and future preclinical and clinical trials of our product candidates may not show sufficient safety, efficacy or adequate quality to obtain or maintain regulatory approvals. Furthermore, success in preclinical and early clinical trials does not ensure that the subsequent trials we plan to conduct will be successful, nor does it predict final results of a confirmatory trial. If our study data do not consistently or sufficiently demonstrate the safety or efficacy of any of our product candidates, the regulatory approvals for such product candidates could be significantly delayed as we work to meet approval requirements, or, if we are not able to meet these requirements, such approvals could be withheld. For example, in 2012, we completed Study 201, a U.S.-based Phase IIb 12-person clinical trial for eteplirsen at 30 mg/kg and 50 mg/kg. Following completion of this study, we initiated Study 202, an ongoing open label extension study with the same participants from Study 201. These trials were initiated, in part, to further demonstrate efficacy and safety, including the production of dystrophin, and explore and identify a more consistently effective dose that may be more appropriate for future clinical trials. While Studies 201 and 202 met their primary endpoints of dystrophin production based on the measurements taken at weeks 24 and 48, respectively, and six-minute walk test results reported for weeks 62, 74, 84, 96 and 120 supported stabilization of disease progression, we cannot provide assurances that data from the ongoing open label extension study will continue to be positive or consistent through the study periods or that the interpretation by regulators, such as the FDA, of the data we collect for our product candidates, including for eteplirsen, will be consistent with our interpretations. For example, on July 10, 2014, we announced the results for week 144 in Study 202, which showed a decline in walking ability at a rate slower than would be expected based on available DMD natural history; however, the decline on the six-minute walk test from baseline, although in prior study results was below 5%, was measured at approximately 8.5%. Additionally, on January 12, 2015, we announced results for week 168 in Study 202, which showed continued ambulation across all patients evaluable on the test, however all patients showed a decline in distance walked on this measure since the week 144 time point. Further, on October 1, 2015 we announced additional clinical efficacy and safety data that demonstrated (i) that eteplirsen provided a statistically significant advantage of 151 meters in the ability of study participants to walk at three years, (ii) that eteplirsen-treated patients (n=8) experienced a slower rate of decline through week 192 than external DMD controls and (iii) the eteplirsen safety profile remains consistent with prior results. If the data from the confirmatory studies for eteplirsen do not produce the safety and efficacy data required by regulatory authorities for a positive advisory committee vote or NDA approval, we may need to continue working with the FDA on the design and subsequent execution of any further studies or analysis we plan to conduct or that may be required to obtain and maintain approval of eteplirsen or our other DMD product candidates. For example, in October 2014, we received meeting minutes from a Type B pre-NDA meeting that took place in September 2014 in which the FDA provided updated guidance regarding the information to be provided as part of, or at the time of, our NDA submission for eteplirsen. The guidance stated that the FDA was requiring additional data as part of the NDA submission, including the results from an independent assessment of dystrophin images and the 168 week clinical data from Study 202. Additionally, the guidance requested more specific data, such as a minimum duration of safety in new patients exposed to eteplirsen, patient-level natural history data to be obtained by us from independent academic institutions and MRI data from a recent study conducted by an independent group. Although, we believe we have now provided the FDA with the additional data and information requested, it may not be consistent with prior results or may not support our NDA generally, a positive advisory committee vote or the approval of our eteplirsen NDA submission.

Table of Contents

We currently rely on third parties in the manufacturing process to produce our product candidates and our dependence on these parties, or our inability to engage third parties to meet manufacturing needs for large-scale clinical trials or potential commercial needs within sufficient timelines, may impair the advancement of our research and development programs and potential commercialization of our product candidates.

We do not currently have the internal ability to undertake the manufacturing process for our product candidates in the quantities needed to conduct our research and development programs, supply clinical trials or meet commercial demand. We therefore rely on, and expect for the foreseeable future to continue relying on, a limited number of third parties to manufacture and supply materials (including raw materials and subunits), drug substance (API) and drug product, as well as to perform additional steps in the manufacturing process, such as the filling and labeling of vials and storage of our product candidates. There are a limited number of third parties with facilities and capabilities suited for the manufacturing process of our product candidates which creates a heightened risk that we may not be able to obtain materials and APIs in the quantity and purity that we require. Any interruption of the development or operation of those facilities due to, among other reasons, events such as order delays for equipment or materials, equipment malfunction, quality control and quality assurance issues, regulatory delays and possible negative effects of such delays on supply chains and expected timelines for product availability, production yield issues, shortages of qualified personnel, discontinuation of a facility or business or failure or damage to a facility by natural disasters, could result in the cancellation of shipments, loss of product in the manufacturing process or a shortfall in available product candidates or materials.

If these third parties were to cease providing quality manufacturing and related services to us, and we are not able to engage appropriate replacements in a timely manner, our ability to have our product candidates manufactured in sufficient quality and quantity required for planned preclinical testing, clinical trials and potential commercial use would be adversely affected.

We have not engaged or contracted with all the third parties needed for the production of materials and APIs for any of our product candidates, including eteplirsen, in quantities sufficient for their potential commercial demand or for multiple large-scale clinical trials. In light of the limited number of third parties with the expertise to produce our product candidates, and the underlying materials, we may not be able to, in a timely manner or at all, establish or maintain sufficient commercial manufacturing arrangements on the commercially reasonable terms necessary to provide adequate supply of our product candidates. Further, we may not be able to obtain the significant financial capital that may be required in connection with such arrangements. Even after successfully engaging third parties to execute the manufacturing process for our product candidates, such parties may not comply with the terms and timelines they have agreed to for various reasons, some of which may be out of their or our control, which could impact our ability to execute our business plans on expected or required timelines in connection with the regulatory approval process and potential commercialization. We may also be required to enter into long-term manufacturing agreements that contain exclusivity provisions and/or substantial termination penalties which could have a material adverse effect on our business prior to and after commercialization of any of our product candidates.

The third parties we use in the manufacturing process for our product candidates may fail to comply with cGMP regulations.

Our contract manufacturers are required to produce our materials, APIs and drug products under current Good Manufacturing Practice regulations (cGMP). We and our contract manufacturers are subject to periodic unannounced inspections by the FDA and corresponding state and foreign authorities to ensure strict compliance with cGMP and other applicable government regulations and corresponding foreign requirements. We do not have control over a third-party manufacturer's compliance with these regulations and requirements. In addition, changes in cGMP could negatively impact the ability of our contract manufacturers to complete the manufacturing process of our product

candidates in a compliant manner on the schedule we require for clinical trials or for potential commercial use. The failure to achieve and maintain high quality compliance, including failure to detect or control anticipated or unanticipated manufacturing errors, could result in patient injury or death or product recalls. Any difficulties or delays in our contractors manufacturing and supply of product

S-11

Table of Contents

candidates, or any failure of our contractors to maintain compliance with the applicable regulations and requirements could increase our costs, make us postpone or cancel clinical trials, prevent or delay regulatory approvals by the FDA and corresponding state and foreign authorities, prevent the import and/or export of our products, cause us to lose revenue, result in the termination of the development of a product candidate, or have our product candidates recalled or withdrawn from use.

We may not be able to successfully scale up manufacturing of our product candidates in sufficient quality and quantity or within sufficient timelines, or be able to secure ownership of intellectual property rights developed in this process, which could delay or prevent us from developing or commercializing our product candidates.

To date, our product candidates have been manufactured in small quantities for preclinical studies and early stage clinical trials. As we prepare for larger and later stage clinical trials for our product candidates, including eteplirsen, and potential commercialization, we are working to increase the manufacturing capacity and scale up production of some of the components of our drug products. During 2015, we will continue to increase material and API production capacity to provide the drug product needed for additional eteplirsen trials and studies for our other product candidates (including a placebo-controlled study planned for one or more of our follow-on exon product candidates) and any planned subsequent commercialization, on an accelerated or other pathway. We may not be able to successfully increase manufacturing capacity or scale up the production of materials, APIs and drug products, whether in collaboration with third-party manufacturers or on our own, in a manner that is safe, compliant with cGMP conditions or other applicable legal or regulatory requirements or is cost-effective, or in a time frame required to meet our timelines for clinical trials, potential commercialization and other business plans, or at all. cGMP and other quality issues may arise during our efforts to increase manufacturing capacity and scale up production with our current or any new contract manufacturers. These issues may arise in connection with the underlying materials, the inherent properties of a product candidate itself or the product candidate in combination with other components added during the manufacturing and packaging process or during shipping and storage of the APIs or finished drug product. In addition, in order to release product and demonstrate stability of product candidates for use in late stage clinical trials (and any subsequent drug products for commercial use), our analytical methods must be validated in accordance with regulatory guidelines. We may not be able to successfully validate, or maintain validation of, our analytical methods or demonstrate adequate purity, stability or comparability of the product candidates in a timely or cost-effective manner, or at all. If we are unable to successfully validate our analytical methods or to demonstrate adequate purity, stability or comparability, the development of our product candidates and regulatory approval or commercial launch for any resulting drug products may be delayed, which could significantly harm our business.

During work with our third-party manufacturers to increase manufacturing capacity and scale up production, it is possible that they could make improvements in the manufacturing and scale-up processes for our product candidates. We may not own or be able to secure ownership of such improvements or may have to share the intellectual property rights to those improvements. Additionally, it is possible that we will need additional processes, technologies and validation studies, which could be costly and which we may not be able to develop or acquire from third parties. Any failure to secure the intellectual rights required for the manufacturing process needed for large-scale clinical trials or commercialization of our product candidates could cause significant delays in our business plans or could prevent commercialization of our product candidates.

We are currently winding down our expired U.S. government contract and further development of Ebola and Marburg product candidates may be limited by our ability to obtain additional funding for these programs and by the intellectual property and other rights retained by the U.S. government.

We have historically relied on U.S. government contracts and awards to fund and support certain development programs, including our Ebola and Marburg programs. The July 2010 DoD contract providing funds for our Marburg

program expired in July 2014, and the Ebola portion of the contract was previously terminated by the DoD in 2012 for convenience of the DoD. We are currently involved in contract wind-down activities and may be subject to additional government audits prior to collecting final cost reimbursements and fees owed by the government. If we are not able to complete such audits and other government requirements

S-12

Table of Contents

successfully, the government may withhold some or all of the currently outstanding amounts owed to us. We may explore and evaluate options to continue advancing the development of our Ebola and Marburg product candidates, which may or may not include funding through U.S. government programs. As a result of government budgetary cuts, appropriations and sequestration, among other reasons, the viability of the government and its agencies as a partner for further development of our Ebola and Marburg programs, or other programs, is uncertain. The options for us to further develop product candidates that were previously developed under contracts with the U.S. government with third parties may be limited or difficult in certain respects given that, after termination or expiration of a U.S. government contract, the government has broad license rights in intellectual property developed under such contract. Therefore, the U.S. government may have the right to develop all or some parts of product candidates we have developed under a U.S. government contract after such contract has terminated or expired.

We may not be able to successfully conduct clinical trials due to various process-related factors which could negatively impact our business plans.

The successful start and completion of any of our clinical trials within time frames consistent with our business plans is dependent on various factors, which include, but are not limited to, our ability to:

recruit and retain employees, consultants or contractors with the required level of expertise;

recruit and retain sufficient patients needed to conduct a clinical trial:

Participant enrollment and retention is a function of many factors, including the size of the relevant population, the proximity of participants to clinical sites, activities of patient advocacy groups, the eligibility criteria for the trial, the existence of competing clinical trials, the availability of alternative or new treatments, side effects from the therapy, lack of efficacy, personal issues and ease of participation;

timely and effectively contract with (under reasonable terms), manage and work with investigators, institutions, hospitals and the contract research organizations (CROs) involved in the clinical trial:

Negotiating contracts and other related documents with clinical trial parties and Institutional Review Boards (IRBs), such as informed consents, CRO agreements and site agreements, can be subject to extensive negotiations that could cause significant delays in the clinical trial process. In addition, terms may vary significantly among different trial sites and CROs and may subject the Company to various risks;

ensure adherence to trial designs and protocols agreed upon and approved by regulatory authorities and applicable legal and regulatory guidelines;

manage or resolve unforeseen adverse side effects during a clinical trial;

conduct the clinical trials in a cost effective manner, including managing foreign currency risk in clinical trials conducted in foreign jurisdictions and cost increases due to unforeseen or unexpected complications such as enrollment delays, or needing to outsource certain Company functions during the clinical trial; and

execute clinical trial designs and protocols approved by regulatory authorities without deficiencies.

If we are not able to manage the clinical trial process successfully, our business plans could be delayed or be rendered unfeasible for us to execute within our planned or required time frames, or at all.

We have incurred operating losses since our inception and we may not achieve or sustain profitability.

We incurred an operating loss of \$42.1 million for three months ended June 30, 2015. Our accumulated deficit was \$782.4 million as of June 30, 2015. Substantially all of our revenue to date has been derived from research and development contracts with the DoD, the last of which expired in July 2014. We have not yet

S-13

Table of Contents

generated any material revenue from product sales and have generally incurred expenses related to research and development of our technology and product candidates, from general and administrative expenses that we have incurred while building our business infrastructure. We anticipate that our expenses will increase substantially if and as we:

continue our research, preclinical and clinical development of our product candidates;

respond to and satisfy requests and requirements from regulatory authorities in connection with development and potential approval of our product candidates;

acquire or in-license other product candidates;

initiate additional clinical trials for our product candidates;

seek marketing approvals for our product candidates that successfully complete clinical trials;

ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;

maintain, expand and protect our intellectual property portfolio;

increase manufacturing capabilities including capital expenditures related to our real estate facilities and entering into manufacturing agreements;

hire additional clinical, quality control and scientific personnel; 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 achieve and maintain profitability depends on our ability to raise additional capital, partner with third parties for one or more of our programs, complete development of our product candidates, obtain regulatory approvals and market our approved products, if any. It is uncertain when, if ever, we will become profitable and if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the Company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

If the FDA does not approve our eteplirsen NDA, our business may be negatively impacted and we may suffer financial losses in connection with winding down and terminating contracts, manufacturing commitments and

employees hired in connection with our current and planned activities in preparation for a potential commercial launch.

Given the potential commercialization timelines, we have commenced certain pre-launch and commercialization investments and activities including negotiating and entering into supply and other commercial agreements, scaling up manufacturing and hiring certain positions needed for pre-launch and commercial activities and operations. If the FDA delays or does not provide approval for our eteplirsen NDA, or we need to delay or discontinue our development and commercialization plans for eteplirsen for other reasons, our business may be negatively impacted and we may incur financial losses in connection with winding down our or terminating the investments, contracts and commitments we enter into for the purpose of positioning ourselves for a commercial launch of eteplirsen.

We will need additional funds to conduct our planned research, development and manufacturing efforts. If we fail to attract significant capital or fail to enter into strategic relationships, we may be unable to continue to develop our product candidates.

We will likely require additional capital from time to time in the future in order to continue the development of product candidates in our pipeline and to expand our product portfolio. The actual amount of funds that we may need will be determined by many factors, some of which are beyond our control. These factors include the

Table of Contents

success of our research and development efforts, the status of our preclinical and clinical testing, costs and timing relating to securing regulatory approvals and obtaining new patent rights, regulatory changes, competitive and technological developments in the market and future commercialization expenses related to any product sales, marketing, manufacturing and distribution. An unforeseen change in these factors, or others, might increase our need for additional capital.

We would expect to seek additional financing from the sale and issuance of equity or equity-linked or debt securities, and we cannot predict that financing will be available when and as we need financing or that, if available, the financing terms will be commercially reasonable. In addition, if the FDA delays or ultimately denies approval of our eteplirsen NDA, raising additional funds may be difficult or challenging. If we are unable to obtain additional financing when and if we require it or on commercially reasonable terms, this would have a material adverse effect on our business and results of operations.

If we are able to consummate such financings, the trading price of our common stock could be adversely affected and/or the terms of such financings may adversely affect the interests of our existing stockholders. To the extent we issue additional equity securities or convertible securities, our existing stockholders could experience substantial dilution in their economic and voting rights. For example, on April 29, 2014, we sold 2,650,000 shares of our common stock in an underwritten public offering at a price to the public of \$38.00 per share. Additional 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.

Further, we may also enter into relationships with pharmaceutical or biotechnology companies to perform research and development with respect to our technologies, research programs, conduct clinical trials or market our product candidates. Other than preclinical collaborations with academic or research institutions and government entities for the development of additional exon-skipping product candidates for the treatment of DMD and clinical collaboration for a product candidate for the treatment of influenza, we currently do not have a strategic relationship with a third party to perform research or development using our technologies or assist us in funding the continued development and commercialization of any of our programs or product candidates. If we were to have such a strategic relationship, such third party may require us to issue equity to such third party, 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.

Our indebtedness resulting from our credit and security agreement with MidCap Financial could adversely affect our financial condition or restrict our future operations.

On June 26, 2015, the Company entered into a credit and security agreement with MidCap Financial that provides a senior secured term loan of \$20.0 million, which may be increased by an additional \$20.0 million upon the acceptance by the FDA of the new drug application for eteplirsen. This indebtedness could have important consequences, including:

requiring the Company to maintain pledged cash in favor of MidCap Financial equal to not less than the lesser of the outstanding term loans or (a) \$15.0 million prior to the increase in the term loan by an additional \$20.0 million and (b) \$30.0 million thereafter;

limiting our flexibility in planning for, or reacting to, changes in our business and our industry;

placing us at a competitive disadvantage compared to our competitors who have less debt or competitors with comparable debt at more favorable interest rates;

limiting our ability to borrow additional amounts for working capital, capital expenditures, research and development efforts, acquisitions, debt service requirements, execution of our business strategy and other purposes; and

resulting in an acceleration of the maturity of such term loans upon the occurrence of a material adverse change or another default under the credit and security agreement.

S-15

Table of Contents

Any of these factors could materially and adversely affect our business, financial condition and results of operations. In addition, if we incur additional indebtedness, the risks related to our business and our ability to service our indebtedness would increase.

The estimates and judgments we make, or the assumptions on which we rely, in preparing our consolidated financial statements could prove inaccurate.

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. Such estimates and judgments include those related to revenue recognition, accrued expenses, assumptions in the valuation of stock-based compensation and accounting for and valuation of liability classified warrants. We base our estimates on historical experience, facts and circumstances known to us and on various other assumptions that we believe to be reasonable under the circumstances. We cannot provide assurances, however, that our estimates, or the assumptions underlying them, will not change over time or otherwise prove inaccurate. If this is the case, we may be required to restate our consolidated financial statements, which could in turn subject us to securities class action litigation. Defending against such potential litigation relating to a restatement of our consolidated financial statements would be expensive and would require significant attention and resources of our management. Moreover, our insurance to cover our obligations with respect to the ultimate resolution of any such litigation may be inadequate. As a result of these factors, any such potential litigation could have a material adverse effect on our financial results and cause our stock price to decline, which could in turn subject us to securities class action litigation.

Our ability to use net operating loss carryforwards and other tax attributes to offset future taxable income may be limited as a result of future transactions involving our common stock.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an ownership change is subject to limitations on its ability to utilize its pre-change net operating losses and certain other tax assets to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders increases by more than 50 percentage points over such stockholders' lowest percentage ownership during the testing period, which is generally three years. An ownership change could limit our ability to utilize our net operating loss and tax credit carryforwards for taxable years including or following such ownership change. Limitations imposed on the ability to use net operating losses and tax credits to offset future taxable income could require us to pay U.S. federal income taxes earlier than we estimated than would have otherwise been required if such limitations were not in effect and could cause such net operating losses and tax credits to expire unused, in each case reducing or eliminating the benefit of such net operating losses and tax credits and potentially adversely affecting our financial position. Similar rules and limitations may apply for state income tax purposes.

We rely on third parties to provide services in connection with our preclinical and clinical development programs. The inadequate performance by or loss of any of these service providers could affect our product candidate development.

Several third parties provide services in connection with our preclinical and clinical development programs, including in vitro and in vivo studies, assay and reagent development, immunohistochemistry, toxicology, pharmacokinetics, clinical assessments, data monitoring and management, statistical analysis and other outsourced activities. If these service providers do not adequately perform the services for which we have contracted or cease to continue operations and we are not able to quickly find a replacement provider or we lose information or items associated with our product candidates, our development programs may be delayed.

S-16

Table of Contents

If we fail to retain our key personnel or are unable to attract and retain additional qualified personnel, our future growth and our ability to compete would suffer.

We are highly dependent on the efforts and abilities of the principal members of our senior management. Additionally, we have scientific personnel with significant and unique expertise in RNA-targeted therapeutics and related technologies. The loss of the services of any one of the principal members of our managerial team or staff may prevent us from achieving our business objectives.

Our CEO and President resigned on March 31, 2015 and we have appointed an interim CEO. No assurance can be made about the impact that this change in management will have on the Company and its business plans (including our regulatory and clinical plans and relationships) nor as to when we will hire a permanent CEO. The existing management team is actively managing the business in accordance with a business strategy approved by the board of directors.

The competition for qualified personnel in the biotechnology field is intense, and our future success depends upon our ability to attract, retain and motivate such personnel. In order to develop and commercialize our products successfully, we will be required to retain key management and scientific employees. In certain instances, we may also need to expand or replace our workforce and our management ranks. In addition, we rely on certain consultants and advisors, including scientific and clinical advisors, to assist us in the formulation and advancement of our research and development programs. Our consultants and advisors may be employed by other entities or have commitments under consulting or advisory contracts with third parties that limit their availability to us, or both. If we are unable to attract, assimilate or retain such key personnel, our ability to advance our programs would be adversely affected.

If we are unable to effectively manage our growth, execute our business strategy and implement compliance controls and systems, the trading price of our common stock could decline. Any failure to establish and maintain effective internal control over financial reporting could adversely affect investor confidence in our reported financial information.

We anticipate continued growth in our business operations due, in part, to advancing our product candidates. This future growth could create a strain on our organizational, administrative and operational infrastructure. Our ability to manage our growth properly and maintain compliance with all applicable rules and regulations will require us to continue to improve our operational, legal, financial and management controls, as well as our reporting systems and procedures. We may not be able to build the management and human resources and infrastructure necessary to support the growth of our business. The time and resources required to implement systems and infrastructure that may be needed to support our growth is uncertain, and failure to complete implementation in a timely and efficient manner could adversely affect our operations.

For example, although there was no material error in our consolidated financial statements, in connection with our assessment of the effectiveness of internal control over financial reporting as of December 31, 2013, our management identified a material weakness in our internal control over financial reporting. We designed and implemented controls to address the material weakness that was identified. However, we cannot provide assurances that material weaknesses in our internal control over financial reporting will not be identified in the future. Any failure to maintain or implement new or improved internal controls, or any difficulties that we may encounter in their maintenance or implementation, could result in additional material weaknesses or material misstatements in our consolidated financial statements and cause us to fail to meet our reporting obligations or prevent fraud, which could cause the trading price of our common stock to decline. We may not be able to build the human resources and infrastructure necessary to support the growth of our business or to appropriately implement our compliance controls and procedures. The time and resources required to build up our human resources and implement systems and infrastructure that may be needed

to support our growth and compliance with applicable rules and regulations is uncertain, and failure to complete these in a timely and efficient manner could adversely affect our operations.

S-17

Table of Contents

We may engage in future acquisitions or collaborations with other entities that increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We actively evaluate various strategic transactions on an ongoing basis, including licensing or acquiring complementary products, technologies or businesses. Potential acquisitions or collaborations with other entities may entail numerous risks, including increased operating expenses and cash requirements, assimilation of operations and products, retention of key employees, diversion of our management's attention and uncertainties in our ability to maintain key business relationships of the acquired entities. In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

Our success, competitive position and future revenue, if any, depend in part on our ability and the abilities of our licensors to obtain and maintain patent protection for our technologies and product candidates, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights and to operate without infringing on the proprietary rights of third parties.

We currently hold various issued patents and exclusive rights to issued patents and own and have licenses to various patent applications, in each case in the United States as well as rights under European patents and patent applications. We anticipate filing additional patent applications both in the United States and in other countries. The patent process, however, is subject to numerous risks and uncertainties, and we can provide no assurance that we will be successful in obtaining and defending patents or in avoiding infringement of the rights of others. Even when our patent claims are allowed, the claims may not issue, or in the event of issuance, may not be sufficient to protect the technology owned by or licensed to us or our collaborators. Even if our patents and patent applications do provide our product candidates and platform technology with a basis for exclusivity, we and our collaborators may not be able to develop or commercialize such product candidates or platform technology due to patent positions held by a third party.

We may not be able to obtain and maintain patent protection for our product candidates necessary to prevent competitors from commercializing competing product candidates. Our patent rights might be challenged, invalidated, circumvented or otherwise might not provide any competitive advantage, and we might not be successful in challenging the patent rights of our competitors through litigation or administrative proceedings. For example, in July 2014, the Patent Trial and Appeal Board (the "PTAB") of the USPTO declared patent interferences between certain patents held by Sarepta (under license from the University of Western Australia, "UWA") and patent applications held by Prosensa (under license from Academisch Ziekenhuis Leiden, "AZL") related to exon 51 and exon 53 skipping therapies designed to treat DMD. In particular, the PTAB declared Interference No. 106,008, which identifies Sarepta's/UWA's U.S. Patent Nos. 7,807,816 and 7,960,541, both covering eteplirsen, as interfering with Prosensa's/AZL's U.S. Application No. 13/550,210. The PTAB also declared Interference No. 106,007, which identifies Sarepta's/UWA's U.S. Patent No. 8,455,636, covering SRP-4053, as interfering with Prosensa's/AZL's U.S. Application No. 11/233,495. In September 2014, the PTAB declared a third patent interference relating to certain methods concerning the exon 51 skipping therapies that are the subject of Interference No. 106,008. In particular, the PTAB declared Interference No. 106,013, which identifies Sarepta's/UWA's U.S. Patent No. 8,486,907, which covers certain methods of using eteplirsen, as interfering with Prosensa's/AZL's U.S. Application No. 14/198,992. In addition, in a September 2014 Order in Interference No. 106,007, the PTAB authorized us to file a motion with the PTAB, which we filed in November 2014, requesting the declaration of a fourth interference relating to certain methods concerning the exon 53 skipping therapies that are the subject of Interference No. 106,007, including SRP-4053, and between Sarepta's/UWA's U.S. Patent No. 8,455,636 and Prosensa's/AZL's U.S. Application No. 14/248,279. On September 29, 2015, we received notice that the PTAB had issued a decision in Interference No. 106,103 that resulted in a judgment against, and an order for, the cancellation of Sarepta's/UWA's U.S. Patent No. 8,486,907 that covers certain methods of using eteplirsen thereby leaving open the possibility of Prosensa's/AZL's competing U.S.

Application No. 14/198,992 to issue and potentially providing the basis for Prosensa to allege that our product candidate, eteplirsen, infringes a patent granted from this application. We intend to appeal this

S-18

Table of Contents

decision to the U.S. Court of Appeals for the Federal Circuit. We cannot make any assurances about the outcome of the two remaining proceedings (Interference No. 106,007 and Interference No. 106,008) or appeals of any of these three interferences. Any additional adverse rulings, which, in the case of Interference No. 106,007 and Interference No. 106,008 could come at any time, could result in a decline in our stock price. If final resolution of the interferences and related appeals are not in our favor, then the Sarepta/UWA patents and any other Sarepta patents or applications also found to be interfering may be invalidated, and as a result, we may not have any patent-based exclusivity available for our product candidates, which may have a material negative impact on our business plans. In addition, if final resolution of the interferences and related appeals are not in our favor, then the USPTO may issue the Prosensa/AZL patent applications resulting in the grant of one or more patents that may provide a basis for Prosensa to allege that our product candidates, eteplirsen and/or SRP-4053, infringe such patents. In addition, these interferences, appeals and any subsequent litigation may require significant financial resources that we may have planned to spend on other Company objectives, resulting in delays or other negative impacts on such other objectives. In addition, Prosensa may continue to evaluate other opportunities to challenge our intellectual property rights or seek to broaden their patent positions in an attempt to cover our product candidates in the United States and in other jurisdictions. We are also aware of certain pending and granted claims that have been issued to Prosensa in Japan and certain other countries outside of Europe and the United States that may provide the basis for Prosensa or other parties to assert that eteplirsen infringes on such claims. Because we have not yet initiated an invalidation proceeding in Japan, the outcome and timing of any such proceeding cannot be predicted or determined as of the date of this report.

As a matter of public policy, there might be significant pressure on governmental bodies to limit the scope of patent protection or impose compulsory licenses for disease treatments that prove successful. Additionally, jurisdictions other than the United States might have less restrictive patent laws than the United States, giving foreign competitors the ability to exploit these laws to create, develop and market competing products. The USPTO and patent offices in other jurisdictions have often required that patent applications concerning pharmaceutical and/or biotechnology-related inventions be limited or narrowed substantially to cover only the specific innovations exemplified in the patent application, thereby limiting the scope of protection against competitive challenges. Accordingly, even if we or our licensors are able to obtain patents, the patents might be substantially narrower than anticipated.

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted, and may also affect patent litigation. The USPTO has issued regulations and procedures to govern administration of the Leahy-Smith Act, but many of the substantive changes to patent law associated with the Leahy-Smith Act have only recently become effective. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

The full impact of several recent U.S. Supreme Court decisions relating to patent law is not yet known. For example, on March 20, 2012, in *Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc.*, the Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patentable subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to patent certain biomarker-related method claims. Additionally, on June 13, 2013, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA molecules were held to be valid. The effect of the decision on patents for other isolated natural products is uncertain and, as with the Leahy-Smith Act, these decisions could increase the uncertainties and

costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

S-19

Table of Contents

Our business prospects will be impaired if third parties successfully assert that our product candidates or technologies infringe proprietary rights of such third parties.

Our competitors may make significant investments in competing technologies, and might have or obtain patents that limit, interfere with or eliminate our ability to make, use and sell our product candidates in important commercial markets.

If our product candidates or technologies infringe enforceable proprietary rights of others, we could incur substantial costs and may have to:

obtain rights or licenses from others, which might not be available on commercially reasonable terms or at all;

abandon development of an infringing product candidate;

redesign product candidates or processes to avoid infringement;

pay damages; and/or

defend litigation or administrative proceedings which might be costly whether we win or lose, and which could result in a substantial diversion of financial and management resources.

Any of these events could substantially harm our potential earnings, financial condition and operations. Prosensa, which is developing competitive pipeline products, has rights to patent claims that, absent a license, may preclude us from commercializing eteplirsén in several jurisdictions. Prosensa has rights to European Patent No. EP 1619249, for example. We opposed this patent in the Opposition Division of the European Patent Office (EPO), and the Opposition Division maintained certain claims of this patent relating to the treatment of DMD by skipping dystrophin exons 51 and 46, which may provide a basis to maintain that commercialization of eteplirsén in Europe would infringe on such patent. Both we and Prosensa have appealed the Opposition Division decision, submitted briefs in support of our respective positions and have also submitted responses to each other's briefs. Prosensa filed arguments with the EPO in response to Sarepta's previously filed briefs. The Opposition Division decision, if maintained at the appeals level, could have a substantial effect on our business and leaves open the possibility that Prosensa or other parties that have rights to such patent could assert that our product candidate, eteplirsén, infringes on such patent. The timing and outcome of appeal cannot be predicted or determined as of the date of this report. If as part of any appeal in the European Union we are unsuccessful in invalidating Prosensa's claims that were maintained by the Opposition Division or if claims previously invalidated by the Opposition Division are restored on appeal, our ability to commercialize both eteplirsén and other therapeutic candidates for our pan-exon strategy could be materially impaired.

We are also aware of existing patent claims Prosensa is pursuing in the United States, including those involved in the interferences declared by the USPTO in July 2014 and September 2014 and discussed in these risk factors, and others that it has or is pursuing in other countries, that where granted may provide the basis for Prosensa or other parties to assert that commercialization of eteplirsén and certain other of our product candidates would infringe on such claims.

The DMD patent landscape is continually evolving and multiple parties, including both commercial entities and academic institutions, may have rights to claims or may be pursuing additional claims that could provide these parties a basis to assert that our product candidates infringe on the intellectual property rights of such parties. Similarly, we may be able to assert that certain activities engaged in by these parties infringe on our current or future patent rights. There has been, and we believe that there will continue to be, significant litigation in the biopharmaceutical and pharmaceutical industries regarding patent and other intellectual property rights. We also cannot be certain that other third parties will not assert patent infringement in the future with respect to any of our development programs.

S-20

Table of Contents

We face intense competition and rapid technological change, which may result in others discovering, developing or commercializing competitive products.

The biotechnology and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. We are aware of many pharmaceutical and biotechnology companies that are actively engaged in research and development in areas related to antisense technology and other RNA technologies, or that are developing alternative approaches to or therapeutics for the disease indications on which we are focused. Some of these competitors are developing or testing product candidates that now, or may in the future, compete directly with our product candidates. For example, we believe that companies including Alnylam Pharmaceuticals, Inc., Isis Pharmaceuticals, Inc., Roche Innovation Center Copenhagen (formerly Santaris Pharma A/S) and Nippon Shinyaku Co. Ltd. share a focus on RNA-targeted drug discovery and development. Competitors with respect to our exon-skipping DMD program, or eteplirsen, include BioMarin Pharmaceuticals (which acquired Prosensa), Nippon Shinyaku, Daiichi Sankyo and Shire plc; and other companies such as PTC Therapeutics and Summit plc have also been working on DMD programs.

We may face competitive risks arising from the Prosensa exon skipping platform and product candidate pipeline, which may include limitations on our ability to gain market share in the DMD space or other diseases targeted by our exon skipping platform and product candidate pipeline. For example, BioMarin Pharmaceuticals completed its rolling NDA submission for and announced the FDA's filing decision of the NDA submission for drisapersen, an exon 51 skipping product candidate that directly competes with eteplirsen, our lead product candidate.

Other potential competitors include large, fully integrated pharmaceutical companies and more established biotechnology companies that have significantly greater resources and expertise in research and development, manufacturing, testing, obtaining regulatory approvals and marketing. Also, academic institutions, government agencies and other public and private research organizations conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and marketing. It is possible that these competitors will succeed in developing technologies that are more effective than our product candidates or that would render our technology obsolete or noncompetitive. Our competitors may, among other things:

develop safer or more effective products;

implement more effective approaches to sales and marketing;

develop less costly products;

obtain regulatory approval more quickly;

have access to more manufacturing capacity;

develop products that are more convenient and easier to administer;

form more advantageous strategic alliances; or

establish superior intellectual property positions.

We may be subject to product liability claims and our insurance may not be adequate to cover damages.

We currently have no products that have been approved for commercial sale; however, the current and future use of our product candidates by us and our collaborators in clinical trials, expanded access programs, the sale of any products in the future, or the use of our products under emergency use vehicles may expose us to liability claims inherent to the manufacture, clinical testing, marketing and sale of medical products. These claims might be made directly by consumers or healthcare providers or indirectly by pharmaceutical companies, our collaborators or others selling such products. Regardless of merit or eventual outcome, we may experience financial losses in the future due to such product liability claims. We have obtained limited general commercial liability insurance coverage for our clinical trials. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for any of our product candidates. However, we may not

S-21

Table of Contents

be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against all losses. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Our operations involve the use of hazardous materials, and we must comply with environmental laws, which can be expensive, and may affect our business and operating results.

Our research and development activities involve the use of hazardous materials, including organic and inorganic solvents and reagents. Accordingly, we are subject to federal, state and local laws and regulations governing the use, storage, handling, manufacturing, exposure to and disposal of these hazardous materials. In addition, we are subject to environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of bio-hazardous materials. Although we believe that our activities conform in all material respects with such environmental laws, there can be no assurance that violations of these laws will not occur in the future as a result of human error, accident, equipment failure or other causes. Liability under environmental, health and safety laws can be joint and several and without regard to fault or negligence. The failure to comply with past, present or future laws could result in the imposition of substantial fines and penalties, remediation costs, property damage and personal injury claims, loss of permits or a cessation of operations, and any of these events could harm our business and financial condition. We expect that our operations will be affected by other new environmental, health and workplace safety laws on an ongoing basis, and although we cannot predict the ultimate impact of any such new laws, they may impose greater compliance costs or result in increased risks or penalties, which could harm our business.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur a liability and our research and development programs and the development of our product candidates could be delayed.

We may incur substantial costs in connection with litigation and other disputes.

In the ordinary course of business we may, and in some cases have, become involved in lawsuits and other disputes such as securities claims, intellectual property challenges, including interferences declared by the USPTO, and employee matters. It is possible that we may not prevail in claims made against us in such disputes even after expending significant amounts of money and company resources in defending our positions in such lawsuits and disputes. The outcome of such lawsuits and disputes is inherently uncertain and may have a negative impact on our business, financial condition and results of operations.

Table of Contents

Risks Related to Our Common Stock

Our stock price is volatile and may fluctuate due to factors beyond our control.

The market prices for and trading volumes of securities of biotechnology companies, including our securities, has been historically volatile. Historically, our stock has had significant swings in trading prices, in particular in connection with our public communications regarding feedback received from regulatory authorities. For example, over the last twelve months, in a single day, our stock has increased as much as 60% in a single day or decreased as much as 32% in a single day. We expect that our stock could have a material swing in its trading price in connection with the upcoming advisory committee meeting for eteplirsen, including a decline in trading price if research analysts, investors or others who follow us view any developments related to the advisory committee meeting negatively. The market has from time to time experienced significant price and volume fluctuations unrelated to the operating performance of particular companies. The market price of our common stock may fluctuate significantly due to a variety of factors, including but not limited to:

discussions at, the outcome of and other matters related to the advisory committee meeting for eteplirsen;

the timing of our submissions to regulatory authorities and regulatory decisions and developments including any decision by the FDA regarding our NDA for eteplirsen;

positive or negative results from or regulatory interpretations of testing and clinical trials by ourselves, strategic partners, our competitors or other companies with investigational drugs targeting the same, similar or related diseases to those targeted by our product candidates;

delays in beginning and completing preclinical and clinical studies for potential product candidates;

delays in entering or failing to enter into strategic relationships with respect to development and/or commercialization of our product candidates or entry into strategic relationships on terms that are not deemed to be favorable to our Company;

technological innovations or commercial product introductions by ourselves or competitors;

changes in applicable government regulations or regulatory requirements in the approval process;

developments concerning proprietary rights, including patents and patent litigation matters, such as developments in the interferences declared by the USPTO, including in the near term any outcomes of ongoing interference proceedings and over the longer term the outcomes from any related appeals;

public concern relating to the commercial value, efficacy or safety of any of our products;

our ability to obtain funds, through the issuance of equity or equity linked securities or incurrence of debt, or other corporate transactions;

comments by securities analysts;

developments in litigation such as the stockholder lawsuits against us;

changes in senior management such as the resignation of our former CEO earlier this year and appointment of an interim CEO; or

general market conditions in our industry or in the economy as a whole.

Broad market and industry factors may seriously affect the market price of a company's stock, including ours, regardless of actual operating performance. In addition, in the past, following periods of volatility in the overall market and the market price of a particular company's securities, securities class action litigation has often been instituted against these companies. Such litigation could result in substantial costs and a diversion of our management's attention and resources.

Table of Contents

Provisions of our certificate of incorporation, bylaws and Delaware law might deter acquisition bids for us that might be considered favorable and prevent or frustrate any attempt to replace or remove the then-current management and board of directors.

Certain provisions of our certificate of incorporation and bylaws may make it more difficult for a third party to acquire control of us or effect a change in our board of directors and management. These provisions include:

when the board is comprised of six or more directors, classification of our board of directors into two classes, with one class elected each year;

directors may only be removed for cause by the affirmative vote of majority of the voting power of all the then-outstanding shares of voting stock;

prohibition of cumulative voting of shares in the election of directors;

right of the board of directors to elect directors to fill a vacancy created by the expansion of the board of directors or the resignation, death, disqualification or removal of a director;

express authorization of the board of directors to make, alter or repeal our bylaws;

prohibition on stockholder action by written consent;

advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at stockholder meetings;

the ability of our board of directors to authorize the issuance of undesignated preferred stock, the terms and rights of which may be established and shares of which may be issued without stockholder approval, including rights superior to the rights of the holders of common stock; and

a super-majority (66 2/3%) of the voting power of all of the then-outstanding shares of capital stock are required to amend, rescind, alter or repeal our bylaws and certain provisions of our certificate of incorporation.

In addition, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These and other provisions in our certificate of incorporation and our bylaws and in the Delaware General Corporation Law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors.

We expect our operating results to fluctuate in future periods, which may adversely affect our stock price.

Our quarterly operating results have fluctuated in the past, and we believe they will continue to do so in the future. Our operating results may fluctuate due to the variable nature of our revenue and research and development expenses. Likewise, our research and development expenses may experience fluctuations as a result of the timing and magnitude of expenditures incurred in support of our DMD and other proprietary drug development programs. In one or more future periods, our results of operations may fall below the expectations of securities analysts and investors. In that event, the market price of our common stock could decline.

A significant number of shares of our common stock are issuable pursuant to outstanding stock awards, and we expect to issue additional stock awards and shares of common stock in the future. Exercise of these awards and sales of shares will dilute the interests of existing security holders and may depress the price of our common stock.

As of June 30, 2015, there were 41,515,793 shares of common stock outstanding and outstanding awards to purchase 7.0 million shares of common stock under various incentive stock plans. Additionally, as of June 30, 2015, there were 2.0 million shares of common stock available for future issuance under our Amended and Restated 2011 Equity Incentive Plan, 0.2 million shares of common stock

Table of Contents

available for issuance under our 2013 Employee Stock Purchase Plan and 0.4 million shares of common stock available for issuance under our 2014 Employment Commencement Incentive Plan. We may issue additional common stock and warrants from time to time to finance our operations. We may also issue additional shares to fund potential acquisitions or in connection with additional stock options or other equity awards granted to our employees, officers, directors and consultants under our Amended and Restated 2011 Equity Incentive Plan, our 2013 Employee Stock Purchase Plan or our 2014 Employment Commencement Incentive Plan. The issuance of additional shares of common stock or warrants to purchase common stock and the perception that such issuances may occur or exercise of outstanding warrants or options may have a dilutive impact on other stockholders and could have a material negative effect on the market price of our common stock.

S-25

Table of Contents

FORWARD-LOOKING STATEMENTS

This prospectus supplement and the Securities and Exchange Commission (the SEC) filings that are incorporated by reference into this prospectus supplement contain or incorporate by reference forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. You can generally identify these forward-looking statements by forward-looking words such as believe, anticipate, expect, intend, plan, will, may, estimate, continue, ongoing, predict, potential, likely, seek and other similar expressions, as well as variations or negative forms of these words. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other forward-looking information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements include, but are not limited to:

our expectations regarding the timing of research, development, preclinical and clinical trial results and analyses relating to the safety profile and potential clinical benefits of our product candidates, including eteplirsen, our PMO chemistries, our other PMO-based chemistries and our other RNA-targeted technologies;

our expectations regarding additional data and analysis collected by us on eteplirsen;

our expectations regarding the FDA interpretation of our data and information on our product candidates, PMO and PMO-based chemistries and RNA-targeted technologies and the impact of the FDA's interpretations on our FDA submissions (including our investigational new drug applications (INDs) and NDAs), filing decisions by the FDA, advisory committee recommendations, and FDA product approval decisions and related timelines;

our estimates regarding how long our currently available cash, cash equivalents and investments will be sufficient to finance our operations and business plans and statements about our future capital needs;

our current and planned investment in, and activities in preparation for, a potential commercial launch of eteplirsen, including negotiating and entered into commercial and supply contracts, scaling up manufacturing and hiring for pre-launch and commercial positions and the impact of winding down or terminating these commitments if the FDA does not approve our eteplirsen NDA;

our ability to raise additional funds to support our business plans and the impact of our credit and security agreement with MidCap Financial on our financial condition and future operations;

our expectations regarding our ability to become a leading developer and marketer of PMO-based and RNA-targeted therapeutics and commercial viability of our product candidates, chemistries and technologies;

the potential safety, efficacy, potency and utility of our product candidates, chemistries and technologies in the treatment of DMD and in rare, infectious and other diseases;

our expectations regarding the timing, completion and receipt of results from our ongoing development programs for our pipeline of product candidates including their potential consistency with prior results;

our ability to effectively manage the clinical trial process for our product candidates on a timely basis, including our ability to conduct a placebo-controlled confirmatory study for eteplirsen in the U.S. using an exon 53 skipping product candidate that depends on our ability to satisfactorily and timely respond to FDA requests with respect to preclinical data on the exon 53 skipping product candidate;

our expectations regarding our ability to engage a number of manufacturers with sufficient capability and capacity to meet our manufacturing needs, including with respect to the manufacture of subunits, drug substance (APIs) and drug product, within the time frames and quantities needed to provide our product candidates, including eteplirsen, to patients in larger scale clinical trials or in potential commercial quantities, and meet regulatory and Company quality control requirements;

S-26

Table of Contents

the impact of regulations as well as regulatory decisions by the FDA and other regulatory agencies on our business, including with respect to our eteplirsen NDA and any issuance of an Emergency Use Authorization (EUA) for our product candidates intended to treat Ebola virus and Marburg virus, as well as the development of our product candidates and our financial and contractual obligations;

our expectations regarding the potential markets for our product candidates;

our expectations regarding our manufacturing and scale-up techniques and our ability to synthesize and purify our product candidates to adequately support clinical development and potential commercialization;

the potential acceptance of our product candidates, if introduced, in the marketplace;

the possible impact of competing products on our product candidates and our ability to compete against such products;

the impact of potential difficulties in product development, manufacturing, or the commercialization of our product candidates, including difficulties in establishing the commercial infrastructure necessary for the commercialization of eteplirsen;

our expectations regarding partnering opportunities and other strategic transactions;

the extent of protection that our patents provide and our pending patent applications may provide, if patents issue from such applications, to our technologies and programs;

our plans and ability to file and progress to issue additional patent applications to enhance and protect our new and existing technologies and programs;

our ability to invalidate some or all of the claims of patents issued to competitors and pending patent applications if issued to competitors, and the potential impact of those claims on the potential commercialization of our product candidates;

our ability to successfully challenge the patent positions of our competitors and successfully defend our patent positions in the actions that the United States Patent and Trademark Office (USPTO) may take or has taken with respect to our patent claims or those of third parties, including with respect to interferences that have been declared between our patents and patent applications held by Prosensa Holding N.V. (Prosensa), which is now owned by BioMarin Pharmaceuticals, Inc., relating to eteplirsen and SRP-4053 and our expectations regarding the impact of these interferences on our business plans, including our current commercialization plans for eteplirsen and SRP-4053;

our ability to operate our business without infringing the intellectual property rights of others;

our ability to enter into contracts, including collaborations or licensing agreements, with respect to our technology and product candidates, with third parties, including government entities;

our estimates regarding future revenues, research and development expenses, other expenses, capital requirements and payments to third parties;

the timing and outcomes of ongoing interference proceedings and related appeals;

the impact of litigation on us, including actions brought by stockholders;

our ability to attract and retain key employees needed to execute our business plans and strategies and our expectations regarding our ability to manage the impact of any loss of key employees;

our ability to comply with applicable environmental laws and regulations;

our expectations relating to potential funding from government and other sources for the development of some of our product candidates;

our beliefs and expectations regarding milestone, royalty or other payments that could be due to third parties under existing agreements; and

S-27

Table of Contents

our succession plan, including the search for a permanent full-time Chief Executive Officer (CEO) and the effect that the changes in management could have on the Company, its business plans and its regulatory and clinical discussions and relationships.

All forward-looking statements contained herein are expressly qualified in their entirety by this cautionary statement, the risk factors set forth under the heading Risk Factors in this prospectus supplement, and in the section entitled Risk Factors incorporated herein by reference to our most recent Annual Report on Form 10-K, and our subsequent filings with the SEC, incorporated by reference in this prospectus supplement (see Where You Can Find Additional Information). These forward-looking statements speak only as of the date of this prospectus supplement. Except to the extent required by applicable laws and regulations of the SEC, we undertake no obligation to update these forward-looking statements to reflect new information, events or circumstances after the date of this prospectus supplement or to reflect the occurrence of unanticipated events. In light of these risks and uncertainties, the forward-looking events and circumstances described in this prospectus supplement may not occur and actual results could differ materially from those anticipated or implied in the forward-looking statements. Accordingly, you are cautioned not to place undue reliance on these forward-looking statements.

S-28

Table of Contents

USE OF PROCEEDS

We anticipate that the net proceeds to us, after deducting underwriting discounts and commissions and estimated expenses payable by us, from the assumed sale of 3,157,362 shares of our common stock offered hereby, at an assumed public offering price of \$39.59 per share, the closing price on the Nasdaq Global Select Market on October 2, 2015, will be approximately \$118.75 million, or approximately \$136.56 million if the underwriters exercise in full their option to purchase an assumed 473,604 additional shares of common stock.

We intend to use the net proceeds from this offering principally for product and commercial development, manufacturing, any business development activities and other general corporate purposes. The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including the status of our product development and clinical trial efforts, regulatory approvals, competition and our ability to obtain government funding or other non-dilutive financing for the development of certain of our product candidates. We reserve the right to change the use of proceeds as a result of certain contingencies such as competitive developments, opportunities to acquire technologies or products and other factors. Pending application of the proceeds of sale of the securities, we intend to invest the net proceeds of the sale in short-term, investment-grade, interest-bearing instruments.

Table of Contents

**MATERIAL U.S. FEDERAL TAX CONSIDERATIONS FOR
NON-U.S. HOLDERS OF COMMON STOCK**

The following is a summary of certain material U.S. federal income and estate tax considerations relating to the purchase, ownership and disposition of our common stock by Non-U.S. Holders (defined below), but does not purport to be a complete analysis of all the potential tax considerations. This summary is based upon the Internal Revenue Code of 1986, as amended (the Code), the Treasury regulations promulgated or proposed thereunder and administrative and judicial interpretations thereof, all as of the date hereof and all of which are subject to change at any time, possibly on a retroactive basis. This summary is limited to the tax consequences to those persons who hold our common stock as capital assets within the meaning of Section 1221 of the Code.

This summary does not purport to deal with all aspects of U.S. federal income and estate taxation that might be relevant to particular Non-U.S. Holders in light of their particular investment circumstances or status, nor does it address specific tax considerations that may be relevant to particular persons (including, for example, financial institutions, broker-dealers, insurance companies, partnerships or other pass-through entities, certain U.S. expatriates, tax-exempt organizations, controlled foreign corporations, passive foreign investment companies, corporations that accumulate earnings to avoid U.S. federal income tax, or persons in special situations, such as those who have elected to mark securities to market or those who hold common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment). In addition, this summary does not address U.S. federal alternative minimum, the unearned income Medicare contribution tax, certain estate and gift tax considerations or considerations under the tax laws of any state, local or non-U.S. jurisdiction.

This summary is for general information only. Non-U.S. Holders are urged to consult their tax advisors concerning the U.S. federal income and estate taxation, state, local and non-U.S. taxation and other tax consequences to them of the purchase, ownership and disposition of our common stock, as well as the application of state, local and non-U.S. income and other tax laws.

For purposes of this summary, a Non-U.S. Holder means a beneficial owner of common stock that for U.S. federal income tax purposes is not an entity treated as a partnership and is not:

an individual who is a citizen or resident of the U.S.,

a corporation (or other entity taxable as a corporation) created or organized under the laws of the U.S., any state thereof, or the District of Columbia,

an estate the income of which is subject to U.S. federal income tax regardless of its source, or

a trust if (a) a court within the U.S. is able to exercise primary supervision over the administration of the trust, and one or more U.S. persons have the authority to control all substantial decisions of the trust, or (b) a valid election to be treated as a U.S. person is in effect with respect to such trust.

If a partnership, or an entity or arrangement treated as a partnership for U.S. federal income tax purposes, holds common stock, the tax treatment of a partner in the partnership generally will depend upon the partner's tax status and

upon the activities of the partnership. Accordingly, partnerships and other entities that are classified as partnerships for U.S. federal income tax purposes that hold our common stock and partners in such partnerships should consult their tax advisors.

Distributions on Our Common Stock

As discussed under **Dividends** above, we do not currently expect to pay dividends. In the event that we do make a distribution of cash or property with respect to our common stock, any such distributions will be treated as a dividend for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). If a distribution exceeds our current and

Table of Contents

accumulated earnings and profits, the excess will be treated first as a tax-free return of capital to the extent of the Non-U.S. Holder's tax basis in our common stock and thereafter as capital gain from the sale or exchange of such stock. Any such distribution would also be subject to the discussion below under the section titled "Additional Withholding and Information Reporting Requirements." Dividends paid to a Non-U.S. Holder generally will be subject to a 30% U.S. federal withholding tax unless such Non-U.S. Holder provides us or our agent, as the case may be, with a properly executed:

1. U.S. Internal Revenue Service (IRS) Form W-8BEN or W-8BEN-E (or successor form) claiming, under penalties of perjury, a reduction in withholding under an applicable income tax treaty, or
2. IRS Form W-8ECI (or successor form) stating that a dividend paid on common stock is not subject to withholding tax because it is effectively connected with a U.S. trade or business of the Non-U.S. Holder (in which case such dividend generally will be subject to regular graduated U.S. tax rates as described below).

The certification described above must be provided to us or another applicable withholding agent prior to the payment of the dividends and must be updated periodically. The certification requirement also may require a Non-U.S. Holder that provides an IRS form or that claims treaty benefits to provide its U.S. taxpayer identification number. Special certification and other requirements apply in the case of certain Non-U.S. Holders that are intermediaries or pass-through entities for U.S. federal income tax purposes.

Each Non-U.S. Holder is urged to consult its tax advisor about the specific methods for satisfying these requirements. A claim for exemption will not be valid if the person receiving the applicable form has actual knowledge or reason to know that the statements on the form are false.

If dividends are effectively connected with a U.S. trade or business of the Non-U.S. Holder (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment), the Non-U.S. Holder, although exempt from the withholding tax described above (provided that the certifications described above are satisfied), will be subject to U.S. federal income tax on such dividends on a net income basis in the same manner as if it were a resident of the United States. In addition, if such Non-U.S. Holder is a non-U.S. corporation and dividends are effectively connected with its U.S. trade or business (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment), such Non-U.S. Holder may be subject to an additional branch profits tax equal to 30% (unless reduced by an applicable income treaty) in respect of such effectively-connected income.

If a Non-U.S. Holder is eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty, such holder may obtain a refund or credit of any excess amount withheld by timely filing an appropriate claim for refund with the IRS.

Disposition of Our Common Stock

Subject to the discussion below under the section titled "Additional Withholding and Information Reporting Requirements", in general, a Non-U.S. Holder will not be subject to U.S. federal income tax or withholding tax on gain recognized on a sale, exchange or other taxable disposition of a share of our common stock, unless:

the gain is effectively connected with a trade or business of the Non-U.S. Holder in the United States (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment);

the Non-U.S. Holder is a nonresident alien who is present in the United States for 183 days or more in the taxable year of the disposition and meets certain other conditions; or

we are or have been a United States real property holding corporation, as defined in the Code (a USRPHC), at any time within the shorter of the five-year period preceding the disposition and the Non-U.S. Holder's holding period in the share of our common stock.

S-31

Table of Contents

We believe we are not, and do not anticipate becoming, a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property relative to the fair market value of other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, a Non-U.S. Holder would not be subject to U.S. federal income tax on a sale, exchange or other taxable disposition of our common stock so long as our common stock continues to be regularly traded on an established securities market and such Non-U.S. Holder does not own and is not deemed to own (directly, indirectly or constructively) more than 5% of our common stock at any time during the shorter of the five year period ending on the date of disposition and the holder's holding period.

If a Non-U.S. Holder is engaged in a trade or business in the U.S. and gain recognized by the Non-U.S. Holder on a sale or other disposition of our common stock is effectively connected with the conduct of such trade or business, the Non-U.S. Holder will generally be subject to regular U.S. income tax as if the Non-U.S. Holder were a U.S. person, subject to an applicable income tax treaty providing otherwise. Additionally, a non-U.S. corporation may also, under certain circumstances, be subject to an additional branch profits tax imposed at a rate of 30% (or, if applicable, a lower income tax treaty rate). Non-U.S. Holders whose gain from dispositions of our common stock may be effectively connected with the conduct of a trade or business in the United States are urged to consult their tax advisors with respect to the U.S. tax consequences of the purchase, ownership and disposition of our common stock.

A nonresident alien who is subject to U.S. federal income tax because such individual was present in the United States for 183 days or more in the taxable year of the taxable disposition of our common stock will be subject to a flat 30% tax on the gain derived from such disposition, which may be offset by U.S. source capital loss.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS and to each Non-U.S. Holder certain information including the Non-U.S. Holder's name, address and taxpayer identification number, the aggregate amount of distributions on our common stock paid to that Non-U.S. Holder during the calendar year and the amount of tax withheld, if any.

Backup withholding tax is imposed on dividends and certain other types of payments to certain U.S. persons (currently at a rate of 28%). In general, backup withholding tax will not apply to payments of dividends on common stock or proceeds from the sale of common stock payable to a Non-U.S. Holder if the certification described above under "Distributions on Our Common Stock" is duly provided by such Non-U.S. Holder or the Non-U.S. Holder otherwise establishes an exemption, provided that the payor does not have actual knowledge or reason to know that the Non-U.S. Holder is a U.S. person or that the conditions of any claimed exemption are not satisfied. Certain information reporting may still apply to distributions even if an exemption from backup withholding is established. Copies of any information returns reporting the distributions to a Non-U.S. Holder and any withholding also may be made available to the tax authorities in the country in which a Non-U.S. Holder resides under the provisions of an applicable income tax treaty.

Backup withholding is not an additional tax and any amounts withheld under the backup withholding tax rules from a payment to a Non-U.S. Holder will be allowed as a refund or a credit against such Non-U.S. Holder's U.S. federal income tax liability, provided that the requisite procedures are followed.

Non-U.S. Holders are urged to consult their tax advisors regarding their particular circumstances and the availability of and procedure for obtaining an exemption from backup withholding.

Table of Contents

Additional Withholding and Information Reporting Requirements

Sections 1471 through 1474 of the Code and related Treasury Regulations, together with other Treasury Department or IRS guidance issued thereunder, and intergovernmental agreements, legislation, rules and other official guidance adopted pursuant to such intergovernmental agreements (commonly referred to as FATCA) generally impose a U.S. federal withholding tax of 30% on payments to certain non-U.S. entities (including certain intermediaries), including dividends on our common stock and, on or after January 1, 2017 (which, under recent Treasury guidance, is expected to be delayed until on or after January 1, 2019), the gross proceeds from a sale or other disposition of shares of our common stock, unless such persons comply with a complicated U.S. information reporting, disclosure and certification regime. This regime requires, among other things, a broad class of persons to enter into agreements with the IRS to obtain, disclose and report information about their investors and account holders. An intergovernmental agreement between the United States and an applicable foreign country may, however, modify these requirements. Prospective investors should consult their own tax advisors regarding the possible impact of these rules on their investment in our common stock, and the possible impact of these rules on the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of this 30% withholding tax under FATCA.

U.S. Federal Estate Tax

Common stock owned or treated as owned by an individual who is a Non-U.S. Holder at the time of death generally will be included in the individual's gross estate for U.S. federal estate tax purposes and may be subject to U.S. federal estate tax unless an applicable estate or other tax treaty provides otherwise.

Table of Contents**DILUTION**

Purchasers of common stock offered by this prospectus supplement and the accompanying prospectus will suffer immediate and substantial dilution in the net tangible book value per share of common stock. Our net tangible book value as of June 30, 2015 was approximately \$159.4 million, or approximately \$3.84 per share of common stock. Net tangible book value per share represents the amount of total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of June 30, 2015.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the assumed sale of 3,157,362 shares of common stock in this offering at an assumed public offering price of \$39.59 per share (the last reported sale price on the Nasdaq Global Select Market on October 2, 2015), and after deduction of the estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2015 would have been approximately \$278.1 million, or \$6.23 per share of common stock. This represents an immediate increase in net tangible book value of \$2.39 per share of common stock to our existing shareholders and an immediate dilution in net tangible book value of \$33.36 per share of common stock to investors participating in this offering. The following table illustrates this per share dilution:

Assumed public offering price per share		\$ 39.59
Net tangible book value per share as of June 30, 2015	\$ 3.84	
Increase per share attributable to this offering	\$ 2.39	
As adjusted net tangible book value per share as of June 30, 2015, after giving effect to this offering	\$ 6.23	
Dilution per share to new investors participating in this offering	\$ 33.36	

Each \$1.00 increase (decrease) in the assumed public offering price of \$39.59 per share, the last reported sale price of our common stock on the NASDAQ Global Select Market on October 2, 2015, would (decrease) increase the number of shares of common stock to be issued by us in this offering by (77,787) and 81,818, respectively, assuming the aggregate dollar amount of shares offered by us, as set forth on the cover page of this prospectus, remains the same. We may also increase or decrease the aggregate dollar amount of shares we are offering. Each increase (decrease) of \$1.0 million of shares offered by us would increase (decrease) the net proceeds of this offering by approximately \$1.0 million, assuming that the assumed public offering price remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

The above table is based on 41,515,793 shares of our common stock outstanding as of June 30, 2015 and excludes the following:

6,659,633 shares of our common stock issuable upon the exercise of stock options outstanding at under our 2002 Equity Incentive Plan, our 2011 Equity Incentive Plan and certain non-plan option grants;

124,783 shares of restricted stock awards issuable upon vesting under our 2011 Equity Incentive Plan;

170,000 shares subject to stock appreciation rights under our 2011 Equity Incentive Plan;

2,006,202 shares of our common stock available for future issuance under our 2011 Equity Incentive Plan and

421,025 shares of common stock issuable upon the exercise of stock options outstanding under our 2014 Employment Commencement Incentive Plan.

To the extent that any options or warrants are exercised, new options are issued under our equity incentive plans, or we otherwise issue additional shares of common stock in the future, there will be further dilution to new investors.

S-34

Table of Contents

If the underwriters exercise in full their option to purchase an assumed 473,604 additional shares of common stock at an assumed public offering price of \$39.59 per share, the as adjusted net tangible book value after this offering would be \$6.55 per share, representing an increase in net tangible book value of \$2.72 per share to existing stockholders and immediate dilution in net tangible book value of \$33.04 per share to investors purchasing our common stock in this offering at the public offering price.

S-35

Table of Contents**UNDERWRITING**

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus, the underwriters named below have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

Name	Number of Shares
Credit Suisse Securities (USA) LLC	
Morgan Stanley & Co. LLC	
Total	

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' option to purchase additional shares described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to \$18,750,000 of additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to \$18,750,000 of additional shares of common stock.

	Per Share	Total	
		No Exercise	Full Exercise
Public offering price	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately \$300,000. We have agreed to reimburse the underwriters for expense relating to clearance of this offering with the Financial Industry Regulatory Authority up to \$40,000.

Our common stock is listed on The NASDAQ Global Select Market under the symbol SRPT.

We and all directors and officers have agreed that, without the prior written consent of Credit Suisse Securities (USA) LLC and Morgan Stanley & Co. LLC, we and they will not, during the period ending 60 days after the date of this prospectus (the restricted period):

offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of common stock;

S-36

Table of Contents

file any registration statement with the Securities and Exchange Commission relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or

enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock.

In addition, we and each such person agrees that, without the prior written consent of Credit Suisse Securities (USA) LLC and Morgan Stanley & Co. LLC, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph relating to our directors and officers and our shareholders do not apply to:

transfers or dispositions of common stock acquired in this offering or acquired in open market transactions after this offering;

transfers or dispositions of shares of common stock as a bona fide gift;

transfers of shares of common stock to any trust for the benefit of immediate family members;

distributions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to limited partners or stockholders;

the establishment of a trading plan that satisfies the requirements of Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period; and

transfers or dispositions of shares of common stock or any security convertible into common stock by will or other testamentary document or by intestacy.

provided further that (i) in the case of any transfer or distribution as described in the second, third or fourth bullet point above, the recipient shall agree to be subject to the restrictions described in the immediately preceding paragraph and no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period.

In addition, the restrictions described in the paragraph above relating to us do not apply to:

the shares to be sold in this offering;

the issuance of equity awards pursuant to our benefit plans, qualified equity incentive plans or other compensation plans as such plans are in existence on the date of, and described in, this prospectus or is hereafter approved by our shareholders;

the issuance of options to induce personnel to accept employment with us (whether or not pursuant to a plan), which in the aggregate shall not exceed 3% of our outstanding common stock; and

the issuance of common stock pursuant to the valid exercises of options, warrants or rights outstanding on the date of this prospectus.

Credit Suisse Securities (USA) LLC and Morgan Stanley & Co. LLC, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice. When determining whether or not to release common stock and other securities from lock-up agreements, Credit Suisse Securities (USA) LLC and Morgan Stanley & Co. LLC will consider, among other factors, the holder's reasons for requesting the release, the number of shares of common stock and other securities for which the release is being requested and market conditions at the time.

S-37

Table of Contents

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option. The underwriters can close out a covered short sale by exercising the option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the option. The underwriters may also sell shares in excess of the option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The underwriters may agree to allocate a number of shares of common stock for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

NASDAQ Global Select Market Listing

The shares are listed on the NASDAQ Global Select Market under the symbol SRPT.

Table of Contents

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (FSMA) received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit

S-39

Table of Contents

prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

S-40

Table of Contents

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon by Ropes & Gray LLP, Boston, Massachusetts. Certain legal matters in connection with this offering will be passed upon for the underwriters by Goodwin Procter LLP, Boston Massachusetts.

EXPERTS

The consolidated financial statements of Sarepta Therapeutics, Inc. and subsidiaries as of December 31, 2014, 2013 and 2012, and for each of the years in the three-year period ended December 31, 2014, 2013 and 2012, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2014 have been incorporated by reference herein in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed a registration statement on Form S-3 with the SEC for the shares of common stock offered by this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus, including the information incorporated by reference herein and therein, do not include all of the information contained in the registration statement. You should refer to the registration statement and its exhibits for additional information.

We file annual, quarterly and current reports, proxy statements and other information with the SEC under the Exchange Act. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge on our website at <http://www.sarepta.com> under the Investor Relations SEC Filings caption. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on our website is not part of this prospectus supplement.

You should rely only on the information provided in, and incorporated by reference in, this prospectus supplement and the accompanying prospectus and the registration statement to which this prospectus supplement and accompanying prospectus form a part. We have not authorized anyone else to provide you with different information. Our securities are not being offered in any jurisdiction where the offer is not permitted. The information contained in documents that are incorporated by reference in this prospectus supplement is accurate only as of the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

Table of Contents

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus supplement and the accompanying prospectus. We incorporate by reference the following information or documents that we have filed with the SEC:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 (including the portions of our proxy statement for our 2015 annual meeting of shareowners incorporated by reference therein), filed with the SEC on February 26, 2015;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2015 and June 30, 2015, filed with the SEC on May 7, 2015 and August 6, 2015, respectively;

our Current Reports on Form 8-K, as filed with the SEC on January 12, 2015 (with respect to Item 5.02 only), April 2, 2015, April 20, 2015, June 3, 2015, June 29, 2015, June 30, 2015, July 2, 2015 and October 1, 2015 (with respect to Item 5.02 only); and

the description of our common stock contained in our Current Report on Form 8-K12B filed with the SEC on June 6, 2013.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement and accompanying prospectus from the date of the filing of such reports and documents.

Any statement contained in any document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or accompanying prospectus modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement and accompanying prospectus.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus supplement and accompanying prospectus is delivered, upon written or oral request, a copy of any or all documents that are incorporated by reference into this prospectus supplement and accompanying prospectus, but not delivered with the prospectus supplement and accompanying prospectus, other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus supplement and accompanying prospectus incorporates. You should direct written requests to: Sarepta Therapeutics, Inc., 215 First Street, Suite 415, Cambridge, MA 02142, or you may call us at (617) 274-4000.

Table of Contents

PROSPECTUS

Sarepta Therapeutics, Inc.

\$200,000,000

Common Stock, Preferred Stock, Debt Securities, Warrants and Units

Sarepta Therapeutics, Inc. or certain selling securityholders may, from time to time offer, in one or more classes or series, separately or together, and in amounts, at prices and on terms to be set forth in one or more supplements to this prospectus, common stock, preferred stock, debt securities, warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units comprised of two or more other securities.

We refer to the common stock, preferred stock, debt securities, warrants and units registered hereunder collectively as the securities in this prospectus. We will offer our securities in amounts, at prices and on terms determined at the time of the offering of any such security.

The prospectus provides a general description of the securities we or any selling securityholder may offer. The specific terms of each series or class of the securities will be set forth in the applicable prospectus supplement and will include, as applicable: (i) in the case of common stock, any public offering price; (ii) in the case of preferred stock, the specific title and any dividend, liquidation, redemption, conversion, voting and other rights and any public offering price; (iii) in the case of debt securities, the specific terms of such debt securities; (iv) in the case of warrants, the duration, offering price, exercise price and detachability; and (v) in the case of units, the constituent securities comprising the units, the offering price and detachability.

We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference before you invest in any of our securities. This prospectus may not be used to sell securities unless accompanied by a prospectus supplement.

Our common stock is listed on The NASDAQ Global Select Market under the symbol SRPT. On February 23, 2015, the last reported sale price on The NASDAQ Global Select Market was \$15.48 per share. There is currently no market for the other securities we may offer.

Investing in our securities involves a high degree of risk. Please carefully read the information under the headings Risk Factors beginning on page 3 of this prospectus before you invest in our securities. This information may also be included in any supplement, any related free writing prospectus and/or any other future filings we make with the Securities and Exchange Commission that are incorporated by reference into this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

We may offer and sell these securities to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continuous or delayed basis. In addition, certain selling securityholders may offer and sell our securities from time to time. We will provide specific information about any selling securityholders in one or more supplements to this prospectus. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names, and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections entitled Plan of Distribution and About This Prospectus for more information. The price to the public of those securities and the net proceeds we or any selling securityholders expect to receive from that sale will also be set forth in a prospectus supplement. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such series of securities.

The date of this prospectus is May 5, 2015.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	1
<u>THE COMPANY</u>	2
<u>RISK FACTORS</u>	3
<u>FORWARD-LOOKING STATEMENTS</u>	4
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	6
<u>USE OF PROCEEDS</u>	7
<u>SELLING SECURITY HOLDERS</u>	8
<u>GENERAL DESCRIPTION OF SECURITIES WE MAY SELL</u>	9
<u>PLAN OF DISTRIBUTION</u>	23
<u>LEGAL MATTERS</u>	26
<u>EXPERTS</u>	26
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	26
<u>INFORMATION INCORPORATED BY REFERENCE</u>	27
<u>DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES</u>	28

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf process, we or any selling securityholder may, from time to time, offer or sell any combination of the securities described in this prospectus in one or more offerings.

This prospectus provides you with a general description of the securities offered by us or any selling securityholder. Each time we or any selling securityholder sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information about the terms of that offering. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add to, update or change information contained in the prospectus or in any documents that we have incorporated by reference into this prospectus, and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in the prospectus supplement or the related free writing prospectus.

You should only rely on the information contained or incorporated by reference in this prospectus and any prospectus supplement or any related free writing prospectus. We have not authorized any other person to provide you with different information. You should read the entire prospectus and any prospectus supplement and any related issuer free writing prospectus, as well as the documents incorporated by reference into this prospectus or any prospectus supplement, before making an investment decision. The prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and any accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security. We do not imply or represent by delivering this prospectus that Sarepta Therapeutics, Inc., or its business, financial condition or results of operations, are unchanged after the date on the front of this prospectus or that the information in this prospectus is correct as any time after such date. In this prospectus, unless the context indicates otherwise, the terms company, we, us, and our refer to Sarepta Therapeutics, Inc. and its subsidiaries.

Table of Contents

THE COMPANY

We are a biopharmaceutical company focused on the discovery and development of unique RNA-targeted therapeutics for the treatment of rare, infectious and other diseases. Our highly-differentiated RNA-targeted technologies work at the most fundamental level of biology. Applying our proprietary and innovative platform technologies, we are able to target a broad range of diseases and disorders through distinct RNA-targeted mechanisms of action. We are primarily focused on rapidly advancing the development of our potentially disease-modifying Duchenne muscular dystrophy (DMD) drug candidates, including our lead DMD product candidate, eteplirsen, designed to skip exon 51. We are also developing therapeutics using our technology for the treatment of drug-resistant bacteria and infectious, rare and other human diseases.

We were incorporated in the State of Oregon on July 22, 1980 and reincorporated into the State of Delaware on June 6, 2013. Our principal executive offices are located at 215 First Street, Suite 415, Cambridge, MA 02142 and our telephone number is (617) 274-4000. We maintain an Internet website at www.sarepta.com. We have not incorporated the information on our website by reference into this prospectus, and you should not consider it to be a part of this prospectus.

We carry on our business directly and through our subsidiaries. Throughout this prospectus, unless the context specifies or implies otherwise, the terms Company, Sarepta, we, us, and our refer to Sarepta Therapeutics, Inc. and its subsidiaries.

Table of Contents

RISK FACTORS

Investment in any securities offered pursuant to this prospectus involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K, any subsequent Quarterly Reports on Form 10-Q and any Current Reports on Form 8-K we file after the date of this prospectus, together with any amendments or supplements thereto and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in any applicable prospectus supplement or free writing prospectus, before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. Please also refer to the section below titled Forward-Looking Statements. Additional risks not known to us or that we believe are immaterial may also significantly impair our business operations and could result in a loss of all or part of your investment in the offered securities.

Table of Contents

FORWARD-LOOKING STATEMENTS

This prospectus and the SEC filings that are incorporated by reference into this prospectus contain or incorporate by reference forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. You can generally identify these forward-looking statements by forward-looking words such as believe, anticipate, expect, intend, plan, will, may, estimate, could, continue, ongoing, predict, potential and other well as variations or negatives of these words. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other forward-looking information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements include, but are not limited to:

our expectations regarding the timing of research, development, preclinical and clinical trial results and analyses relating to the safety profile and potential clinical benefits of our product candidates, including eteplirsen, our phosphorodiamidate morpholino oligomer (PMO) chemistries, our other PMO-based chemistries and our other RNA-targeted technology;

our expectations regarding additional data and analysis collected by us on eteplirsen, the Food and Drug Administration s (FDA) interpretation of this additional information and the impact of such data or interpretation on our new drug application (NDA) filing plans and timelines;

our estimates regarding how long our currently available cash, cash equivalents and investments will be sufficient to finance our operation and business plans and statements about our future capital needs;

our expectations regarding our ability to become a leading developer and marketer of PMO-based and RNA targeted therapeutics and commercial viability of our product candidates, chemistries and technologies;

the potential safety, efficacy, potency and utility of our product candidates, chemistries and technologies in the treatment of DMD and rare and infectious diseases, and their potential to treat a broad number of other human diseases;

our expectations regarding the timing, completion and receipt of results from our ongoing development programs for our pipeline of product candidates including their potential consistency with prior results;

our ability to effectively manage the clinical trial process for our product candidates on a timely basis, such as our confirmatory studies for eteplirsen;

our expectations regarding our ability to engage a number of manufacturers with sufficient capability and capacity to meet our manufacturing needs, including with respect to the manufacture of subunits, drug substance (API s) and drug product, within the time frames and quantities needed to provide our product

candidates, including eteplirsen, to patients in larger scale clinical trials or in potential commercial quantities, and meet regulatory and Company quality control requirements;

the impact of regulations as well as regulatory decisions by the FDA and other regulatory agencies on our business, including with respect to the finalization of the pivotal clinical study design for eteplirsen, NDA submissions and the issuance of an Emergency Use Authorization (EUA) for our product candidate intended to treat Marburg virus, as well as the development of our product candidates and our financial and contractual obligations;

our expectations regarding the potential markets for our product candidates;

the potential acceptance of our product candidates, if introduced, in the marketplace;

the possible impact of competing products on our product candidates and our ability to compete against such products;

the impact of potential difficulties in product development, manufacturing, or the commercialization of our product candidates, including difficulties in establishing the commercial infrastructure necessary for the commercialization of eteplirsen;

Table of Contents

our expectations regarding partnering opportunities and other strategic transactions;

the extent of protection that our patents provide and our pending patent applications may provide, if patents issue from such applications, to our technologies and programs;

our plans and ability to file and progress to issue additional patent applications to enhance and protect our new and existing technologies and programs;

our ability to invalidate some or all of the claims of patents issued to competitors and pending patent applications if issued to competitors, and the potential impact of those claims on the potential commercialization of our product candidates;

our ability to enter into contracts, including collaborations or licensing agreements, with respect to our technology and product candidates, with third parties, including government entities;

our estimates regarding future revenues, research and development expenses, other expenses, capital requirements and payments to third parties;

our ability to successfully challenge the patent positions of our competitors and successfully defend our patent positions in the actions that the United States Patent and Trademark Office (USPTO) may take or has taken with respect to our patent claims or those of third parties, including with respect to interferences that have been declared between our patents and patent applications held by Prosensa Holding N.V. (Prosensa), which is now owned by BioMarin Pharmaceuticals, Inc., relating to eteplirsen and SRP-4053 and our expectations regarding the impact of these interferences on our business plans, including our current commercialization plans for eteplirsen and SRP-4053;

our ability to operate our business without infringing the intellectual property rights of others;

the impact of litigation on us, including actions brought by stockholders;

our ability to attract and retain key employees needed to execute our business plans and strategies and our expectations regarding our ability to manage the impact of any loss of key employees;

our ability to comply with applicable environmental laws and regulations;

our expectations relating to the potential funding from government and other sources for the development of some of our product candidates, including those targeting Ebola and Marburg viruses;

our beliefs and expectations regarding milestone, royalty or other payments that could be due to third parties under existing agreements; and

other factors set forth in the section entitled "Risk Factors" incorporated by reference to our most recent Annual Report on Form 10-K, any subsequent Quarterly Reports on Form 10-Q and any Current Reports on Form 8-K we file after the date of this prospectus.

All forward-looking statements contained herein are expressly qualified in their entirety by this cautionary statement and the risk factors incorporated by reference into this prospectus. These forward-looking statements speak only as of the date of this prospectus. Except to the extent required by law or the rules and regulations of the U.S. Securities and Exchange Commission, we undertake no obligation to update these forward-looking statements to reflect new information, events or circumstances after the date of this prospectus or to reflect the occurrence of unanticipated events. In light of these risks and uncertainties, the forward-looking events and circumstances described in this prospectus may not occur and actual results could differ materially from those anticipated or implied in the forward-looking statements. Accordingly, you are cautioned not to place undue reliance on these forward-looking statements.

Table of Contents**RATIO OF EARNINGS TO FIXED CHARGES**

The following table sets forth, for the periods presented, our ratio of earnings to fixed charges and our ratio of earnings to combined fixed charges and preferred stock dividends. For purposes of computing the ratio of earnings to fixed charges and the ratio of earnings to combined fixed charges and preferred stock dividends, earnings consist of income or loss from continuing operations before income taxes and fixed charges. Fixed charges consist of interest expense and an estimate of the interest component of rent expense. In each of the periods presented, earnings were insufficient to cover fixed charges and combined fixed charges and deemed dividends on preferred stock and the extent of such deficiencies in each period is shown below. You should read these ratios in connection with our consolidated financial statements, including the notes to those statements, incorporated by reference in this prospectus.

	Year Ended December 31,				
	2010	2011	2012	2013	2014
Ratio of earnings to fixed charges (1)					
Deficiency of earnings available to cover fixed charges	\$ (32,177)	\$ (2,318)	\$ (121,287)	\$ (111,985)	\$ (135,789)
Ratio of earnings to combined fixed charges and preferred stock dividends (1)					
Deficiency of earnings available to cover combined fixed charges and preferred stock dividends	\$ (32,177)	\$ (2,318)	\$ (121,287)	\$ (111,985)	\$ (135,789)

- (1) The ratio of earnings to fixed charges and the ratio of earnings to combined fixed charges and preferred stock dividends represent the number of times that fixed charges and combined fixed charges and preferred stock dividends, respectively, are covered by earnings. In each of the periods presented, earnings were negative and calculation of such ratios is not meaningful.

Table of Contents

USE OF PROCEEDS

Unless we state otherwise in the applicable prospectus supplement, we intend to use the net proceeds from the sale of the securities for one or more of the following purposes:

to fund research and development, including clinical trials and expansion of manufacturing capacity;

to finance capital expenditures and capacity expansions; and/or

for general corporate purposes and working capital.

Until we apply the proceeds from a sale of securities to their intended purposes, we may invest these proceeds in highly liquid, investment grade securities. We cannot predict whether the proceeds invested will yield a favorable return.

The specific allocations of the proceeds we receive from the sale of our securities will be described in the applicable prospectus supplement.

Table of Contents

SELLING SECURITY HOLDERS

Information about selling securityholders, if any, including their identities and the common stock to be registered on their behalf, will be set forth in any applicable prospectus supplement, in a post-effective amendment or in filings we make with the SEC under the Exchange Act that are incorporated by reference into this prospectus.

All of the shares of common stock currently held by the selling securityholders were acquired in transactions that were completed prior to the date of the filing of the registration statement of which this prospectus is a part and were issued and outstanding prior to the date of the filing of the registration statement of which this prospectus is a part. Selling securityholders shall not sell any of our common stock pursuant to this prospectus until we have identified such selling securityholders, any relationship any selling securityholder has had with us in the three years prior to any such sale, the total number of shares held by each selling securityholder before and after the sale and the number of shares of common stock being offered for resale by such selling securityholders in a subsequent prospectus supplement. However, the selling securityholders may sell or transfer all or a portion of their common stock pursuant to any available exemption from the registration requirements of the Securities Act.

Table of Contents

GENERAL DESCRIPTION OF SECURITIES WE MAY SELL

We or any selling securityholder may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, either individually or in units, from time to time under this prospectus, together with any applicable prospectus supplement and related free writing prospectus, in amounts, at prices and on terms to be determined by market conditions at the time of offering. If we issue any debt securities at a discount from their original stated principal amount, then, for purposes of calculating the total dollar amount of all securities issued under this prospectus, we will treat the initial offering price of the debt securities as the total original principal amount of the debt securities. Each time we or any selling securityholder offer securities under this prospectus, we will provide offerees with a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities being offered, including, to the extent applicable:

designation or classification;

aggregate principal amount or aggregate offering price;

maturity, if applicable;

original issue discount, if any;

rates and times of payment of interest or dividends, if any;

conversion or exchange prices or rates, if any, and if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;

ranking;

restrictive covenants, if any;

voting or other rights, if any; and

important United States federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a

part.

We or any selling securityholder may sell the securities to or through underwriters, dealers or agents or directly to purchasers or as otherwise set forth below under Plan of Distribution. We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Each prospectus supplement will set forth the names of any underwriters, dealers, agents or other entities involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them, details regarding any over-allotment option granted to them, and net proceeds to us. The following is a summary of the securities that we may offer with this prospectus.

For the complete terms of our common stock and preferred stock, please refer to our articles of incorporation and bylaws that are incorporated by reference into the registration statement of which this prospectus is a part or may be incorporated by reference in this prospectus or any applicable prospectus supplement. The summary below and that contained in any applicable prospectus supplement or any related free writing prospectus are qualified in their entirety by reference to our articles of incorporation and bylaws, as in effect at the time of any offering of securities under this prospectus.

Table of Contents

COMMON STOCK

We are authorized to issue 50,000,000 shares of common stock, par value \$0.0001 per share, of which 41,311,512 shares were issued and outstanding as of the date of this prospectus. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a majority of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that is outstanding at the time of the dividend. In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. All shares of common stock will, when issued, be duly authorized, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to the rights of the holders of shares of any series of preferred stock that the Company may designate and issue in the future.

PREFERRED STOCK

We are authorized to issue up to 3,333,333 shares of preferred stock, par value \$0.0001 per share, of which no shares are issued and outstanding as of the date of this prospectus, in one or more series. Our board of directors may, without further action by our stockholders, from time to time, direct the issuance of shares of preferred stock in one or more series and may, at the time of issuance, determine the rights, preferences and limitations of each series, including voting rights, dividend rights and redemption and liquidation preferences. Satisfaction of any dividend preferences of outstanding shares of our preferred stock would reduce the amount of funds available for the payment of dividends on shares of our common stock. Holders of shares of our preferred stock may be entitled to receive a preference payment in the event of any liquidation, dissolution or winding-up of our Company before any payment is made to the holders of shares of our common stock. In some circumstances, the issuance of shares of preferred stock may render more difficult or tend to discourage a merger, tender offer or proxy contest, the assumption of control by a holder of a large block of our securities or the removal of incumbent management. The issuance of preferred stock with voting and conversion rights could adversely affect the voting power of holders of common stock and reduce the likelihood that holders of shares of our common stock will receive dividend payments and payments upon liquidation.

If we offer a specific class or series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

the title and stated value;

the number of shares offered, the liquidation preference per share and the purchase price;

the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

the provisions for redemption, if applicable;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated) and exchange period;

Table of Contents

voting rights, if any, of the preferred stock;

a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of the Company; and

any material limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the Company.

The preferred stock offered by this prospectus, when issued, will not have, or be subject to, any preemptive or similar rights.

Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law

Certain provisions of Delaware law, our certificate of incorporation and our bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, encourage persons seeking to acquire control of us to first negotiate with our board of directors and the holders of our capital stock.

Delaware Law

We are subject to Section 203 of the Delaware General Corporation Law. This statute regulating corporate takeovers prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for three years following the date that the stockholder became an interested stockholder, unless:

prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

upon completion of the transaction that resulted in the interested stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (a) shares owned by persons who are directors and also officers, and (b) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is any person who, together with such person's affiliates and associates (i) owns 15% or more of a corporation's voting securities or (ii) is an affiliate or associate of a corporation and was the owner of 15% or more of the corporation's voting securities at any time within the three year period immediately preceding a business combination of the corporation governed by Section 203. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may discourage takeover attempts that might result in a premium over the market price for the shares of common stock held by our stockholders.

Staggered board of directors

Our certificate of incorporation and our bylaws divide our board of directors into two classes with staggered two-year terms, when the board is comprised of more than six members. Seven individuals currently serve on our

Table of Contents

board of directors, which is divided into two classes. At each annual meeting of stockholders, a class of directors is to be elected for a two-year term to succeed the directors of the same class whose terms are then expiring. As a result, a portion of our board of directors will be elected each year. Our bylaws authorize our board of directors to fix the number of directors from time to time by a resolution of the majority of our board of directors, provided the board shall consist of a minimum of one and a maximum of seven members. The division of our board of directors into two classes with staggered two-year terms may delay or prevent a change of our management or a change in control. Between stockholder meetings, directors may be removed by a vote of a majority of the voting power of all outstanding shares of voting stock only for cause, and the board of directors may appoint new directors to fill the vacancies. Under our certificate of incorporation and bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office unless our board of directors determines by resolution that any such vacancies or newly created directorships shall be filled by the stockholders. These provisions may prevent a stockholder from removing incumbent directors and simultaneously gaining control of the board of directors by filling the resulting vacancies with its own nominees. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder action; special meeting of stockholders; advance notice requirements for stockholder proposals and director nominations

Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our president or our board of directors, or by our president at the request of holders of not less than one-tenth of all outstanding shares of capital stock. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-majority voting

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Certain provisions of our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 66 2/3% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 66 2/3% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Transfer Agent

The transfer agent for our common stock is Computershare Trust Company, N.A.

Table of Contents

Listing

Our common stock is quoted on The NASDAQ Global Select Market under the trading symbol SRPT.

DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series. The senior debt securities and the subordinated debt securities are together referred to in this prospectus as the debt securities. We may issue debt securities under an indenture to be entered between us and a trustee. The indenture does not limit the amount of securities that may be issued under it and provides that debt securities may be issued in one or more securities. Our board of directors or a committee designated by the board will determine the terms of the debt securities being offered. This prospectus contains only general terms and provisions of the debt securities. The applicable prospectus supplement will describe the particular terms of the debt securities offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the debt securities being offered, as well as the complete indenture that contains the terms of the debt securities. The form of indenture has been filed as an exhibit to the registration statement of which this prospectus is a part, and any supplemental indenture or forms of debt securities containing the terms of debt securities we offer under this prospectus will be filed as an exhibit to the registration statement of which this prospectus is a part, or will be incorporated by reference from another report that we file with the SEC.

The debt securities will be issued under an indenture between us and a trustee. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

the title and ranking of the debt securities (including the terms of any subordination provisions);

the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;

any limit on the aggregate principal amount of the debt securities;

Table of Contents

the date or dates on which the principal of the securities of the series is payable;

the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;

the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;

the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;

the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;

the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;

whether the debt securities will be issued in the form of certificated debt securities or global debt securities;

the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;

the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;

the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;

if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index or financial index;

any provisions relating to any security provided for the debt securities;

any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;

any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;

any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;

Table of Contents

the provisions, if any, relating to conversion or exchange of any securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange; and

any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depository, or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a book-entry debt security), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a certificated debt security) as set forth in the applicable prospectus supplement. Except as set forth under the heading Global Debt Securities and Book-Entry System below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see Global Securities.

Global Securities

The debt securities of any series may be represented, in whole or in part, by one or more global securities. Each global security will:

be registered in the name of a depositary, or its nominee, that we will identify in a prospectus supplement;

be deposited with the depositary or nominee or custodian; and

Table of Contents

bear any required legends.

No global security may be exchanged in whole or in part for debt securities registered in the name of any person other than the depositary or any nominee unless:

the depositary has notified us that it is unwilling or unable to continue as depositary or has ceased to be qualified to act as depositary;

an event of default is continuing with respect to the debt securities of the applicable series; or

any other circumstance described in a prospectus supplement has occurred permitting or requiring the issuance of any such security.

As long as the depositary, or its nominee, is the registered owner of a global security, the depositary or nominee will be considered the sole owner and holder of the debt securities represented by the global security for all purposes under the indentures. Except in the above limited circumstances, owners of beneficial interests in a global security will not be:

entitled to have the debt securities registered in their names;

entitled to physical delivery of certificated debt securities; or

considered to be holders of those debt securities under the indenture.

Payments on a global security will be made to the depositary or its nominee as the holder of the global security. Some jurisdictions have laws that require that certain purchasers of securities take physical delivery of such securities in definitive form. These laws may impair the ability to transfer beneficial interests in a global security.

Institutions that have accounts with the depositary or its nominee are referred to as participants. Ownership of beneficial interests in a global security will be limited to participants and to persons that may hold beneficial interests through participants. The depositary will credit, on its book-entry registration and transfer system, the respective principal amounts of debt securities represented by the global security to the accounts of its participants.

Ownership of beneficial interests in a global security will be shown on and effected through records maintained by the depositary, with respect to participants' interests, or any participant, with respect to interests of persons held by participants on their behalf.

Payments, transfers and exchanges relating to beneficial interests in a global security will be subject to policies and procedures of the depositary. The depositary policies and procedures may change from time to time. Neither any trustee nor we will have any responsibility or liability for the depositary's or any participant's records with respect to beneficial interests in a global security.

Payment and Paying Agents

Unless otherwise indicated in a prospectus supplement, the provisions described in this paragraph will apply to the debt securities. Payment of interest on a debt security on any interest payment date will be made to the person in whose name the debt security is registered at the close of business on the regular record date. Payment on debt securities of a particular series will be payable at the office of a paying agent or paying agents designated by us. However, at our option, we may pay interest by mailing a check to the record holder. The trustee will be designated as our initial paying agent.

We may also name any other paying agents in a prospectus supplement. We may designate additional paying agents, change paying agents or change the office of any paying agent. However, we will be required to maintain a paying agent in each place of payment for the debt securities of a particular series.

Table of Contents

All moneys paid by us to a paying agent for payment on any debt security that remain unclaimed for a period ending the earlier of:

10 business days prior to the date the money would be turned over to the applicable state; or

at the end of two years after such payment was due, will be repaid to us. Thereafter, the holder may look only to us for such payment.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection In the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a successor person) unless:

we are the surviving corporation or the successor person (if other than Sarepta Therapeutics) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and

immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

Event of Default means with respect to any series of debt securities, any of the following:

default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);

default in the payment of principal of any security of that series at its maturity;

default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or we and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;

certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of our company; and

any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

Table of Contents

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee will be under no obligation to exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in exercising such right of power. (Section 7.1(e)) Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and

the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered reasonable indemnity or security, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the

Table of Contents

trustee shall mail to each Securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify and amend the indenture or the debt securities of any series without the consent of any holder of any debt security:

to cure any ambiguity, defect or inconsistency;

to comply with covenants in the indenture described above under the heading Consolidation, Merger and Sale of Assets ;

to provide for uncertificated securities in addition to or in place of certificated securities;

to make any change that does not adversely affect the rights of any holder of debt securities;

to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;

to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or

to comply with requirements of the Commission in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;

reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;

reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;

reduce the principal amount of discount securities payable upon acceleration of maturity;

waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);

make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;

make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or

waive a redemption payment with respect to any debt security. (Section 9.3)

Table of Contents

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

we may omit to comply with the covenant described under the heading Consolidation, Merger and Sale of Assets and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and

any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (covenant defeasance).

The conditions include:

depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and

delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result

Table of Contents

of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

Covenant Defeasance and Events of Default. In the event we exercise our option to effect covenant defeasance with respect to any series of debt securities and the debt securities of that series are declared due and payable because of the occurrence of any Event of Default, the amount of money and/or U.S. government obligations or foreign government obligations on deposit with the trustee will be sufficient to pay amounts due on the debt securities of that series at the time of their stated maturity but may not be sufficient to pay amounts due on the debt securities of that series at the time of the acceleration resulting from the Event of Default. However, we shall remain liable for those payments. (Section 8.4)

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York without regard to conflict of law principles that would result in the application of any law other than the laws of the State of New York. (Section 10.10)

WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. Our board of directors or a committee designated by the board will determine the terms of the warrants. This prospectus contains only general terms and provisions of the warrants. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Specific warrant agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each warrant agreement relating to warrants offered under this prospectus.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;

the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;

the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;

the date on which the right to exercise the warrants will commence and the date on which the right will expire;

United States federal income tax consequences applicable to the warrants; and

any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Table of Contents

Holders of equity warrants will not be entitled:

to vote, consent or receive dividends;

receive notice as shareholders with respect to any meeting of shareholders for the election of our directors or any other matter; or

exercise any rights as shareholders of Sarepta Therapeutics, Inc.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

UNITS

We may issue units consisting of our common stock or preferred stock, debt securities and/or warrants to purchase any of these securities in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

the title of the series of units;

identification and description of the separate constituent securities comprising the units;

the price or prices at which the units will be issued;

the date, if any, on and after which the constituent securities comprising the units will be separately transferable;

a discussion of certain United States federal income tax considerations applicable to the units; and

any other terms of the units and their constituent securities.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities offered through this prospectus (i) to or through underwriters or dealers, (ii) directly to purchasers, including our affiliates, (iii) through agents, or (iv) through a combination of any these methods. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices. The prospectus supplement will include the following information:

the terms of the offering;

the names of any underwriters or agents;

the name or names of any managing underwriter or underwriters;

the purchase price of the securities;

the net proceeds from the sale of the securities;

any delayed delivery arrangements;

any underwriting discounts, commissions or agency fees and other items constituting underwriters or agents compensation;

any initial public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any commissions paid to agents.

We may engage in at-the-market offerings into an existing trading market in accordance with Rule 415(a)(4). Any at-the-market offering will be through an underwriter or underwriters acting as principal or agent for us.

We may issue to the holders of our common stock on a pro rata basis for no consideration, subscription rights to purchase shares of our common stock or preferred stock. These subscription rights may or may not be transferable by shareholders. The applicable prospectus supplement will describe the specific terms of any offering of our common or preferred stock through the issuance of subscription rights, including the terms of the subscription rights offering, the terms, procedures and limitations relating to the exchange and exercise of the subscription rights and, if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering

of common or preferred stock through the issuance of subscription rights.

Sale Through Underwriters or Dealers

If underwriters are used in the sale, the underwriters will acquire the securities for their own account, including through underwriting, purchase, security lending or repurchase agreements with us. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions. Underwriters may sell the securities in order to facilitate transactions in any of our other securities (described in this prospectus or otherwise), including other public or private transactions and short sales. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise indicated in the prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all the offered securities if they purchase any of them. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers.

Table of Contents

If dealers are used in the sale of securities offered through this prospectus, we will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale. The prospectus supplement will include the names of the dealers and the terms of the transaction.

Direct Sales and Sales Through Agents

We may sell the securities offered through this prospectus directly. In this case, no underwriters or agents would be involved. Such securities may also be sold through agents designated from time to time. The prospectus supplement will name any agent involved in the offer or sale of the offered securities and will describe any commissions payable to the agent. Unless otherwise indicated in the prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

We may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. The terms of any such sales will be described in the prospectus supplement.

Delayed Delivery Contracts

If the prospectus supplement indicates, we may authorize agents, underwriters or dealers to solicit offers from certain types of institutions to purchase securities at the public offering price under delayed delivery contracts. These contracts would provide for payment and delivery on a specified date in the future. The contracts would be subject only to those conditions described in the prospectus supplement. The applicable prospectus supplement will describe the commission payable for solicitation of those contracts.

Market Making, Stabilization and Other Transactions

Unless the applicable prospectus supplement states otherwise, each series of offered securities will be a new issue and will have no established trading market. We may elect to list any series of offered securities on an exchange. Any underwriters that we use in the sale of offered securities may make a market in such securities, but may discontinue such market making at any time without notice. Therefore, we cannot assure you that the securities will have a liquid trading market.

Any underwriter may also engage in stabilizing transactions, syndicate covering transactions and penalty bids in accordance with Rule 104 under the Securities Exchange Act. Stabilizing transactions involve bids to purchase the underlying security in the open market for the purpose of pegging, fixing or maintaining the price of the securities. Syndicate covering transactions involve purchases of the securities in the open market after the distribution has been completed in order to cover syndicate short positions.

Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the securities to be higher than it would be in the absence of the transactions. The underwriters may, if they commence these transactions, discontinue them at any time.

Derivative Transactions and Hedging

We, the underwriters or other agents may engage in derivative transactions involving the securities. These derivatives may consist of short sale transactions and other hedging activities. The underwriters or agents may acquire a long or

short position in the securities, hold or resell securities acquired and purchase options or futures on the securities and other derivative instruments with returns linked to or related to changes in the price of the securities. In order to facilitate these derivative transactions, we may enter into security lending or repurchase agreements with the underwriters or agents. The underwriters or agents may effect the derivative transactions

Table of Contents

through sales of the securities to the public, including short sales, or by lending the securities in order to facilitate short sale transactions by others. The underwriters or agents may also use the securities purchased or borrowed from us or others (or, in the case of derivatives, securities received from us in settlement of those derivatives) to directly or indirectly settle sales of the securities or close out any related open borrowings of the securities.

Electronic Auctions

We may also make sales through the Internet or through other electronic means. Since we may from time to time elect to offer securities directly to the public, with or without the involvement of agents, underwriters or dealers, utilizing the Internet or other forms of electronic bidding or ordering systems for the pricing and allocation of such securities, you will want to pay particular attention to the description of that system we will provide in a prospectus supplement.

Such electronic system may allow bidders to directly participate, through electronic access to an auction site, by submitting conditional offers to buy that are subject to acceptance by us, and which may directly affect the price or other terms and conditions at which such securities are sold. These bidding or ordering systems may present to each bidder, on a so-called real-time basis, relevant information to assist in making a bid, such as the clearing spread at which the offering would be sold, based on the bids submitted, and whether a bidder's individual bids would be accepted, prorated or rejected. For example, in the case of debt security, the clearing spread could be indicated as a number of basis points above an index treasury note. Of course, many pricing methods can and may also be used.

Upon completion of such an electronic auction process, securities will be allocated based on prices bid, terms of bid or other factors. The final offering price at which securities would be sold and the allocation of securities among bidders would be based in whole or in part on the results of the Internet or other electronic bidding process or auction.

General Information

Agents, underwriters, and dealers may be entitled, under agreements entered into with us, to indemnification by us against certain liabilities, including liabilities under the Securities Act. Our agents, underwriters, and dealers, or their affiliates, may be customers of, engage in transactions with or perform services for us, in the ordinary course of business.

Table of Contents

LEGAL MATTERS

Ropes & Gray LLP, Boston, Massachusetts will provide us with an opinion as to certain legal matters in connection with the securities being offered hereby. Additional legal matters may be passed on for us, or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Sarepta Therapeutics, Inc. and subsidiaries as of December 31, 2014 and 2013, and for each of the years in the three-year period ended December 31, 2014, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2014 have been incorporated by reference herein in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge on our website at <http://www.sarepta.com> under the Investor Relations SEC Filings caption. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on our website is not part of this prospectus.

Table of Contents

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. We incorporate by reference the following information or documents that we have filed with the SEC (excluding those portions of any Form 8-K that are not deemed filed pursuant to the General Instructions of Form 8-K):

our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 (including the portions of our proxy statement for our 2015 annual meeting of shareowners incorporated by reference therein), filed with the SEC on February 26, 2015; and

the description of our common stock contained in our Current Report on Form 8-K12B filed with the SEC on June 6, 2013.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

Any statement contained in any document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any prospectus supplement modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, a copy of any or all documents that are incorporated by reference into this prospectus, but not delivered with the prospectus, other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus incorporates. You should direct written requests to: Sarepta Therapeutics, Inc., 215 First Street, Suite 415, Cambridge, MA 02142, or you may call us at (617) 274-4080.

Table of Contents

**DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT
LIABILITIES**

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers or controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable. If a claim for indemnification against such liabilities (other than the payment by us of expenses incurred or paid by a director or officer of our company in the successful defense of the action, suit or proceeding) is asserted by a director or officer in connection with securities which may have been registered, we will, unless in the opinion of our counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by us is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issues.

Table of Contents

\$125,000,000

Common Stock

Prospectus Supplement

Credit Suisse

Morgan Stanley

October , 2015