

Sarepta Therapeutics, Inc.
Form 424B5
March 05, 2019
Table of Contents

**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-229934**

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

Subject to completion, dated March 5, 2019

Prospectus Supplement

(To Prospectus dated February 28, 2019)

\$350,000,000

Sarepta Therapeutics, Inc.

Common Stock

We are offering \$350 million of shares of our common stock in this offering.

Our common stock is listed on the Nasdaq Global Select Market under the symbol SRPT. On March 4, 2019, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$145.48 per share.

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

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-7 of this prospectus supplement, page 4 of the accompanying prospectus and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

We have granted the underwriters an option to purchase up to \$52.5 million 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 \$ and the total proceeds, before expenses, to us will be \$.

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 , 2019.

Goldman Sachs & Co. LLC

The date of this prospectus supplement is , 2019.

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-6
<u>RISK FACTORS</u>	S-7
<u>FORWARD-LOOKING STATEMENTS</u>	S-9
<u>USE OF PROCEEDS</u>	S-12
<u>MATERIAL U.S. FEDERAL TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK</u>	S-13
<u>DILUTION</u>	S-17
<u>UNDERWRITING</u>	S-18
<u>LEGAL MATTERS</u>	S-23
<u>EXPERTS</u>	S-23
<u>WHERE YOU CAN FIND ADDITIONAL INFORMATION</u>	S-23
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	S-23

ACCOMPANYING PROSPECTUS

	Page
<u>ABOUT THIS PROSPECTUS</u>	1
<u>THE COMPANY</u>	2
<u>RISK FACTORS</u>	4
<u>FORWARD-LOOKING STATEMENTS</u>	4
<u>USE OF PROCEEDS</u>	5
<u>GENERAL DESCRIPTION OF SECURITIES WE MAY SELL</u>	6
<u>PLAN OF DISTRIBUTION</u>	21
<u>LEGAL MATTERS</u>	24
<u>EXPERTS</u>	24
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	24
<u>INFORMATION INCORPORATED BY REFERENCE</u>	24

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**. 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 filed before the date of this prospectus supplement, 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-7 of this prospectus supplement, the financial statements and related notes, and the other information that we incorporate by reference herein, including Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2018.

Sarepta Therapeutics, Inc.

Overview

We are a commercial-stage biopharmaceutical company focused on helping patients through the discovery and development of unique RNA-targeted therapeutics, gene therapy and other genetic therapeutic modalities for the treatment of rare diseases. Applying our proprietary, highly-differentiated and innovative technologies, and through collaborations with our strategic partners, we are developing potential therapeutic candidates for a broad range of diseases and disorders, including Duchenne muscular dystrophy (DMD), Limb-girdle muscular dystrophies (LGMDs), Mucopolysaccharidosis type IIIA (MPS IIIA) and Pompe.

Our Commercial Product

Our first commercial product in the U.S., EXONDYS 51[®] (eteplirsen) Injection (EXONDYS 51), was granted accelerated approval by the United States Food and Drug Administration (FDA) on September 19, 2016. EXONDYS 51 is indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. EXONDYS 51 uses our phosphorodiamidate morpholino oligomer (PMO) chemistry and exon-skipping technology to skip exon 51 of the dystrophin gene. Exon skipping is intended to promote the production of an internally truncated but functional dystrophin protein. We are in the process of assessing and conducting various EXONDYS 51 clinical trials, including studies that are required to comply with regulatory New Drug Applications (NDA) and studies we need to conduct to comply with our post-marketing FDA requirements/commitments to verify and describe the clinical benefit of EXONDYS 51.

EXONDYS 51 targets the most frequent series of mutations that cause DMD. Approximately 13% of DMD patients are amenable to exon 51 skipping. For the years ended December 31, 2018, 2017 and 2016, we recorded net revenue of \$301.0 million, \$154.6 million and \$5.4 million, respectively, related to the sale of EXONDYS 51.

Our Pipeline

A summary description of our main product candidates, including those in collaboration with our strategic partners, is as follows:

Golodirsen (SRP-4053) uses our PMO chemistry and exon-skipping technology to skip exon 53 of the DMD gene. Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA, resulting in exclusion, or skipping, of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping.

S-1

Table of Contents

We are enrolling and dosing patients in ESSENCE (4045-301), our Phase 3 placebo controlled confirmatory trial in patients who have a confirmed mutation of the DMD gene that is amenable to exon 45 or 53 skipping using casimersen and golodirsen, respectively. Golodirsen is also being evaluated in a Phase 1/2 trial having two parts. Part I of the Phase 1/2 trial has been completed, and Part II, an open-label portion of the trial, is expected to be completed in 2019 (Study 4053-101). In September 2017, we announced positive results of an analysis that included biopsies of the bicep muscle at baseline and on-treatment at the Part II, Week 48 time point. The 4053-101 interim trial results demonstrated statistical significance on all primary and secondary biological endpoints.

In December 2018, we completed the submission of our rolling NDA to the FDA seeking accelerated approval for golodirsen. The FDA accepted the NDA and granted priority review status for golodirsen with a targeted regulatory action date of August 19, 2019. The FDA also indicated that it does not intend to conduct an advisory board for golodirsen.

Casimersen (SRP-4045) uses our PMO chemistry and exon-skipping technology to skip exon 45 of the DMD gene. Casimersen is designed to bind to exon 45 of dystrophin pre-mRNA, resulting in exclusion, or skipping, of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 45 skipping. We are enrolling and dosing patients in ESSENCE, further described above. We have completed a dose titration portion (Phase 1) and the open-label portion (Phase 2) of a Sarepta sponsored Phase 1/2 clinical trial studying casimersen (4045-101). We anticipate submitting an NDA to the FDA for casimersen in 2019 if we believe the results of an interim dystrophin analysis in the ESSENCE study are positive.

SRP-5051 uses our next-generation chemistry platform, cell-penetrating peptide-conjugated PMO (PPMO), and our exon-skipping technology to skip exon 51 of the dystrophin gene. The PPMO technology features covalent attachment of a cell-penetrating peptide to a PMO with the goal of enhanced delivery into the cell. In pre-clinical research, our proprietary class of PPMO compounds demonstrated an increase in dystrophin production and a more durable response compared to PMO. In addition, PPMO treatment in non-human primates results in high levels of exon-skipping in skeletal, cardiac and smooth muscle tissues. Pre-clinical trials also indicate that PPMOs may require less frequent dosing than PMOs, and that PPMOs could potentially be tailored to reach other organs beyond muscle.

In the fourth quarter of 2017, we received clearance from the FDA and commenced a first-in-human, single ascending dose, trial for the treatment of DMD using SRP-5051 in patients who are amenable to exon 51 skipping. We expect to complete this trial in 2019.

SRP-9001 (micro-dystrophin gene therapy program), in collaboration with Nationwide Children's Hospital (Nationwide), aims to express micro-dystrophin a smaller but still functional version of dystrophin. A unique, engineered micro-dystrophin is used because naturally-occurring dystrophin is too large to fit in an adeno-associated virus (AAV) vector. SRP-9001, developed in collaboration with Nationwide, employs the AAVrh74 vector, which is designed to be systemically and robustly delivered to skeletal, diaphragm and cardiac muscle without promiscuously crossing the blood brain barrier, which we believe makes it a strong candidate to treat peripheral neuromuscular diseases. An MHCK7 promoter was chosen for its ability to robustly express in the heart, which is critically important for patients with DMD, who typically die from pulmonary or cardiac complications. Lastly, the transgene was designed to maintain spectrin-like repeats 2 and 3, which has been reported to be critical to maintaining muscle force.

In the fourth quarter of 2017, an investigational new drug (IND) application for the micro-dystrophin gene therapy program, in collaboration with Nationwide, was cleared by the FDA, and a Phase 1/2a clinical trial in individuals with DMD was initiated. On October 3, 2018, Nationwide presented what we believe to be positive updated results from the Phase 1/2a clinical trial in four individuals with DMD enrolled in the trial. In the

S-2

Table of Contents

fourth quarter of 2018, we commenced a placebo-controlled trial with the goal to establish the functional benefits of micro-dystrophin expressions. We plan to conduct a confirmatory trial using commercial supply of SRP-9001 by the end of 2019, pending regulatory feedback.

MYO-101. We are collaborating with Myonex Therapeutics, Inc. (Myonex) to develop gene therapy programs for various types of LGMDs. All the Myonex programs use the AAVrh.74 vector, the same vector used in the micro-dystrophin gene therapy program, to transfect a restorative gene. The most advanced of Myonex product candidates, MYO-101, aims to treat LGMD2E, also known as beta-sarcoglycanopathy, a severe and debilitating form of LGMD characterized by progressive muscle fiber loss, inflammation and muscle fiber replacement with fat and fibrotic tissue. MYO-101 is designed to transfect a gene that codes for and restores beta-sarcoglycan protein with the goal of restoring the dystroglycan complex. MYO-101 has generated positive pre-clinical safety and efficacy data utilizing the AAVrh.74 vector. Myonex commenced a Phase 1/2a trial of MYO-101 in the fourth quarter of 2018, and on February 27, 2019, we announced positive two-month data from the first three-patient cohort dosed in the MYO-101 trial.

GALGT2. An additional gene therapy program for DMD and other muscular dystrophies, also in collaboration with Nationwide, aims to express the enzyme GALGT2 from an AAV vector. We believe that GALGT2 modifies the dystrophin associated protein complex (DAPC) and up-regulates utrophin (a protein significantly homologous to dystrophin) to protect muscle from damage in the absence of dystrophin. We believe that the micro-dystrophin and GALGT2 technologies have the potential to treat all or nearly all DMD patients regardless of mutation.

In the fourth quarter of 2017, an IND application for GALGT2 was cleared by the FDA, and a Phase 1/2a clinical trial testing GALGT2 for the treatment of DMD was initiated.

LYS-SAF 302. We are collaborating with Lysogene S.A. (Lysogene) to develop a gene therapy, LYS-SAF302, to treat MPS IIIA. LYS-SAF302 is an AAV-mediated gene therapy, the goal of which is to replace the faulty N-sulfoglucosamine sulfohydrolase (SGSH) gene with a healthy copy of the gene. LYS-SAF302 employs the AAVrh10 virus, chosen for its ability to target the central nervous system (CNS). Proof-of-concept was established in MPS IIIA pre-clinical models demonstrating strong expression, broad distribution and the ability of the compound to correct lysosomal storage defects by producing the missing enzyme. Safety data from an IND-enabling toxicity and a biodistribution Good Laboratory Practice trial showed that, at any dose level evaluated, LYS-SAF302 was not associated with unexpected mortality, change in clinical signs, body weight, behavior or macroscopic findings in the brain.

The first patient has been dosed in AAVance, a global Phase 2/3 clinical trial of LYS-SAF302, aiming at evaluating the effectiveness of a one-time delivery of a AAVrh10 virus carrying the N-SGSH gene.

Neurotrophin 3 (CMT Type 1A). A gene therapy program in collaboration with Nationwide that aims to express neurotrophin 3 (NT-3) encoding the NTF3 gene to treat Charcot-Marie-Tooth (CMT) neuropathies, including CMT type 1A. We believe that the delivery of NT-3 may have applicability to other sub-types of CMT in addition to other neuropathies and muscle-wasting diseases. Pre-clinical research has shown the ability of the NT-3 gene construct to regenerate nerves. Further pre-clinical research is under way to explore its potential. A clinical trial to test NT-3 gene therapy is planned to commence dosing in 2019 for CMT type 1A, pending regulatory feedback. We believe that the delivery of NT-3 may have applicability to other sub-types of CMT in addition to other muscle-wasting diseases.

Programs in Collaboration with Lacerta. Our collaboration with Lacerta Therapeutics, Inc. (Lacerta) utilizes proprietary AAV capsid variants and a scalable vector manufacturing platform to develop treatments for CNS and lysosomal storage diseases. The lead candidate, still in discovery phase, is a gene therapy approach with a novel AAV

variant for the treatment of Pompe disease.

S-3

Table of Contents

CRISPR/Cas9. We are exploring, in collaboration with Duke University, the gene-editing technology CRISPR/Cas9 that aims to restore dystrophin expression by removing or excising exons directly from the dystrophin gene to correct out-of-frame mutations. CRISPR/Cas9 technology can also potentially be used to fix stop codon mutations in the dystrophin gene so that dystrophin can be translated to a function protein. This program is in the discovery phase.

The chart below summarized the status of our more advanced programs, including those with our strategic partners:

Our pipeline includes 25 programs at various stages of pre-clinical and clinical development, reflecting our aspiration to apply our multifaceted approach and expertise in precision genetic medicine to make a profound difference in the lives of patients suffering from rare diseases.

Manufacturing

We have developed proprietary state-of-the-art Chemistry, Manufacturing and Controls (CMC) and manufacturing capabilities that allow synthesis and purification of our product candidates to support both clinical development as well as commercialization. Our current main focus in manufacturing is to continue scaling up production of our PMO-based therapies and optimizing manufacturing for PPMO and gene therapy-based product candidates. We have entered into certain manufacturing and supply arrangements with third-party suppliers which will in part utilize these capabilities to support production of certain of our product candidates and their components. In 2017, we opened a facility in Andover, Massachusetts, which significantly enhances our research and development manufacturing capabilities. However, we currently do not have internal large scale Good Manufacturing Practices (GMP) manufacturing capabilities to produce our product and product candidates for commercial and/or clinical use. For our current and future manufacturing needs, we have entered

Table of Contents

into supply agreements with specialized contract manufacturing organizations (each a CMO) to produce custom raw materials, the active pharmaceutical Ingredients and finished goods for our product candidates. All of our CMO partners have extensive technical expertise, GMP experience and experience manufacturing our specific technology.

Corporate Information

We were originally incorporated in the State of Oregon on July 22, 1980 and, on June 6, 2013, we reincorporated in the State of Delaware. 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.

S-5

Table of Contents

THE OFFERING

Common stock offered by us	\$350 million of shares of our common stock.
Option to purchase additional shares of common stock	We have granted the underwriters an option to purchase up to \$52.5 million of additional shares from us within 30 days of the date of this prospectus supplement.
Common stock to be outstanding immediately after this offering	shares (or shares if the underwriters exercise in full their option to purchase additional shares)
Use of proceeds	We intend to use the net proceeds from this offering principally for the continuation and initiation of further clinical trials, commercialization, manufacturing, business development activities, including the potential licensing or acquisition of complementary products, technologies and entities, and other general corporate purposes. Please see Use of Proceeds .
Risk factors	You should read carefully the information set forth under Risk Factors herein and in our Annual Report on Form 10-K for a discussion of factors that you should consider before deciding to invest in our common stock.
Nasdaq Global Select Market symbol	SRPT
The number of shares of our common stock to be outstanding immediately after this offering as shown above is based on 71,071,887 shares outstanding as of December 31, 2018. This number of shares excludes the following:	

8,391,171 shares of our common stock issuable upon the exercise of stock options outstanding under our 2002 Equity Incentive Plan, our Amended and Restated 2011 Equity Incentive Plan (2011 Equity Incentive Plan), our 2014 Employment Commencement Incentive Plan (2014 Equity Incentive Plan) and our 2018 Equity Incentive Plan;

251,298 shares of restricted stock units issuable upon vesting under our 2011 Equity Incentive Plan, our 2014 Equity Incentive Plan and our 2018 Equity Incentive Plan;

100,000 shares subject to stock appreciation rights under our 2011 Equity Incentive Plan;

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850,390 shares of our common stock available for future issuance under our 2014 Equity Incentive Plan;

163,266 shares of our common stock available for future issuance under our 2013 Employee Stock Purchase Plan; and

4,412,446 shares of our common stock available for future issuance under our 2018 Equity Incentive Plan.

S-6

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 as well as other information in this prospectus supplement and the documents incorporated by reference herein before deciding whether to invest in our securities. See **Where You Can Find Additional Information**. The risks and uncertainties described below and incorporated by reference herein are not the only ones we face. If any such risks actually occur, 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 and in the documents incorporated by reference herein as a result of different factors, including the risks we face described below and in the documents incorporated by reference herein. Other events that we do not currently anticipate or that we currently deem immaterial also affect our results of operations and financial condition.*

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 principally for the continuation and initiation of clinical trials, commercialization, manufacturing, business development activities including the potential licensing or acquisition of complementary products and technologies 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, particularly sales by our directors, executive officers and significant stockholders, or the perception that these sales could occur, could cause the market price of our common stock to decline and may make it more difficult for you to sell your common stock at a time and price that you deem appropriate. 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.

We and our executive officers and directors have entered into lock-up agreements with the underwriters under which we and they have agreed, subject to specified exceptions, not to sell, directly or indirectly, any shares of common stock without the permission of the underwriters for a period of 60 days and 30 days, respectively, following the date of this prospectus. We refer to such period as the lock-up period. The specified exceptions include allowing our officers and directors to sell shares of common stock pursuant to existing Rule 10b5-1 trading plans. When the lock-up period expires, we and our directors and officers subject to a lock-up agreement will be able to sell our shares in the public market. In addition, the underwriters may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements at any time and for any reason. Sales of a substantial number of such shares upon expiration of the lock-up agreements, the perception that such sales may occur, or early release of these agreements, could cause our market price to fall or make it more difficult for you to sell your common stock at a time and price

that you deem appropriate.

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

S-7

Table of Contents

the common stock you purchase in this offering. Based on a net tangible book value of our common stock of \$14.36 per share as of December 31, 2018, if you purchase shares of common stock in this offering at the public offering price of \$ per share, 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 carry-forwards 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, which transaction may include this offering, may result in material additional limitations on our ability to use our net operating loss and tax credit carry-forwards.

As of December 31, 2018, we had U.S. federal and state net operating loss (NOL) carry-forwards of \$438.5 million and \$503.3 million, respectively, available to reduce future taxable income, which expire between 2019 and 2038. 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 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 carry-forwards will be subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended (the Code), and similar state laws. Such limitations may result in expiration of a portion of the NOL carry-forwards incurred prior to 2018 before utilization and may be substantial. We may 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. If such change has occurred or does occur, the tax benefits related to the NOL carry-forwards may be limited or lost. Under the Tax Cuts and Jobs Act, NOLs generated after December 31, 2017 will not be subject to expiration. In addition, the deduction for NOLs in any taxable year is limited to 80% of current year taxable year income in respect of NOLs generated during or after 2018.

Table of Contents

FORWARD-LOOKING STATEMENTS

This prospectus supplement 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, potent similar expressions, as 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 belief that our proprietary technology platforms and collaborations can be used to develop novel pharmaceutical products to treat a broad range of diseases and address key currently unmet medical needs;

our intention to leverage our technology platforms, organizational capabilities, collaborations and resources to lead the field of precision genetic medicines, including the treatment of rare, neuromuscular and other diseases, with a diversified portfolio of product candidates;

our intention to focus on building our gene therapy engine, advancing the development of and potentially commercialize additional exon-skipping product candidates, investing in our next-generation precision medicine, ensuring appropriate capitalization and nurturing our culture;

our expectations regarding the continued growth of our business operations due, in part, to the commercialization of EXONDYS 51;

our technologies and programs, including those with strategic partners, and their respective potential benefits, including our PMO based compounds potential to be designed to create more, less, or none of certain proteins, or produce analogues of endogenous proteins; the potential of our PPMO to be tailored to reach other organs beyond muscle and result in enhanced delivery into the cell with less frequent dosing than PMOs; the benefits of the unique design of the AAVrh74 vector, the MHCK7 promoter and the transgene, our belief that GALGT2 modifies the dystrophin associated protein complex and up-regulates utrophin to protect muscle from damage in the absence of dystrophin; and the potential of micro-dystrophin and GALGT2 to treat all or nearly all DMD patients regardless of mutation;

our belief that our partnerships with manufacturers will provide us access to additional commercial manufacturing capacity for our micro-dystrophin DMD gene therapy program, as well as a manufacturing platform for future gene therapy programs, and our belief that our current network of manufacturing partners are able to fulfil the requirements of our commercial plan;

our plan to continue building out our network for commercial distribution in jurisdictions in which eteplirsen is approved;

estimated timelines and milestones for 2019 and beyond, including an expected FDA action date of August 19, 2019 for golodirsen, the expectation to complete the open-label portion of our golodirsen trial (4053-101) in 2019, filing an NDA to the FDA for casimersen in 2019, completing a first-in-human, single ascending dose trial for SRP-5051, conducting a confirmatory trial for our micro-dystrophin gene therapy program using commercial supply of SRP-9001 by the end of 2019 and commencing dosing in the clinical trial to test NT-3 gene therapy in 2019 for CMT type 1A;

our belief that the delivery of NT-3 may have applicability to other subtypes of CMT in addition to other neuropathies and muscle-wasting diseases;

the timely completion and satisfactory outcome of our post-marketing requirements and commitments, including verification of a clinical benefit for EXONDYS 51 in confirmatory trials;

S-9

Table of Contents

our plan to seek follow up European Medicines Agency (EMA) scientific advice in 2019 to explore a potential approach for EMA approval of eteplirsen;

our ability to further secure long term supply of EXONDYS 51 and our product candidates to satisfy our planned commercial, managed access programs, named patient programs and clinical needs;

our belief that our current network of manufacturing partners is able to produce raw materials and active pharmaceutical ingredients in the quantities that we require, and are capable of continuing to expand capacity as needed;

the impact of regulations and regulatory decisions by the FDA and other regulatory agencies on our business, as well as the development of our product candidates and our financial and contractual obligations;

the possible impact of any competing products on the commercial success of EXONDYS 51 and our product candidates and our ability to compete against such products;

our ability to enter into research, development or commercialization alliances with universities, hospitals, independent research centers, non-profit organizations, pharmaceutical and biotechnology companies and other entities for specific molecular targets or selected disease indications and our ability to selectively pursue opportunities to access certain intellectual property rights that complement our internal portfolio through license agreements or other arrangements;

our expectations regarding the potential benefits of the partnership, licensing and/or collaboration arrangements and other strategic arrangements and transactions we have entered into or may enter into in the future;

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, and our ability to obtain and maintain patent protection for 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 belief that our owned and licensed patents and patent applications provide us with a competitive advantage;

our belief that our current facilities in Cambridge, Andover and Burlington, Massachusetts and Dublin and Columbus, Ohio are suitable and will provide sufficient capacity to meet the projected needs of our business

for the next 12 months;

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

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

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

our ability to comply with applicable environmental laws and regulations; and

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

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. Please

Table of Contents

reference 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-11

Table of Contents

USE OF PROCEEDS

We expect to receive approximately \$350 million from the sale of shares of common stock offered hereby before deducting underwriting discounts and commissions and estimated offering expenses payable by us, or approximately \$402.5 million if the underwriters exercise their option in full to purchase up to \$52.5 million of additional shares of common stock.

We intend to use the net proceeds from this offering principally for the continuation and initiation of further clinical trials, commercialization, manufacturing, business development activities, including the potential licensing or acquisition of complementary products, technologies and entities, 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, products or entities 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 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.

Dividends

We did not declare or pay cash dividends on our common stock in 2018, 2017 or 2016. We currently expect to retain future earnings, if any, to finance the operation and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors.

S-13

Table of Contents

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 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 U.S. 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 U.S. (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment);

S-14

Table of Contents

the Non-U.S. Holder is a nonresident alien who is present in the U.S. 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.

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 U.S. 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 U.S. 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.

S-15

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, unless such persons comply with a complicated U.S. information reporting, disclosure and certification regime. Pursuant to recently proposed regulations, upon which a tax payer can rely, the withholding tax does not apply to gross proceeds from the sale or other disposition of our common stock. 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 U.S. 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 neither a citizen nor a resident of the United States for U.S. federal estate tax purposes 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 December 31, 2018 was approximately \$1,020.7 million, or approximately \$14.36 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 December 31, 2018.

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 sale of _____ shares of common stock in this offering at a price of \$ _____ per share, and after deduction of the estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2018 would have been approximately \$ _____ million, or \$ _____ per share of common stock. This represents an immediate increase in net tangible book value of \$ _____ per share of common stock to our existing shareholders and an immediate dilution in net tangible book value of \$ _____ 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		\$
Net tangible book value per share as of December 31, 2018	\$ 14.36	
Increase per share attributable to this offering	\$	
As adjusted net tangible book value per share as of December 31, 2018, after giving effect to this offering		\$
Dilution per share to new investors participating in this offering		\$

The above table is based on 71,071,887 shares of our common stock outstanding as of December 31, 2018 and excludes the following:

8,391,171 shares of our common stock issuable upon the exercise of stock options outstanding under our 2002 Equity Incentive Plan, our 2011 Equity Incentive Plan, our 2014 Equity Incentive Plan and our 2018 Equity Incentive Plan;

251,298 shares of restricted stock units issuable upon vesting under our 2011 Equity Incentive Plan, our 2014 Equity Incentive Plan and our 2018 Equity Incentive Plan;

100,000 shares subject to stock appreciation rights under our 2011 Equity Incentive Plan;

850,390 shares of our common stock available for future issuance under our 2014 Equity Incentive Plan;

163,266 shares of our common stock available for future issuance under our 2013 Employee Stock Purchase Plan; and

4,412,446 shares of our common stock available for future issuance under our 2018 Equity 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.

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

S-17

Table of Contents**UNDERWRITING**

We are offering the shares of common stock described in this prospectus supplement through the underwriters named below. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

Name	Number of Shares
Goldman Sachs & Co. LLC	
Morgan Stanley & Co. LLC	
Total	

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The underwriters propose to offer the shares of common stock directly to the public at the public offering price set forth on the cover page of this prospectus supplement. After the public offering of the shares, the offering price and other selling terms may be changed by the underwriters.

The underwriters have a 30 day option to buy up to \$52.5 million of additional shares of common stock from us. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ per share. The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ per share of common stock. The following table shows the per share and total underwriting discounts and commissions we will pay to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	No Exercise	Full Exercise
Per share	\$	\$
Total to be paid by us	\$	\$

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$ million. We have agreed to reimburse the underwriters up to an aggregate of \$10,000 for fees incurred by them in connection with any required filings with the Financial Industry Regulatory Authority.

We and our directors and executive officers have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which we and each of these persons or entities for a period of 60 days and 30 days, respectively, after the date of this prospectus supplement, may not, subject to limited exceptions, including the ability to sell shares under currently existing Rule 10b5-1 trading plans, without

S-18

Table of Contents

the prior written consent of the underwriters (i) 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 our common stock or any other securities convertible into or exercisable or exchangeable for shares of our common stock or (ii) 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, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of shares of our common stock or such other securities, in cash or otherwise.

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

Our common stock is listed on the Nasdaq Global Market under the symbol `SRPT`.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters' option referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option. 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 that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on the Nasdaq Global Select Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on the Nasdaq Global Select Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the

absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

S-19

Table of Contents

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

Other Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the Company and to persons and entities with relationships with the Company, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the Company (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the Company. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

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 our common shares may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of our common shares may be made at any time under the following exemptions under the Prospectus Directive:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined in 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 our common shares 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 our common shares to be offered so as to enable an investor to decide to purchase our common shares, 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 (as amended), including by Directive 2010/73/EU, and includes any relevant implementing measure in the Relevant Member State.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

S-20

Table of Contents

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 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.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or

S-21

Table of Contents

invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

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, New York, New York.

EXPERTS

The consolidated financial statements of Sarepta Therapeutics, Inc. and subsidiaries as of December 31, 2018 and 2017, and for each of the years in the three-year period ended December 31, 2018, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2018 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>. 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.

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, 2018, filed with the SEC on February 28, 2019;

S-23

Table of Contents

the portions of our Definitive Proxy Statement filed with the SEC on April 26, 2018 that are incorporated by reference in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017;

our Current Reports on Form 8-K, as filed with the SEC on February 14, 2019 and February 27, 2019 (except, with respect to each of the foregoing, for portions of such reports which were deemed to be furnished and not filed); 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 filed before the date of this prospectus supplement 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.

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 27, 2019, the last reported sale price on The Nasdaq Global Select Market was \$151.68 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 heading Risk Factors beginning on page 4 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 February 28, 2019.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	1
<u>THE COMPANY</u>	2
<u>RISK FACTORS</u>	4
<u>FORWARD-LOOKING STATEMENTS</u>	4
<u>USE OF PROCEEDS</u>	5
<u>GENERAL DESCRIPTION OF SECURITIES WE MAY SELL</u>	6
<u>PLAN OF DISTRIBUTION</u>	21
<u>LEGAL MATTERS</u>	24
<u>EXPERTS</u>	24
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	24
<u>INFORMATION INCORPORATED BY REFERENCE</u>	24
<u>SIGNATURES</u>	II-5
<u>SIGNATURES AND POWERS OF ATTORNEY</u>	II-6

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. We take no responsibility for, and can provide no assurance as to the reliability of, any information that others may give you. 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 otherwise requires, Sarepta, the Company, we, us, our and similar names refer to Sarepta Therapeutics, Inc. and its subsidiaries.

Table of Contents

THE COMPANY

Our Business

We are a commercial-stage biopharmaceutical company focused on helping patients through the discovery and development of unique RNA-targeted therapeutics, gene therapy and other genetic therapeutic modalities for the treatment of rare diseases.

Applying our proprietary, highly-differentiated and innovative technologies, and through collaborations with our strategic partners, we are developing potential therapeutic candidates for a broad range of diseases and disorders, including Duchenne muscular dystrophy (DMD), Limb-girdle muscular dystrophies (LGMDs), Mucopolysaccharidosis type IIIA (MPS IIIA) and Pompe.

Our first commercial product in the U.S., EXONDYS 51[®] (eteplirsen) Injection (EXONDYS 51), was granted accelerated approval by the United States Food and Drug Administration (FDA) on September 19, 2016. EXONDYS 51 is indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. EXONDYS 51 uses our phosphorodiamidate morpholino oligomer (PMO) chemistry and exon-skipping technology to skip exon 51 of the dystrophin gene. Exon skipping is intended to promote the production of an internally truncated but functional dystrophin protein.

In addition to our commercial-stage product, we have PMO-based product candidates in clinical development designed to treat those patients with DMD who have genetic mutations amenable to skipping exon 53 of the Duchenne gene (SRP-4053) and exon 45 of the Duchenne gene (SRP-4045) (golodirsen and casimersen, respectively). We also have other product candidates in discovery and preclinical development that are designed to skip other exons.

The PMO chemistry platform is highly adaptable, and we have developed next-generation PMO-based chemistries for advancing RNA-targeted therapeutics. These next-generation chemistries are specifically designed to enhance tissue targeting, intracellular delivery, target selectivity and drug potency. One of these novel technologies is based on cell-penetrating peptide-conjugated PMO (PPMO). The PPMO features covalent attachment of a cell-penetrating peptide to a PMO with the goal of enhanced delivery into the cell. Our most advanced PPMO product candidate is SRP-5051, which is designed to treat DMD in patients with genetic mutations amenable to exon 51 skipping.

As part of our multifaceted approach to DMD, we are also exploring gene therapy technologies to treat DMD. In collaboration with Nationwide Children's Hospital, we are testing a product candidate, SRP-9001, that aims to express a smaller but still functional version of dystrophin (micro-dystrophin). We use a unique adeno-associated virus (AAV) vector called AAVrh74 to transport the transgene the genetic material that will make the protein of interest to the target cells. Micro-dystrophin is used because naturally-occurring dystrophin is too large to fit in an AAV.

In 2018, through a number of strategic collaboration and licensing arrangements, we expanded our pipeline to include programs that aim to treat a broad range of rare diseases in addition to DMD, such as LGMDs, Charcot-Marie-Tooth, MPS IIA and Pompe disease. Our pipeline includes 25 programs at various stages of pre-clinical and clinical development, reflecting our aspiration to apply our multifaceted approach and expertise in precision genetic medicine to make a profound difference in the lives of patients suffering from rare diseases.

Corporate Information

We were originally incorporated in the State of Oregon on July 22, 1980, and on June 6, 2013, we reincorporated in the State of Delaware. Our principal executive offices are located at 215 First Street, Suite 415, Cambridge, MA

02142 and our telephone number is (617) 274-4000. On July 12, 2012, our common stock began

Table of Contents

trading under the symbol SRPT on the Nasdaq Global Market. Our common stock is quoted on the Nasdaq Global Select Market under the same symbol. 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.

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.

FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and any information incorporated by reference into this prospectus or such prospectus supplement may contain certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act) and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act). 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, likely, seek and other similar expressions, as well as variations or negatives of these words. You can also identify forward-looking statements by the fact that they do not relate strictly to historical or current facts. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes to differ materially from current expectations. These statements are likely to relate to, among other things, the commercialization of EXONDYS 51, the development and commercialization of our product candidates, the timeline for clinical development, commercialization and regulatory approval of our product candidates, the expected timing for the reporting of data from on-going trials, the structure of our planned or pending clinical trials, additional planned studies, our rights to develop or commercialize our products or product candidates and our ability to finance contemplated development activities and fund operations for a specified period of time.

Forward-looking statements are not guarantees of future performance and our actual results could differ materially from the results discussed in the forward-looking statements we make. In particular, you should consider the numerous risks described in our Annual Report on Form 10-K for the year ended December 31, 2018 and any subsequent Quarterly Report on Form 10-Q, each incorporated by reference in this prospectus, and in the Risk Factors section in the applicable prospectus supplement. See Where You Can Find More Information.

As a result of these and other factors, we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. The forward-looking statements contained in this prospectus reflect our views as of the date hereof. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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 the continuation and initiation of further clinical trials, commercialization, manufacturing and business development activities;

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 and any material amounts of other funds necessary to accomplish the specified purposes for with the proceeds are to be obtained will be described in the applicable prospectus supplement.

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 99,000,000 shares of common stock, par value \$0.0001 per share, of which 71,071,887 shares were issued and outstanding as of December 31, 2018. 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 December 31, 2018, 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 the 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;

Table of Contents

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

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;

Table of Contents

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

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;

Table of Contents

be deposited with the depositary or nominee or custodian; and

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.

Table of Contents

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.

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;

Table of Contents

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)

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)

Table of Contents

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 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;

Table of Contents

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)

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

Table of Contents

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 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;

Table of Contents

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.

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.

Table of Contents

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, 2018 and 2017, and for each of the years in the three-year period ended December 31, 2018, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2018, 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>. 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.

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:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, filed with the SEC on February 28, 2019;

our Current Reports on Form 8-K, as filed with the SEC on February 14, 2019 and February 27, 2019 (except, with respect to each of the foregoing, for portions of such reports which were deemed to be furnished and not filed); 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 the offering of securities described in the applicable prospectus supplement, 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

Table of Contents

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

\$350,000,000

Common Stock

Prospectus Supplement

Goldman Sachs & Co. LLC

Morgan Stanley