Sarepta Therapeutics, Inc.
Form 424B5
December 12, 2012
Table of Contents

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Registration No. 333-184807

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

SUBJECT TO COMPLETION, DATED DECEMBER 12, 2012

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated November 7, 2012)

Sarepta Therapeutics, Inc.

Shares of Common Stock

We are offering shares of our common stock in this offering.

Our common stock is listed on The NASDAQ Global Market under the symbol SRPT. On December 11, 2012, the last reported sale price of our common stock was $25.92 per share.

Investing in our common stock involves significant risks. See Risk Factors beginning on page S-5 of this prospectus supplement and page 10 of the accompanying prospectus.

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

	Per Share	Total
Public Offering Price	$	$
Underwriting discounts and commissions	$	$
Proceeds to us, before expenses	$	$

We estimate the total expenses of this offering, excluding the underwriting discounts and commissions, will be approximately $. We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to a total of additional shares of our common stock at the public offering price per share, less the underwriting discounts and commissions, to cover any over-allotments.

We anticipate that delivery of the shares will be made through the facilities of the Depository Trust Company on or about December , 2012 subject to customary closing conditions.

Sole Book-Running Manager

Lazard Capital Markets

Prospectus supplement dated December , 2012.

Table of Contents

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

ACCOMPANYING PROSPECTUS

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is the prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under Where You Can Find Additional Information on page S-33 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference therein.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. We have not, and the underwriters have not, authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. 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.

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-6 of this prospectus supplement, the financial statements, and related notes, and the other information that we incorporated by reference herein, including our Annual Report on Form 10-K and any subsequent Quarterly Report on Form 10-Q which are incorporated by reference in this prospectus supplement.

Sarepta Therapeutics, Inc.

Overview

We are a biopharmaceutical company focused on the discovery and development of unique RNA-based therapeutics for the treatment of rare and infectious diseases. Applying our proprietary, highly-differentiated and innovative platform technologies, we are able to target a broad range of diseases and disorders through distinct RNA-based mechanisms of action. We are primarily focused on rapidly advancing the development of our potentially disease-modifying Duchenne muscular dystrophy drug candidates, including our lead product candidate, eteplirsen. We are also focused on developing therapeutics for the treatment of infectious diseases, including our lead infectious disease program aimed at the development of a drug candidate for the Marburg hemorrhagic fever virus. By building our infectious disease program funded by the U.S. government and leveraging our highly-differentiated, proprietary technology platforms, we are seeking to further develop our research and development competencies and identify additional product candidates.

Our highly-differentiated RNA-based technologies work at the most fundamental level of biology and potentially could have a meaningful impact across a broad range of human diseases and disorders. Our lead program focuses on the development of disease-modifying therapeutic candidates for Duchenne muscular dystrophy, or DMD, a rare genetic muscle-wasting disease caused by the absence of dystrophin, a protein necessary for muscle function. Currently, there are no disease-modifying therapies available for DMD. Eteplirsen is our lead therapeutic candidate for DMD and if we are successful in our development efforts, eteplirsen will address a severe unmet medical need. We recently completed a U.S.-based Phase IIb clinical trial for eteplirsen that was initiated in August 2011. Following completion of this study, we initiated an open label extension study with the same participants from the original Phase IIb placebo controlled trial.

In April 2012, we announced the results from our DMD Phase IIb clinical trial which determined that treatment with eteplirsen met the primary efficacy endpoint in the Phase IIb study. Eteplirsen administered once weekly at 30mg/kg over 24 weeks resulted in a statistically significant (p £ 0.002) increase in novel dystrophin (22.5% dystrophin-positive fibers as a percentage of normal) compared to no increase in the placebo group. Restoration of dystrophin expression and dystrophin positive fibers is believed to be critical for successful disease-modifying treatment of individuals with DMD. In the study, a shorter duration of eteplirsen treatment, 12 weeks, did not show a significant increase in novel dystrophin (0.79% dystrophin-positive fibers as a percentage of normal; p-value NS), despite administration of the drug at a higher dose (50mg/kg once weekly). No significant improvements in clinical outcomes in the treated groups were observed compared to placebo.

On July 24, 2012, we announced interim results from our DMD open label extension study which indicated that treatment with eteplirsen over 36 weeks achieved a significant clinical benefit on the primary clinical outcome, the 6-minute walk test (6MWT), over a placebo/delayed treatment cohort in our Phase IIb open

Table of Contents

label extension study. Eteplirsen administered once weekly at 50mg/kg over 36 weeks resulted in a 69.4 meter benefit compared to patients who received placebo for 24 weeks followed by 12 weeks of treatment with eteplirsen. In the predefined prospective analysis of the study s intent-to-treat population on the primary clinical outcome measure, the change in 6MWT distance from baseline, eteplirsen-treated patients who received 50mg/kg of the drug weekly demonstrated a decline of 8.7 meters in distance walked from baseline (mean=396.0 meters), while patients who received placebo/delayed-eteplirsen treatment for 36 weeks showed a decline of 78.0 meters from baseline (mean=394.5 meters), for a statistically significant treatment benefit of 69.4 meters over 36 weeks (p £ 0.019). There was no statistically significant difference in the 6MWT between the cohort of patients who received 30mg/kg weekly of eteplirsen and the placebo/delayed treatment cohort. The safety profile of eteplirsen was evaluated across all subjects through the 36 weeks eteplirsen was administered and there were no treatment-related adverse events, no serious adverse events and no discontinuations. Furthermore, no treatment-related changes were detected on any safety laboratory parameters, including several biomarkers for renal function.

On October 3, 2012, we announced 48-week results from our DMD open label extension study which indicated that treatment with eteplirsen met the primary efficacy endpoint, increase in novel dystrophin, and achieved a significant clinical benefit on the primary clinical outcome, the 6MWT, over the placebo/delayed treatment cohort in our Phase IIb extension trial. Eteplirsen administered once weekly at either 30 mg/kg or 50 mg/kg for 48 weeks (n=8) resulted in a statistically significant increase ($p<0.001$) in dystrophin-positive fibers to 47.0% of normal. The placebo/delayed treatment cohort, which had received 24 weeks of eteplirsen at either 30 mg/kg or 50 mg/kg following 24 weeks of placebo (n=4), also showed a statistically significant increase in dystrophin-positive fibers to 38.3% of normal ($p<0.009$). Eteplirsen administered once weekly at 50 mg/kg over 48 weeks resulted in an 89.4 meter benefit compared to patients who received placebo for 24 weeks followed by 24 weeks of treatment with eteplirsen in the open-label extension. In the predefined prospective analysis of the study s intent-to-treat population on the primary clinical outcome measure, the change in 6MWT distance from baseline, eteplirsen-treated patients who received 50 mg/kg of the drug weekly (n=4) demonstrated an increase of 21.0 meters in distance walked from baseline (mean=396.0 meters), while patients who received placebo/delayed-eteplirsen treatment (n=4) showed a decline of 68.4 meters from baseline (mean=394.5 meters), for a statistically significant treatment benefit of 89.4 meters over 48 weeks ($p=0.016$, using analysis of covariance for ranked data). There was no statistically significant difference between the cohort of patients who received 30 mg/kg weekly of eteplirsen and the placebo/delayed treatment cohort. The safety profile of eteplirsen was evaluated across all subjects through 48 weeks and there were no treatment-related adverse events, no serious adverse events, and no discontinuations. Furthermore, no clinically significant treatment-related changes were detected on any safety laboratory parameters, including several biomarkers for renal function.

On December 7, 2012, we announced updated data from our DMD open label extension study. Patients treated with eteplirsen for 62 weeks and evaluable on ambulatory measures (modified Intent-to-Treat population) maintained a statistically significant clinical benefit on the primary clinical outcome measure, the 6-minute walk test (6MWT), compared to patients who received placebo for 24 weeks followed by 38 weeks of eteplirsen treatment. As reported previously, Study 202 met its primary endpoint of increased novel dystrophin as assessed in muscle biopsies at week 48 and is now in the long-term extension phase in which patients continue to be followed for safety and clinical outcomes.

In the modified Intent-to-Treat (mITT) population, which includes evaluable patients from both the 30mg/kg and 50mg/kg dose cohorts, patients treated with eteplirsen for 62 weeks demonstrated a statistically significant benefit of 62 meters over the placebo/delayed-treatment cohort using a mixed-model repeated measure statistical test. The mITT consisted of 10 of the enrolled 12 patients (4 eteplirsen-treated patients receiving 50 mg/kg weekly, 2 eteplirsen-treated patients receiving 30 mg/kg weekly, and 4 placebo/delayed-treatment patients), and excludes two patients who showed signs of rapid disease progression and lost ambulation by week 24. The eteplirsen treatment cohort (n=6) continued to show disease stabilization and the cohort has

Table of Contents

shown less than a 5% decline in walking distance on the 6-minute walk test from baseline. The placebo/delayed-treatment cohort (n=4) also demonstrated stability in walking distance from week 36 through week 62 with a less than 10 meter change over this timeframe, the period in which dystrophin was likely produced, with confirmation of significant dystrophin levels at week 48 through analysis of muscle biopsies in these patients.

The safety profile of eteplirsen was evaluated across all patients through week 62 and there were no clinically significant treatment-related adverse events, no serious adverse events, and no discontinuations. One patient had a laboratory treatment-related adverse event, a transient elevation of urine protein on a urine dipstick test, however this elevation was not observed on a 24-hour urine protein measurement and resulted in no clinical symptoms or interruption of treatment. This patient did not show elevations of the specific renal markers of cystatin C or KIM-1. Across both the treatment and placebo/delayed treatment cohorts there is evidence of continued stabilization on pulmonary function tests, echocardiogram, muscle strength and clinical laboratory tests over the 62 weeks.

Results from the mITT population, which combines the evaluable eteplirsen-treated patients across the 30mg/kg and 50mg/kg cohorts, have previously been reported and will be used as the primary assessment of ambulatory clinical measures for the remainder of the study. Given there was no significant difference between the 30 mg/kg and 50 mg/kg arms on the production of dystrophin through 48 weeks, this mITT population is the most appropriate to assess dystrophin production and its potential predictive benefits on ambulatory clinical outcomes, such as the 6MWT.

We anticipate initiating enrollment of a pivotal Phase III trial in late 2013.

We are also leveraging the capabilities of our RNA-based technology platforms to develop therapeutics for the treatment of infectious diseases. The U.S. Department of Defense, or DoD, has provided significant financial support for the development of therapeutics against Ebola, Marburg, and influenza viruses. As of September 30, 2012, we had completed all of our then-existing contracts with the U.S. government except for the July 2010 agreement for the development of therapeutics against Ebola and Marburg viruses (the ADHFVT contract). On August 29, 2012, we entered into an additional agreement with DoD related to the Marburg virus to evaluate the feasibility of an intramuscular route of administration using AVI-7288. On October 2, 2012, the Company received notice from DoD that the Ebola portion of the ADHFVT contract was terminated for the convenience of the government due to funding constraints. The Company previously received a stop-work order for the Ebola portion of the ADHFVT contract which was in effect from August 2, 2012 through the termination on October 2, 2012. The termination only applies to the Ebola portion of the ADHFVT contract and the Marburg portion remains in effect.

Corporate Information

We were incorporated in the State of Oregon on July 22, 1980. Our executive office is located at 3450 Monte Villa Parkway, Suite 101, Bothell, Washington 98021 and our telephone number is (425) 354-5038. We maintain an Internet website at www.sareptatherapeutics.com. We have not incorporated the information on our website by reference into this prospectus supplement, and you should not consider it to be a part of this prospectus supplement.

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

Table of Contents

The Offering

Common stock offered by us	shares
Over-allotment option	shares
Common stock to be outstanding immediately after this offering	Shares (or shares if the underwriter exercises in full its over-allotment option to purchase additional shares)
Use of proceeds	We intend to use the net proceeds from the sale of our common stock from time to time hereunder for general corporate purposes, including the continued development of eteplirsen and other product candidates. Please see Use of Proceeds on page S-27.
Risk factors	See Risk Factors beginning on page S-5 of this prospectus supplement for a discussion of factors that you should read and consider before investing in our securities.
NASDAQ Global Market symbol	SRPT

The number of shares of our common stock to be outstanding immediately after this offering as shown above is based on 24,302,261 shares outstanding as of September 30, 2012. This number of shares excludes the following:

- 4,822,090 shares of our common stock reserved for issuance upon the exercise of outstanding warrants with a weighted average exercise price of $9.70 per share, of which 0.9 million shares have been issued upon exercise of such warrants subsequent to September 30, 2012;
- 2,440,470 shares of our common stock issuable upon the exercise of stock options outstanding at September 30, 2012 under our 2002 Equity Incentive Plan, our 2011 Equity Incentive Plan and certain non-plan option grants;
- 38,911 shares of restricted stock units issuable upon vesting under our 2011 Equity Incentive Plan;
- 70,000 shares subject to stock appreciation rights under our 2011 Equity Incentive Plan;
- 1,539,930 shares of our common stock available as of September 30, 2012 for future issuance under our 2011 Equity Incentive Plan; and
- up to an aggregate of $19.0 million in shares of our common stock (or approximately 733,000 shares of common stock assuming a public offering price of $25.92 per share, the last reported sale price on The Nasdaq Global Market on December 11, 2012) to be sold by us through Citadel Securities LLC pursuant to the at-the-market equity offering sales agreement entered into on September 4, 2012, of which $16.9 million (or approximately 555,000 shares) were sold subquent to September 30, 2012.

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 and any subsequent Quarterly Report on Form 10-Q, each of which is or upon filing will be incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future, as well as other information in this prospectus and the documents incorporated by reference herein before deciding whether to invest in our securities. The risks described below are not the only ones we face. If any of the following risks actually occurs, our business, financial condition or results of operations could be adversely affected. In such case, the trading price of our common stock could decline and you could lose all or part of your investment. Our actual results could differ materially from those anticipated in the forward-looking statements made throughout this prospectus supplement as a result of different factors, including the risks we face described below.

Risks Relating to Our Business

Our product candidates are at an early stage of development, and it is possible that none of our product candidates will ever become commercial products.

Our product candidates are in relatively early stages of development. These product candidates will require significant further development, financial resources and personnel to obtain regulatory approval and develop into commercially viable products, if at all. Currently, eteplirsen in DMD and AVI-7288 in Marburg are in active clinical development. AVI-7537 in Ebola was in active clinical development until August 2012, when we received a stop-work order from DoD instructing us to cease all work and ordering of supplies in support of the development of this product candidate. On October 2, 2012, we received notice from DoD that the program for the development of AVI-7537 was terminated for the convenience of the government due to funding constraints. The clinical development of AVI-7100 in influenza is currently paused and the rest of our product candidates are in preclinical development. We expect that much of our effort and many of our expenditures over the next several years will be devoted to development activities associated with eteplirsen and other exon-skipping candidates as part of our larger pan-exon strategy in DMD and our antiviral candidates. With current resources, we may be restricted or delayed in our ability to develop other clinical and preclinical product candidates.

Our ability to commercialize any of our product candidates, including eteplirsen, depends on first receiving required regulatory approvals, and it is possible that we may never receive regulatory approval (including any accelerated approval by the U.S. Food and Drug Administration (the FDA) under Subpart H Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) for any of our product candidates based on an inability to adequately demonstrate the safety and effectiveness of our product candidates, lack of funding, changes in the regulatory landscape, manufacturing or other reasons. Even if a product candidate receives regulatory approval, the resulting product may not gain market acceptance among physicians, patients, healthcare payers and the medical community. Assuming that any of our product candidates receives the required regulatory approvals, commercial success will depend on a number of factors, including:

- establishment and demonstration of clinical efficacy and safety and acceptance of the same by the medical community;
- cost-effectiveness of the product;
- the availability of adequate reimbursement by third parties, including governmental payers such as the Medicare and Medicaid programs, managed care organizations, and private health insurers;
- the product s potential advantage over alternative treatment methods;
- whether the product can be produced in commercial quantities at acceptable costs;

Table of Contents

marketing and distribution support for the product; and

any exclusivities applicable to the product.

To date we have been granted orphan status for two of our product candidates in DMD and for AVI-6002 and AVI-7537 for the treatment of Ebola virus and AVI-6003 and AVI-7288 for the treatment of Marburg virus. We are not guaranteed to receive orphan status for other product candidates in development or product candidates we may develop in the future. Even though we have received orphan status for some of our product candidates, we would not enjoy orphan drug exclusivity for such product candidates in the event that another entity received approval of products with the same active ingredient for the same indication before we receive market approval. Further, application of the orphan drug regulations in the United States and Europe is uncertain and we cannot predict how the respective regulatory bodies will interpret and apply the regulations to our or our competitors product candidates. If a competitor s product receives orphan drug status for an indication that we are targeting, and such product is approved for commercial sales before our product, regulators may interpret our product to be the same drug as the competing product and could prevent us from selling our product in the applicable territories for the competitors orphan exclusivity period. Furthermore, pediatric exclusivity only applies if the product has another form of exclusivity.

If we are unable to develop and commercialize any of our product candidates, if development is delayed or if sales revenue from any product candidate that receives marketing approval is insufficient, we may never reach sustained profitability.

If we are unable to obtain or maintain required regulatory approvals, we will not be able to commercialize our product candidates, our ability to generate revenue will be materially impaired and our business will not be successful.

The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products are subject to extensive regulation by the FDA in the United States, and other regulatory authorities in other countries, with regulations differing from country to country. Marketing of our product candidates in the United States or foreign countries is not permitted until we obtain marketing approval from the FDA or other foreign regulatory authorities, and we may never receive regulatory approval for the commercial sale of any of our product candidates. Obtaining marketing approval is a lengthy, expensive and uncertain process and approval is never assured. As of the date of this prospectus, we have not progressed to the point of preparing or filing the applications necessary to gain regulatory approvals. Further, the FDA and other foreign regulatory agencies have substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for any product candidate we develop. In this regard, even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA or any other foreign regulatory authority. In addition, the FDA or their advisors may disagree with our interpretations of data from preclinical studies and clinical trials. Regulatory agencies may approve a product candidate for fewer indications than requested or may grant approval subject to the performance of post-approval studies for a product candidate. Similarly, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

In addition, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols or other approval strategies to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to Institutional Review Boards (IRBs) or the FDA for review, which may impact the costs, timing or successful completion of a clinical trial. Changes in our approval strategies may require additional studies that were not originally planned. Other factors may also impact our ability to commercialize our product candidates, including, for example, the fact that a therapeutic commercial product utilizing our RNA-based technologies has never been approved by any regulatory authority. Due to these factors, our current product candidates or any of our other future product candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain regulatory approval, which could delay or

Table of Contents

eliminate any potential product revenue by delaying or terminating the potential commercialization of our product candidates.

If we receive regulatory approval for our product candidates, we will also be subject to ongoing FDA obligations and oversight, including adverse event reporting requirements, marketing restrictions and, potentially, other post-marketing obligations, all of which may result in significant expense and limit our ability to commercialize such products. The FDA s policies may also change and additional government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States, or abroad. If we are not able to maintain regulatory compliance, we may be subject to civil and criminal penalties, we may not be permitted to market our products and our business could suffer. Any delay in, or failure to, receive or maintain regulatory approval for any of our product candidates could harm our business and prevent us from ever generating meaningful revenues or achieving profitability. We will need to obtain regulatory approval from authorities in foreign countries to market our product candidates in those countries. We have not filed for regulatory approval to market our product candidates in any foreign jurisdiction. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. If we fail to obtain approvals from foreign jurisdictions, the geographic market for our product candidates would be limited.

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

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate, through extensive preclinical and clinical studies, that the product candidate is safe and effective in humans. Ongoing and future preclinical and clinical trials of our product candidates may not show sufficient safety or efficacy to obtain regulatory approvals.

Phase I clinical trials generally are not designed to test the efficacy of a product candidate but rather are designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the product candidate s side effects at various doses and dosing schedules in healthy volunteers. Delays in establishing the appropriate dosage levels can lead to delays in the overall clinical development of a product candidate. As of the date of this prospectus, we do not believe that we have identified the preferred dose of eteplirsen for individuals with DMD. We plan to evaluate the appropriate dosage in a future confirmatory pivotal study. We recently completed a U.S.-based Phase IIb clinical trial for eteplirsen at 30 mg/kg and 50 mg/kg, higher doses than was initiated in August 2011. Following completion of this study, we initiated an open label extension study with the same participants from the original Phase IIb placebo controlled trial. These trials were initiated, in part, to further explore and identify a more consistently effective dose that may be more appropriate for future clinical trials. We cannot assure you that these efforts will be successful. If a consistently effective dose is found in the U.S.-based clinical trial, we will expect to engage in discussions with regulatory authorities about the design and subsequent execution of any further studies which may be required. Regulatory authorities might require more extensive preclinical or clinical trials than anticipated and conforming to any guidance regulatory authorities provide does not guarantee receipt of marketing approval, even if we believe our preclinical and clinical trials are successful. Such clinical trials might include additional open label extension studies for all participants who have previously received eteplirsen, as well as other participants (e.g., non-ambulatory participants) and any additional placebo-controlled pivotal study or studies. If we are not able to establish an optimal dosage in these trials we may need to conduct additional dose-ranging trials before conducting our pivotal trials of the product. Any such additional clinical trials required by regulatory authorities would increase our costs and delay commercialization of eteplirsen.

Furthermore, success in preclinical and early clinical trials does not ensure that later larger-scale trials will be successful nor does it predict final results. Acceptable results in early trials may not be reproduced in later trials. For example, pivotal trials for eteplirsen will likely involve a larger number of participants to achieve

Table of Contents

statistical significance, will be expensive and will take a substantial amount of time to complete. As a result, we may conduct lengthy and expensive clinical trials of our product candidates, only to learn that the product candidate is not an effective treatment or is not superior to existing approved therapies, or has an unacceptable safety profile, which could prevent or significantly delay regulatory approval for such product candidate.

The Animal Rule is a new and seldom-used approach to seeking approval of a new drug and our infectious disease program may not meet the requirements for this ill-defined path to regulatory approval.

Clinical trials cannot be used to assess the efficacy of most biodefense countermeasures against rare and lethal pathogens due to ethical considerations and the relative infrequency of naturally occurring cases. In the United States, we plan to develop the therapeutic product candidate to treat Marburg virus using the Animal Rule regulatory mechanism. Pursuant to the Animal Rule, the sponsor of a drug product must demonstrate efficacy in animal models and safety in humans. There is no guarantee that the FDA will agree to this approach to the development of our infectious disease product candidate, considering that no validated animal model has been established as predicting human outcomes in the prevention or treatment of any filovirus disease. Animal models represent, at best, a rough approximation of efficacy in humans, and, as such, countermeasures developed using animal models will be untested until their use in humans during an emergency. We have yet to demonstrate the predictive value of our animal studies to the FDA s satisfaction. If we fail to do so, we will have to demonstrate efficacy of AVI-7288 through adequate well-controlled trials in humans in order to obtain regulatory approval of this product in the United States, which, if possible, will greatly add to the time and expense required to commercialize this product. Furthermore, the Animal Rule mechanism has been used only rarely and questions remain regarding the FDA s interpretation and implementation. No novel products have been approved using the Animal Rule. It has thus far been used to extend the indicated use of three previously licensed products which had considerable prior human experience. We do not have any experience successfully navigating this approach to drug approval. Even if the Animal Rule represents a viable approach to seeking approval of AVI-7288, it may present challenges for gaining final regulatory approval for this product candidate, including an extended timeline to approval and less predictable study requirements. In addition, the FDA would require post-marketing human efficacy studies if the countermeasure is used in humans, which would most likely be in the aftermath of a bioterrorist attack. The ability to reliably perform efficacy clinical trials in the midst of a national crisis is uncertain.

The timing and conduct of animal studies may be further constrained given that filoviruses are classified for use only in BSL-4 laboratories. There are limited laboratories and staff world-wide that can work with these live viruses and companies will be competing for the limited availability of this critical infrastructure to test their countermeasures. Furthermore, we anticipate limits in conforming to Good Laboratory Practice (GLP) requirements given the requirement for BSL-4 containment.

We rely on U.S. government contracts to support certain research and development programs and substantially all of our revenue. If the U.S. government fails to fund such programs on a timely basis or at all, or such contracts are terminated, the results of our operations would be materially and adversely affected.

We rely on U.S. government contracts and awards to fund certain development programs, including the Marburg virus which accounts for substantially all of our current revenue. The funding of U.S. government programs is subject to Congressional appropriations. Congress generally appropriates funds on a fiscal year basis even though a program may extend over several fiscal years, as is the case with our DoD contract for the development of our Marburg product candidate. Consequently, programs are often only partially funded initially and additional funds are committed only as Congress makes further appropriations. If appropriations for one of our programs become unavailable, or are reduced or delayed, our contracts may be terminated or adjusted by the government, which could have a negative impact on our future revenue under such contract or subcontract. From time to time, when a formal appropriation bill has not been signed into law before the end of the U.S. government s fiscal year, Congress may pass a continuing resolution that authorizes agencies of the U.S. government to continue to operate, generally at the same funding levels from the prior year, but does not

Table of Contents

authorize new spending initiatives, during a certain period. During such a period, or until the regular appropriation bills are passed, delays can occur in government procurement due to lack of funding and such delays can affect our operations during the period of delay. Additionally, the DoD is planning on hundreds of billions of dollars in cuts to defense spending over the next decade and faces a possible sequestration of an additional $600 billion over the same timeframe beginning in January 2013 unless Congress acts. These cuts would have widespread ramifications including on DoD s procurement and research and development programs. The 2004 Project BioShield Act which created the Special Reserve Fund for use by DHHS to purchase countermeasures over 10 years avoids the uncertainty of the annual appropriations process, but the $5.6 billion appropriation is rapidly depleting and will expire in 2013. Thus, the viability of DHHS as a potential customer hinges in part on Congress taking action to replenish the Special Reserve Fund.

In addition, U.S. government contracts generally also permit the government to terminate the contract, in whole or in part, without prior notice, at the government s convenience or for default based on performance. From time to time, we receive communications from the U.S. government regarding our performance, including requests for us to provide additional information and/or take certain steps to remedy noted deficiencies. While we work closely with our contacts at the U.S. government and believe we can adequately address issues raised through such communications, there is no guarantee that we will be able to adequately respond to all requests or remedy all deficiencies cited. If one of our contracts is terminated for convenience, we would generally be entitled to payments for our allowable costs and would receive some allowance for profit on the work performed. If one of our contracts is terminated for default, we would generally be entitled to payments for our work that has been completed to that point. A termination arising out of our default could expose us to liability and have a negative impact on our ability to obtain future contracts. Furthermore, if we fail to satisfy certain performance or deliverable requirements or to adhere to development timelines, revenues associated with the satisfaction of such requirements or timelines may be delayed or may not be realized.

The termination of one or more of these government contracts, whether due to lack of funding, for convenience, for our failure to perform, or otherwise, or the occurrence of delays or product failures in connection with one or more of these contracts, could negatively impact our financial condition. For example, on October 2, 2012, we received notice from DoD that the program for the development of our Ebola product candidate was terminated for the convenience of the government due to funding constraints. We had previously received a stop-work order for the Ebola program which was in effect from August 2, 2012 through the termination on October 2, 2012. If the government terminates the Marburg development program or contract, our business could be materially and adversely affected. Furthermore, we can give no assurance that we would be able to procure new U.S. government contracts to offset the revenue lost as a result of termination of any of our existing contracts. Even if our Marburg contract is not terminated and is completed, there is no assurance that we will receive future government contracts.

Even if we successfully complete development of our Marburg product candidate, the major, if not only, potential purchaser is the U.S. government. The lack of a commercial market makes us reliant upon the U.S. government to determine and communicate the market for biodefense countermeasures and government purchasing is subject to evolving threat assessments and shifting political priorities, which exacerbate market uncertainties. Within the DoD, the war fighter has evolving requirements specifically related to route of administration and time to treat. Until future studies are completed, it is unclear whether our drug candidate will successfully meet these requirements. If it does not, DoD may choose to terminate the contract. With respect to the civilian sector, Marburg virus is among the top chemical, biological, radiological and nuclear threats to national security, yet DHHS has not defined the civilian requirement, making the broader demand for our drug candidate uncertain.

This expected dependence on government purchases presents additional challenges, since the government is incentivized to negotiate prices for countermeasures to just above their marginal cost of production, which would severely limit our profit potential. If companies resist low prices, governments can, in extreme cases, threaten compulsory licensing or purchase patent-breaching generics.

Table of Contents

Our U.S. government contracts may be terminated and we may be liable for penalties under a variety of procurement rules and regulations and changes in government regulations or practices could adversely affect our profitability, cash balances or growth prospects.

We must comply with laws and regulations relating to the formation, administration and performance of U.S. government contracts, which affect how we do business with our customers. Such laws and regulations may potentially impose added costs on our business and our failure to comply with them may lead to penalties and the termination of our U.S. government contracts. Some significant regulations that affect us include:

- the Federal Acquisition Regulation and supplements, which regulate the formation, administration and performance of U.S. government contracts;
- the Truth in Negotiations Act, which requires certification and disclosure of cost and pricing data in connection with contract negotiations; and
- the Cost Accounting Standards, which impose accounting requirements that govern our right to reimbursement under certain cost-based government contracts.

Our contracts with the U.S. government are subject to periodic review and investigation. If such a review or investigation identifies improper or illegal activities, we may be subject to civil or criminal penalties or administrative sanctions, including the termination of contracts, forfeiture of profits, the triggering of price reduction clauses, suspension of payments, fines and suspension or debarment from doing business with U.S. government agencies. We could also suffer harm to our reputation if allegations of impropriety were made against us, which would impair our ability to win awards of contracts in the future or receive renewals of existing contracts.

In addition, U.S. government agencies routinely audit and review their contractors performance on contracts, cost structure, pricing practices and compliance with applicable laws, regulations and standards. They also review the adequacy of, and a contractor s compliance with, its internal control systems and policies, including the contractor s purchasing, property, estimating, compensation and management information systems. Such audits may result in adjustments to our contract costs, and any costs found to be improperly allocated will not be reimbursed. We have recorded contract revenues based upon costs we expect to realize upon final audit; however, we do not know the outcome of any future audits and adjustments and, if future audit adjustments exceed our estimates, our results of operations could be adversely affected. Additionally, we may be required to enter into agreements and subcontracts with third parties, including suppliers, consultants and other third party contractors in order to satisfy our contractual obligations pursuant to our agreements with the U.S. government. Negotiating and entering into such arrangements can be time-consuming and we may not be able to reach agreement with such third parties. Any such agreement also has to be compliant with the terms of our government grants. Any delay or inability to enter into such arrangements or entering into such arrangements in a manner that is non-compliant with the terms of our grants, may result in violations of our contracts with the U.S. government.

Clinical trials for our product candidates are expensive and time consuming, may take longer than we expect or may not be completed at all, and their outcomes are uncertain.

We have completed a Phase Ib/II clinical trial for eteplirsen in the UK and announced results in October 2010, which were published in The Lancet in July 2011. We have also completed a U.S.-based Phase IIb placebo controlled trial in eteplirsen and announced results in April 2012. Following completion of this study, we initiated an open label extension study with the same participants from the original Phase IIb placebo controlled trial and announced 48-week results on October 3, 2012. We expect to commence additional trials of eteplirsen and other product candidates in the future. Each of our clinical trials requires the investment of substantial planning, expense and time, and the timing of the commencement, continuation and completion of these clinical

Table of Contents

trials may be subject to significant delays relating to various causes, including scheduling conflicts with participating clinicians and clinical institutions, difficulties in identifying and enrolling participants who meet trial eligibility criteria, failure of participants to complete the clinical trial, delay or failure to obtain IRB or other regulatory approval to conduct a clinical trial at a prospective site, unexpected adverse events and shortages of available drug supply. Participant enrollment is a function of many factors, including the size of the relevant population, the proximity of participants to clinical sites, the eligibility criteria for the trial, the existence of competing clinical trials and the availability of alternative or new treatments.

We depend on medical institutions and clinical research organizations, or CROs, to conduct our clinical trials in compliance with Good Clinical Practice, or GCP, and to the extent they fail to enroll participants for our clinical trials, fail to conduct the study to GCP standards or are delayed for a significant time in the execution of our trials, including achieving full enrollment, we may be affected by increased costs, program delays or both, which may harm our business. In addition, we have in the past conducted clinical trials in foreign countries and may do so again in the future, which may subject us to further delays and expenses as a result of increased drug shipment costs, additional regulatory requirements and the engagement of foreign CROs, as well as expose us to risks associated with less experienced clinical investigators who are unknown to the FDA, and different standards of medical care. Foreign currency transactions insofar as changes in the relative value of the U.S. dollar to the foreign currency where the trial is being conducted may impact our actual costs. In addition, for some programs (e.g., DMD and Marburg infection) there are currently no approved drugs to compare against and an agreement about how to measure efficacy has yet to be reached with the FDA and then demonstrated.

Clinical trials must be conducted in accordance with FDA or other applicable foreign government guidelines and are subject to oversight by the FDA, other foreign governmental agencies and IRBs at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of our product candidates produced under current Good Manufacturing Practice, or cGMP, and other requirements in foreign countries, and may require large numbers of participants. The FDA or other foreign governmental agencies or we ourselves could delay, suspend or halt our clinical trials of a product candidate for numerous reasons, including:

- deficiencies in the trial design;
- deficiencies in the conduct of the clinical trial including failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols;
- deficiencies in the clinical trial operations or trial sites resulting in the imposition of a clinical hold;
- the product candidate may have unforeseen adverse side effects, including fatalities, or a determination may be made that a clinical trial presents unacceptable health risks;
- the time required to determine whether the product candidate is effective may be longer than expected;
- fatalities or other adverse events arising during a clinical trial that may not be related to clinical trial treatments;
- the product candidate may appear to be no more effective than current therapies;
- the quality or stability of the product candidate may fail to conform to acceptable standards;
- our inability to produce or obtain sufficient quantities of the product candidate to complete the trials;

Table of Contents

our inability to reach agreement on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

our inability to obtain IRB approval to conduct a clinical trial at a prospective site;

our inability to obtain regulatory approval to conduct a clinical trial;

lack of adequate funding to continue the clinical trial, including the occurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties;

our inability to recruit and enroll individuals to participate in clinical trials for reasons including competition from other clinical trial programs for the same or similar indications; or

our inability to retain participants who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues, or who are lost to further follow-up.

In addition, we may experience significant setbacks in advanced clinical trials, even after promising results in earlier trials, such as unexpected adverse events that occur when our product candidates are combined with other therapies and drugs or given to larger populations, which often occur in later-stage clinical trials. In addition, clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. Also, patient advocacy groups and parents of trial participants may demand additional clinical trials or continued access to drug even if our interpretation of clinical results received thus far leads us to determine that additional clinical trials or continued access are unwarranted. Any disagreement with patient advocacy groups or parents of trial participants may require management s time and attention and may result in legal proceedings being instituted against us, which could be expensive, time-consuming and distracting, and may result in delay of the program. Negative or inconclusive results or adverse medical events, including participant fatalities that may be attributable to our product candidates, during a clinical trial may necessitate that it be redesigned, repeated or terminated. Further, some of our clinical trials may be overseen by an independent data safety monitoring board, or DSMB, and the DSMB may determine to delay or suspend one or more of these trials due to safety or futility findings based on events occurring during a clinical trial. Any such delay, suspension, termination or request to repeat or redesign a trial could increase our costs and prevent or significantly delay our ability to commercialize our product candidates.

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

We had an operating loss of $19.3 million for the nine months ended September 30, 2012, and incurred an operating loss of $35.9 million for the year ended December 31, 2011. As of September 30, 2012, our accumulated deficit was $369.2 million. Our losses have resulted principally from expenses incurred in research and development of our technology and products, from general and administrative expenses that we have incurred while building our business infrastructure and acquired in-process research and development resulting from two acquisitions. We expect to continue to incur significant operating losses in the future as we continue our research and development efforts and seek to obtain regulatory approval of our products. Our ability to achieve profitability depends on our ability to raise additional capital, partner one or more programs, complete development of our products, obtain regulatory approvals and market our products. It is uncertain when, if ever, we will become profitable.

Table of Contents

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

We will require additional capital from time to time in the future in order to continue the development of product candidates in our pipeline and to expand our product portfolio. The actual amount of funds that we will need will be determined by many factors, some of which are beyond our control. These factors include the success of our research and development efforts, the status of our preclinical and clinical testing, costs relating to securing regulatory approvals and the costs and timing of obtaining new patent rights, regulatory changes and competitive and technological developments in the market. An unforeseen change in these factors, or others, might increase our need for additional capital.

We would expect to seek additional financing from the sale and issuance of equity or equity-linked or debt securities, and we cannot predict that financing will be available when and as we need financing or that, if available, the financing terms will be commercially reasonable. If we are unable to obtain additional financing, when and if we require or on commercially reasonable terms, it would have a material adverse effect on our business and results of operations.

If we are able to consummate such financings, the trading price of our common stock could be adversely affected and/or the terms of such financings may adversely affect the interests of our existing shareholders. To the extent we issue additional equity securities, our existing shareholders could experience substantial dilution in their economic and voting rights. For example, through December 10, 2012, we sold an aggregate of approximately 14.0 million shares of our common stock in connection with our December 2007, January 2009, August 2009 and April 2011 financings and September 2012 at-the-market equity offering program and issued warrants to purchase approximately 5.0 million additional shares of our common stock in connection with our December 2007, January 2009 and August 2009 financings, which warrants have been exercised for an aggregate of 1.0 million shares of common stock.

Further, we may also enter into relationships with pharmaceutical or biotechnology companies to perform research and development with respect to our RNA-based technologies, research programs or to conduct clinical trials and to market our product candidates. Other than pre-clinical collaborations with academic/research institutions and a U.S. government entity for the development of additional exon-skipping drug candidates for the treatment of DMD, we currently do not have a strategic relationship with a third party to perform research or development using our RNA-based technologies or assist us in funding the continued development and commercialization of any of our programs or drug candidates other than that with the U.S. government. If we are unable to enter into partnerships or strategic relationships with respect to our technologies or any of our programs or drug candidates on favorable terms it may impede our ability to discover, develop and commercialize our product candidates.

We currently rely on third-party manufacturers and other third parties for production of our drug products and our dependence on these manufacturers may impair the advancement of our research and development programs and the development of our product candidates.

We do not currently have the internal ability to manufacture the product candidates that we need to conduct our clinical trials and we rely upon a limited number of manufacturers to supply our product candidates and the components of our drug substance. We may also need to rely on manufacturers for the production of our product candidates to support our research and development programs. In addition, we rely on other third parties to perform additional steps in the manufacturing process, including filling and labeling of vials and storage of our product candidates. For the foreseeable future, we expect to continue to rely on contract manufacturers and other third parties to produce, fill vials and store sufficient quantities of our product candidates for use in our research and development programs and clinical trials. For each of our eteplirsen and Marburg development programs, based on limited capacity for our specialized manufacturing needs we have had to enter into a sole-source

agreement with multinational manufacturing firms for the production of the API for eteplirsen and Marburg therapeutics. There are a limited number of companies that can produce phosphorodiamidate-linked morpholino oligomer, or PMO, in the quantities and with the quality and purity that we require for our development efforts. This might limit our ability to rapidly expand our programs or commercialize our products. If we are required to seek alternative supply arrangements, the resulting delays and potential inability to find suitable replacements or bring on-line new suppliers could materially and adversely impact our business.

Our product candidates require precise, high-quality manufacturing. The failure to achieve and maintain high quality standards, including failure to detect or control anticipated or unanticipated manufacturing errors could result in patient injury or death or product recalls. Contract drug manufacturers often encounter difficulties involving production yields, quality control and quality assurance and shortages of qualified personnel. If our contract manufacturers or other third parties fail to deliver our product candidates for our research and development programs and for clinical use on a timely basis, with sufficient quality, and at commercially reasonable prices, and we fail to find replacement manufacturers or to develop our own manufacturing capabilities, we may be required to delay or suspend clinical trials, research and development programs or otherwise discontinue development and production of our product candidates. In addition, we depend on certain sole-source third-party vendors for the supply of raw materials used to produce our product candidates. If the third-party suppliers were to cease production or otherwise fail to supply us with quality raw materials and we are unable to contract on acceptable terms for these raw materials with alternative suppliers, our ability to have our product candidates manufactured and to conduct preclinical testing and clinical trials of our product candidates would be adversely affected.

We do not yet have all of the agreements necessary for the supply of our product candidates in quantities sufficient for commercial sale and we may not be able to establish or maintain sufficient commercial manufacturing arrangements on commercially reasonable terms. Securing commercial quantities of our product candidates from contract manufacturers will require us to commit significant capital and resources. We may also be required to enter into long-term manufacturing agreements that contain exclusivity provisions and/or substantial termination penalties. In addition, contract manufacturers have a limited number of facilities in which our product candidates can be produced and any interruption of the operation of those facilities due to events such as equipment malfunction or failure or damage to the facility by natural disasters could result in the cancellation of shipments, loss of product in the manufacturing process or a shortfall in available product candidates.

Our contract manufacturers are required to produce our clinical product candidates under cGMP conditions in order to meet acceptable standards for our clinical trials. If such standards change, the ability of contract manufacturers to produce our product candidates on the schedule we require for our clinical trials may be affected. In addition, contract manufacturers may not perform their obligations under their agreements with us or may discontinue their business before the time required by us to successfully produce and market our product candidates. We and our contract manufacturers are subject to periodic unannounced inspection by the FDA and corresponding state and foreign authorities to ensure strict compliance with cGMP and other applicable government regulations and corresponding foreign standards. We do not have control over a third-party manufacturer s compliance with these regulations and standards. Any difficulties or delays in our contractors manufacturing and supply of product candidates or any failure of our contractors to maintain compliance with the applicable regulations and standards could increase our costs, cause us to lose revenue, make us postpone or cancel clinical trials, prevent or delay regulatory approval by the FDA and corresponding state and foreign authorities, prevent the import and/or export of our product candidates, or cause our products to be recalled or withdrawn.

We may not be able to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing resulting approved drug products, if any.

To date, our product candidates have been manufactured in small quantities for preclinical studies and early stage clinical trials. In order to conduct larger or late-stage scale clinical trials for a product candidate and

Table of Contents

for commercialization of the resulting drug product if that product candidate is approved for sale, we will need to manufacture it in larger quantities. We may not be able to successfully increase the manufacturing capacity for any of our product candidates, whether in collaboration with third-party manufacturers or on our own, in a timely or cost-effective manner or at all. If a contract manufacturer makes improvements in the manufacturing process for our product candidates, we may not own, or may have to share, the intellectual property rights to those improvements. Significant scale-up of manufacturing may require additional validation studies, which are costly and which the FDA must review and approve. In addition, quality issues may arise during those scale-up activities because of the inherent properties of a product candidate itself or of a product candidate in combination with other components added during the manufacturing and packaging process, or during shipping and storage of the finished product or active pharmaceutical ingredients. If we are unable to successfully scale-up manu