Sarepta Therapeutics, Inc.
Form 10-K
March 15, 2013
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2012

Or

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 Or 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission file number: 001-14895

Sarepta Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Oregon	**93-0797222**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**

215 First Street

Suite 007

Cambridge, MA **02142**
(Address of principal executive offices) **(Zip Code)**
Registrant s telephone number, including area code: (857) 242-3700

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

Tile of Each Class	**Name of Exchange on Which Registered**
Common Stock, $0.0001 par value	**The NASDAQ Stock Market LLC**
	(The NASDAQ Global Market)

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

None

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of the registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2012 was approximately $84,275,000.

The number of outstanding shares of the registrant s common stock as of the close of business on February 28, 2013 was 31,831,212.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant has incorporated into Part III of this Annual Report on Form 10-K, by reference, portions of its definitive Proxy Statement for its 2013 annual meeting.

Table of Contents

Sarepta Therapeutics, Inc.

FORM 10-K INDEX

	Page
PART I	1
Item 1. Business	1
Item 1A. Risk Factors	26
Item 1B. Unresolved Staff Comments	44
Item 2. Properties	44
Item 3. Legal Proceedings	45
Item 4. Mine Safety Disclosures	45
PART II	46
Item 5. Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	46
Item 6. Selected Financial Data	48
Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operation	49
Item 7A. Quantitative and Qualitative Disclosures About Market Risk	59
Item 8. Financial Statements and Supplementary Data	59
Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	59
Item 9A. Controls and Procedures	59
Item 9B. Other Information	63
PART III	64
Item 10. Directors, Executive Officers and Corporate Governance	64
Item 11. Executive Compensation	64
Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	64
Item 13. Certain Relationships and Related Transactions, and Director Independence	64
Item 14. Principal Accountant Fees and Services	64
PART IV	65
Item 15. Exhibits, Financial Statement Schedules	65

Table of Contents

PART I

Item 1. Business.

Forward-Looking Information

This Annual Report on Form 10-K, including the Management s Discussion and Analysis of Financial Condition and Results of Operations section in Item 7, and other materials accompanying this Annual Report on Form 10-K contain forward-looking statements or incorporate by reference forward-looking statements. The statements contained in this Annual Report on Form 10-K that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are identified by words such as believe, anticipate, expect, intend, plan, will, may, seek and other similar expressions. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other forward-looking information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements include, but are not limited to:

our expectations regarding the development and clinical benefits of our product candidates;

the results of our research and development efforts and the efficacy of our PMO-based chemistries and other RNA-based technology;

our expectations regarding our ability to become a leading developer and marketer of RNA-based therapeutics;

our expectations regarding the results of preclinical and clinical testing of our product candidates;

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

our expectations regarding initiating a pivotal clinical trial for eteplirsen by the end of 2013 and commencing dosing in this trial early 2014;

our ability to submit IND filings for DMD candidates beyond eteplirsen;

our ability to initiate Phase I multiple ascending dose studies for AVI-7288 for treatment of the Marburg virus in 2013;

the receipt of any required approval from the U.S. Food and Drug Administration, or the FDA, or other regulatory approval for our products;

the potential for our product candidates to qualify for accelerated approval, as breakthrough therapies or as orphan drugs;

the potential for any filings or applications by us for accelerated approval or other designations to be accepted or granted by the FDA;

the effect of regulation by the FDA and other agencies;

our intention to introduce new products;

our expectations regarding the markets, pricing or reimbursement for our products;

acceptance of our products, if introduced, in the marketplace;

the impact of competitive products, product development, commercialization and technological difficulties;

our expectations regarding our ability to commercialize eteplirsen with a relatively small sales force, if eteplirsen is approved for commercial sale;

our expectations regarding partnering opportunities and other strategic transactions;

our ability to increase the scale of our manufacturing to provide our product to patients in larger scale clinical trials or in potential commercial quantities;

Table of Contents

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

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

our plans to file additional patent applications to enhance and protect our existing intellectual property portfolio;

our ability to invalidate some or all of the claims covered by patents issued to competitors;

our estimates regarding our future revenues, research and development expenses, other expenses, payments to third parties and changes in staffing levels;

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

our expectations about funding from the government and other sources; and

other factors set forth below under the heading Risk Factors .

All forward-looking statements are based on information available to us on the date of this Annual Report on Form 10-K and we will not update any of the forward-looking statements after the date of this Annual Report on Form 10-K, except as required by law. Our actual results could differ materially from those discussed in this Annual Report on Form 10-K. The forward-looking statements contained in this Annual Report on Form 10-K, and other written and oral forward-looking statements made by us from time to time, are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in the following discussion and within Part I, Item 1A Risk Factors of this Annual Report on Form 10-K.

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 programs which are primarily funded and supported 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 approved disease-modifying therapies for DMD. Eteplirsen is our lead therapeutic candidate for DMD. If we are successful in our development efforts, eteplirsen will address a severe unmet medical need. Last year, we completed a U.S.- based Phase IIb clinical trial for eteplirsen that was initiated in August 2011. Following completion of this study in early 2012, we initiated an open label extension study that is expected to be completed in late 2013 with the same participants from the original Phase IIb placebo controlled trial. We anticipate initiating a pivotal clinical trial for eteplirsen by the end of 2013 and commencing dosing in this trial early 2014.

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

Table of Contents

support in the past for the development of therapeutics against Ebola, Marburg, Dengue and influenza viruses. We have attracted DoD s support based in part on our ability to rapidly respond to pathogenic threats by quickly identifying, manufacturing and evaluating novel therapeutic candidates as discussed in greater detail in the section captioned Development Programs Infectious Disease Programs Influenza Program below.

The basis for our novel RNA-based therapeutics is our phosphorodiamidate-linked morpholino oligomer, or PMO, chemistries. Unlike other RNA-based therapeutics, which are often used to down-regulate gene expression, our technologies can be used to selectively up-regulate or down-regulate the production of a target protein, or direct the expression of novel proteins involved in human diseases and disorders. Further, we believe the charge-neutral nature of our PMO-based molecules may have the potential to reduce off-target effects, such as immune stimulatory effects often seen in alternative RNA-based technologies. We believe that our highly-differentiated, novel proprietary and innovative RNA-based technology platforms, based on charge neutral morpholino oligomers, may represent a significant improvement over traditional RNA-based technologies.

We were incorporated in the State of Oregon on July 22, 1980. Our executive office is located at 215 First Street, Suite 7 Cambridge, MA 02142 and our telephone number is (857) 242-3700. Our common stock trades on The NASDAQ Global Market under the symbol SRPT. On July 12, 2012, our common stock began trading on The NASDAQ Global Market on a split-adjusted basis following a one-for-six reverse stock split that was effective on July 11, 2012. Unless otherwise noted, all share amounts, share prices and exercise prices included throughout this report give effect to the July 2012 one-for-six reverse stock split.

This Annual Report on Form 10-K includes our trademarks and registered trademarks, including PMO*plus*®, PMO-X, AVI BioPharma®, Sarepta, Sarepta Therapeutics, Cytoporter® and NeuGene®. Each other trademark, trade name or service mark appearing in this Annual Report on Form 10-K belongs to its holder.

Where You Can Find Additional Information

We make available free of charge through our corporate website, www.sareptatherapeutics.com, our annual reports, quarterly reports, current reports, proxy statements and all amendments to those reports as soon as reasonably practicable after such material is electronically filed or furnished with the SEC. These reports may also be obtained without charge by contacting Investor Relations, Sarepta Therapeutics, Inc., 215 First Street, Suite 7, Cambridge, MA 02142, e-mail: investorrelations@sareptatherapeutics.com. Our Internet website and the information contained therein or incorporated therein are not intended to be incorporated into this Annual Report on Form 10-K. In addition, the public may read and copy any materials we file or furnish with the Securities and Exchange Commission, or the SEC, at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 or may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Moreover, the SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding reports that we file or furnish electronically with them at www.sec.gov.

Objectives and Business Strategy

We believe that our highly-differentiated, proprietary RNA-based technology platforms can be used to develop novel pharmaceutical products to treat a broad range of diseases and address key unmet medical needs. We intend to leverage our RNA-based technology platforms, organizational capabilities and resources to become a leading developer and marketer of RNA-based therapeutics, including for the treatment of rare and infectious diseases, with a diversified portfolio of product candidates and approved products. In pursuit of this objective, we intend to engage in the following activities:

- advancing the development of eteplirsen and our other drug candidates for the treatment of DMD to realize the product opportunities of such candidates and provide significant clinical benefits;

- successfully executing our government funded infectious disease therapeutic programs and building on and leveraging our experience with such programs to further develop our research and development capabilities and garner additional external funding; and

Table of Contents

leveraging our highly-differentiated, proprietary RNA-based technology platforms to identify product candidates in additional therapeutic areas and explore various strategic opportunities, including potential partnering, licensing or collaboration arrangements with industry partners.

Development Programs

Our currently active RNA-based drug programs are being clinically evaluated for the treatment of DMD and have also demonstrated promising antiviral activity in infectious diseases such as Marburg and H1N1 influenza in certain animal models. Our active lead product candidates are at various stages of development summarized below.

Program	Indication	Mechanism	Chemistry	Development Stage	Developer / Collaborator
Eteplirsen	DMD (exon 51)	Exon Skipping	PMO	Phase IIb*	Proprietary
AVI-7288	Marburg virus	Translation Suppression	PMO*plus*®	Phase I	Proprietary/U.S. Government
AVI-7100	H1N1 influenza virus	Translation Suppression	PMO*plus*®	Phase I	Proprietary/U.S. Government

* We announced results from our Phase IIb clinical study in eteplirsen in April 2012 and are currently conducting an open label extension phase to this clinical trial.

For purposes of the table, Development Stage indicates the most advanced stage of development that has been completed or is ongoing. In the table above, under the heading Development Stage, Phase IIb indicates clinical safety and efficacy testing in a small patient population, and Phase I indicates initial clinical safety testing in healthy volunteers or a limited patient population, or trials directed toward understanding the mechanisms or metabolism of the drug.

Duchenne Muscular Dystrophy Program

Duchenne muscular dystrophy, or DMD, is one of the most common fatal genetic disorders affecting children (primarily boys) around the world. DMD is a devastating and incurable muscle-wasting disease associated with specific mutations in the gene that codes for dystrophin, a protein that plays a key structural role in muscle fiber function. The absence of dystrophin in muscle cells leads to significant cell damage and ultimately causes muscle cell death and fibrotic replacement. The disease occurs in approximately one in every 3,500 male births worldwide. Females are rarely affected by the disorder. Initial symptoms, which usually appear between the ages of three and five, include progressive muscle weakness of the legs and pelvis, manifested as difficulty walking, running or climbing stairs, which eventually spreads to the arms, neck, and other areas. By age ten, braces may be required for walking, and many individuals require full-time use of a wheelchair before age 12. Eventually muscular degeneration progresses to the point of complete paralysis. Disease progression is also typically associated with respiratory muscle dysfunction and a corresponding difficulty in breathing, which may require ventilatory support, and cardiac muscle dysfunction which may lead to heart failure. DMD is ultimately fatal and death usually occurs before the age of 30. There is currently no approved disease modifying treatment or cure for DMD.

The yearly cost of care for individuals with DMD is high and increases with disease progression. Although DMD is a rare disease, it represents a substantial product opportunity due to the severity and inexorable progression of the symptoms.

Our lead program is designed to address specific gene mutations that result in DMD by forcing the genetic machinery to skip over an adjacent contiguous piece (*i.e.*, one or more exons) of RNA and, thus, restore the ability of the cell to express a new, truncated but functional, dystrophin protein. We believe that the expression of

Table of Contents

this truncated dystrophin protein may restore, prevent or slow deterioration of muscle function, as exemplified by the less severe muscular dystrophy phenotype, called Becker muscular dystrophy.

Eteplirsen. Eteplirsen is an antisense PMO-based therapeutic in clinical development for the treatment of individuals with DMD who have an error in the gene coding for dystrophin that can be treated by skipping exon 51. Eteplirsen targets the most frequent series of mutations that cause DMD. Eteplirsen has been granted orphan drug designation in the United States and European Union. In 2007, the FDA granted eteplirsen fast track status and we are currently evaluating the possibility of seeking certain types of expedited review or approval for eteplirsen. See Government Regulation for additional information.

In October 2010, we announced results from a clinical trial of eteplirsen, AVI Study 28. Data from this study were published in *The Lancet* in July 2011. AVI Study 28 was a Phase Ib/IIa open label, dose-ranging, clinical trial assessing the safety, tolerability, pharmacokinetics and exploratory efficacy of eteplirsen in ambulatory individuals with DMD. Participants in AVI Study 28 were between the ages of five and 15 with errors in the gene coding for dystrophin, which were amenable to treatment by skipping exon 51. Participants were dosed once per week for 12 weeks. A total of 19 participants were enrolled and these individuals were assigned to one of six dose cohorts of 0.5, 1.0, 2.0, 4.0, 10.0 or 20.0 mg/kg. Of the 19 participants enrolled, 18 received at least ten of the 12 doses planned in this trial. After completion of dosing, participants were followed for an additional 14 weeks. Muscle biopsies were taken before treatment and 17 participants had a second biopsy at week 14, two weeks after administration of the final dose. The primary objective of the trial was to assess the safety of eteplirsen at these doses over the 26-week duration of the trial. Secondary trial objectives included assessment of plasma pharmacokinetics, urinary elimination and exploratory endpoints evaluating biological activity and clinical performance. This trial was conducted by investigators in the United Kingdom at the University College London Institute of Child Health / Great Ormond Street Hospital in London and at the Royal Victoria Infirmary in Newcastle-Upon-Tyne. In AVI Study 28, (i) eteplirsen induced exon 51 skipping in all cohorts and new dystrophin protein expression in cohort 3; (ii) eteplirsen was well-tolerated in all participants with no drug-related serious adverse events or severe adverse events, except that one participant exhibited deteriorating cardiac function, which was considered probably disease related; (iii) adverse events were mostly mild or moderate in intensity, not dose-related, and none were considered probably or definitely related to eteplirsen; and (iv) there was no detectable immune response to newly made dystrophin.

Based on the AVI 28 study results, we initiated a Phase IIb trial for eteplirsen in August 2011, AVI 4658-us-201, or Study 201, at Nationwide Children s Hospital in Columbus, Ohio and we announced the results from this study in April 2012. This was a randomized, double-blind, placebo-controlled study to assess the efficacy, safety, tolerability and pharmacokinetics of eteplirsen administered intravenously in two different doses over 24 weeks for the treatment of ambulant boys with DMD. Exploratory clinical measures of ambulation, muscle function and strength were also captured and evaluated during the course of the trial. Study 201 included 12 participants and muscle biopsies of all participants were performed prior to initiation of treatment. The 12 participants with a genotypically-confirmed appropriate genetic mutation were randomized into one of three treatment groups with four participants in each group. The first treatment group received a weekly intravenous administration of eteplirsen at a dose of 50.0 mg/kg. The second treatment group received a weekly intravenous administration of eteplirsen at a dose of 30.0 mg/kg. The third and final treatment group received a weekly administration of placebo. Participants receiving the 50.0 mg/kg dose received a second biopsy at 12 weeks after initiation of treatment, and participants receiving the 30.0 mg/kg dose received a second biopsy at 24 weeks after initiation of treatment. The results from Study 201 determined that treatment with eteplirsen met the primary efficacy endpoint in the study. Eteplirsen administered once weekly at 30mg/kg over 24 weeks resulted in a statistically significant ($p \leq 0.002$) increase in novel dystrophin (22.5% dystrophin-positive fibers as a percentage of normal) compared to no increase in the placebo group. 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.

Table of Contents

All participants in Study 201 were enrolled in an open-label extension study 4658-us-202, or Study 202, following the completion of Study 201 and all participants, including those from the placebo group in Study 201, are receiving either 30.0 mg/kg or 50.0 mg/kg for the duration of Study 202. The purpose of Study 202 is to evaluate the ongoing safety, efficacy and tolerability of eteplirsen. The primary efficacy endpoint was the change from baseline at week 48 in the percentage of dystrophin-positive fibers in muscle biopsy tissue as measured by immunohistochemistry. The primary clinical outcome measure was the change from baseline to week 48 on the six minute walk test, or the 6MWT. Study 202 is now in a long-term extension phase in which patients continue to be followed for safety and clinical outcomes approximately every 12 weeks through week 108 (which includes the original 28 weeks of Study 201).

On July 24, 2012, we announced interim results from Study 202 which indicated that treatment with eteplirsen over 36 weeks achieved a significant clinical benefit on the primary clinical outcome measure, the 6MWT, over a placebo/delayed treatment cohort. 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 ($p \leq 0.019$). 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 Study 202 which indicated that treatment with eteplirsen met the predefined primary efficacy endpoint, increase in novel dystrophin, and achieved a significant clinical benefit on the predefined primary clinical outcome measure, the 6MWT, over the placebo/delayed treatment cohort. 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 ($p<0.009$).

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 at week 48, 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 Study 202 which showed 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 6MWT, compared to patients who received placebo for 24 weeks followed by 38 weeks of eteplirsen treatment. In the 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 ($p \leq 0.007$) of 62 meters over the

Table of Contents

placebo/delayed-treatment cohort using a mixed-model repeated measure statistical test. The mITT population utilized for the 62 week analysis 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 excluded 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 with less than a 5% decline in walking distance on the 6MWT 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 been previously reported and will be used as the primary assessment of ambulatory clinical measures for the remainder of Study 202. 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 are participating in an end of Phase II meeting with the FDA in the first quarter of 2013 to discuss the clinical results from our Phase IIb study of eteplirsen. Based on feedback from the meeting, we will make an initial determination regarding the most appropriate regulatory path for pursuing regulatory review and approval of eteplirsen. Any such initial determination will be further informed by a subsequent Chemistry, Manufacturing and Controls, or CMC, meeting with the agency. Regardless of the registration path ultimately pursued, we anticipate initiating a pivotal clinical trial by the end of 2013 and commencing dosing in early 2014.

Pan-Exon Strategy. In addition to our lead product candidate, eteplirsen, we are pursuing development of additional exon-skipping drugs, to support our broad-based development program for the treatment of DMD.

To support certain IND-enabling activities for an exon 45-skipping therapeutic, we are collaborating with Children s National Medical Center in Washington, D.C. and the Carolinas Medical Center. This collaboration will be funded primarily through two grants, one from DoD s Congressionally Directed Medical Research Program to Children s National Medical Center and the other from the National Institute of Neurological Disorders and Stroke to the Carolinas Medical Center. This funding is intended to pursue the most promising treatments for DMD. The collaboration will support a series of Good Laboratory Practice, or GLP, toxicology studies for an exon 45-skipping drug candidate based on our PMO chemistry.

To support certain clinical proof of concept studies and IND-enabling activities for an exon 53-skipping therapeutic, we announced in November 2012 that we are collaborating with University College London s scientist, Professor Francesco Muntoni, M.D., the Dubowitz Neuromuscular Centre, the Institute of Child Health and other scientists from the European Union and the United States. In connection with this collaboration, the consortium received an E.U. Health Innovation-1 2012 Collaborative research grant to support development of an exon 53-skipping therapeutic, based on our PMO chemistry. Targeting exon 53 with this technology will potentially address one of the most prevalent sets of mutations in DMD that are amenable to exon-skipping (deletion of exons 42-52, 45-52, 47-52, 48-52, 49-52, 50-52, or 52) by potentially restoring the cellular machinery s ability to produce a functional dystrophin protein.

Table of Contents

To support certain IND-enabling activities for an exon 50-skipping therapeutic, we entered into a Cooperative Research and Development Agreement, or CRADA, in August 2012 with the National Institutes of Health, or NIH, which was anticipated to be supported through in-kind research conducted either by the Therapeutics for Rare and Neglected Diseases program or by contract research organizations. We and NIH mutually agreed to terminate the CRADA in February 2013 and we are now developing exon 50 utilizing our own research and development capabilities. We do not anticipate any significant changes in IND filing timelines due to the termination.

These collaborations and our DMD program, which includes eteplirsen, are part of our larger pan-exon strategy for the development of drug candidates to address the most prevalent exon deletions in the DMD population. Because the majority of DMD patients have exon deletions that cluster together, a small number of exon-skipping therapies will potentially be disease-modifying for a relatively large percentage of DMD patients. Approximately 83% of the total DMD population is potentially treatable with exon-skipping therapeutics. Of this 83%, exon 51 skipping is applicable to the largest sub-group, equal to approximately 16%, and skipping of exons 50 and 45 is applicable to approximately 5% and 10%, respectively.

Infectious Disease Programs

With the financial support of the U.S. government, we are currently implementing our RNA-based technology platforms in our infectious disease programs for the development of therapeutics to treat infectious diseases, such as Marburg and influenza. DoD has provided significant financial support for our development of therapeutics designed to treat Ebola, Marburg, and influenza viruses and we recently entered into an agreement with the National Institute of Allergy and Infectious Diseases, or NIAID, part of NIH, under which NIAID will provide clinical support for the development of a therapeutic designed to treat influenza.

Our current arrangement with DoD supporting the development of our Marburg drug candidate provides funding for all clinical and licensure activities necessary to obtain approval of a New Drug Application, or a NDA, by the FDA if DoD exercises all of its options under the arrangement. 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. Under a separate arrangement, DoD similarly provided funding to advance the development of our H1N1 influenza drug candidate through an IND, application with the FDA and to preclinically evaluate its therapeutic potential against H5N1 (avian flu), Tamiflu® resistant H1N1 (pandemic flu) and H3N2 (seasonal flu) which concluded in 2011. In December 2012, we entered into an agreement with NIAID to support the further development of a drug candidate against influenza viruses AVI-7100. Under the agreement, NIAID researchers are allowed to proceed with a Phase I, study to assess the safety, tolerability and pharmacokinetics of single and multiple doses of AVI-7100 in healthy volunteers. Per the terms of the agreement, we will provide AVI-7100 to NIAID and in return, we will have the right to use the data from this clinical study to support future development of AVI-7100.

Without continued government support of these programs we would likely significantly curtail our development efforts. Future funding and support is subject to availability of budgeted funds from DoD and the Department of Health and Human Services, or DHHS, as government support for some of our infectious disease programs has previously been discontinued or not renewed due to government budget constraints. For example, our current arrangement with DoD initially provided for support of the development of our Ebola virus drug candidate; however, on October 2, 2012, the Company received notice from DoD that the Ebola portion of the arrangement 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 arrangement with DoD 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 arrangement with DoD and the Marburg portion remains actively in development under the DoD arrangement. Additionally, the period of performance for our June 2010 H1N1 influenza contract with DoD expired in June 2011 and our subsequent submissions to a DoD request for proposal, or RFP, for funding of the full clinical development of our influenza drug candidate, AVI-7100, were unsuccessful, although additional research for this antiviral program is being conducted by NIAID as described elsewhere in this report.

Table of Contents

In the periods presented in this report, substantially all of our revenues were derived from research and development contracts with and grants from the U.S. government. As of December 31, 2012, we had completed all of our contracts with the U.S. government except for the Marburg portion of the July 2010 agreement for the development of therapeutics against Marburg and Ebola viruses and the August 2012 agreement for the intramuscular administration of our product candidate against the Marburg virus. Pursuant to these agreements, as of December 31, 2012, the remaining funding for the current segments of the contracts is approximately $19.8 million. In addition, if the U.S. government elects to exercise all its options under the agreements, an additional $84.4 million in funding is available. For a more detailed description of our contracts with the U.S. government, see Management s Discussion and Analysis of Financial Condition and Results of Operations U.S. Government Contracts and Note 6 U.S. Government Contracts of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Hemorrhagic Fever Virus Programs. Our infectious disease therapeutic programs use our translation suppression technology and apply our proprietary PMO*plus*® chemistry backbone, an advanced generation of our base PMO chemistry backbone that selectively introduces positive backbone charges to improve selective interaction between the drug and its target. Our translation suppressing technology is based on Translation Suppressing Oligomers, or TSOs, which are PMO-based compounds that stop or suppress the translation of a specific protein by binding to their specific target sequence in mRNA. We are pursuing development and regulatory approval of our Marburg hemorrhagic fever virus product candidates under the FDA s Animal Rule. The Animal Rule provides that under certain circumstances, where it is unethical or not feasible to conduct human efficacy studies, the FDA may grant marketing approval based on adequate and well-controlled animal studies when the results of those studies establish that the drug or biological product is reasonably likely to produce clinical benefit in humans. Demonstration of the product s safety in humans is still required. See Government Regulation Animal Rule for additional information.

Marburg virus. AVI-7288 is designed for post-exposure prophylaxis after documented or suspected exposure to Marburg virus. Marburg hemorrhagic fever is a severe and often fatal disease in humans that was first recognized in 1967. It is caused by an RNA virus of the Filoviridae family and is understood to be endemic to Africa. The Marburg virus is classified as a Category A bioterrorism agent by the Centers for Disease Control and Prevention, or CDC, and was determined to be a material threat to national security by the Secretary of Homeland Security in 2006. Onset of the disease is often sudden and the symptoms include fever, chills, nausea, vomiting, chest pain and diarrhea. Increasingly severe symptoms may also include massive hemorrhaging and multiple organ dysfunction. There are currently no treatments for Marburg virus infection beyond supportive care and the mortality rate is very high. For Marburg virus infection, our lead product candidate is currently AVI-7288. Previously, our lead product candidate for Marburg virus infection was AVI-6003 which is a combination of AVI-7287 and AVI-7288; however, in February 2012, we announced that we received agreement from the FDA to remove AVI-7287 and we are now proceeding with a single oligomer approach, AVI-7288, given that efficacy in non-human primates has been demonstrated to be attributable to this single oligomer. During the 2012 fiscal year, we completed Phase I single ascending-dose studies in healthy volunteers with our candidates for the treatment of Ebola virus and Marburg virus and in July 2012, we announced results from a non-human primate study of the efficacy of AVI-7288. With the support of DoD s Joint Project Manager Transformational Medical Technologies we are also evaluating the feasibility of in intramuscular route of administration using AVI-7288, including an evaluation of the tolerability, pharmacokinetics, and efficacy of intramuscular AVI-7288. In September 2012, we announced that the FDA has granted fast track status for the development of AVI-7288 and our product candidate against Ebola, AVI-7537.

Ebola virus. AVI-7537 is a single agent designed for post-exposure prophylaxis after documented or suspected exposure to the Ebola virus. The hemorrhagic fever caused by the Ebola virus is severe and often fatal in humans and there are currently no treatments for Ebola beyond supportive care. AVI-6002, a combination of AVI-7537 and AVI-7539, was previously our product candidate for the Ebola virus. However, based on our evaluation of the efficacy of AVI-7537 as a single agent versus a combination with AVI-7539 which demonstrated that efficacy could be attributed to the single oligemer AVI-7537, we transitioned our focus to this

Table of Contents

product candidate in 2012. Although we believe AVI-7537 has the potential to be a therapeutic option for the Ebola virus, we suspended our development efforts with respect to our Ebola program after the August 2012 stop-work order and subsequent termination by DoD of support for this program in 2012. The termination only applies to the Ebola portion of our arrangement with DoD and the Marburg portion remains in effect.

Development Status of Hemorrhagic Fever Virus Programs. Non-human primates infected with Marburg virus and treated with our precursor product candidate, AVI-6003, achieved 100% survival and primates infected with Ebola virus and treated with, AVI-6002, achieved 80% survival, in each case compared to universal lethality in both control groups. In addition to survival, primates treated with AVI-6002 and AVI-6003 have demonstrated decreases in levels of viremia, in harmful inflammatory indicators and in virus induced liver damage. Additional data have also demonstrated that the surviving animals were resistant to viral infection after subsequent injection with the virus.

During the 2012 fiscal year, Sarepta completed Phase I single ascending-dose studies in healthy adult volunteers with its drug candidates for the treatment of Ebola virus and Marburg virus demonstrating positive safety data for each therapeutic candidate. In February 2012, we announced positive safety results from all six cohorts of our Phase I single ascending dose trials of AVI-6002 and AVI-6003. For each group, safety, clinical laboratory and renal biomarker results through five days after treatment were reviewed by an independent Data and Safety Monitoring Board, or DSMB, which issued recommendations for both studies to progress as planned to multiple ascending dose studies after no safety concerns were identified. The Phase I single ascending dose trials were designed to characterize the safety, tolerability and pharmacokinetics of each therapeutic candidate in healthy adult volunteers. In the two studies, a total of 60 healthy human subjects (five per group) were enrolled into six sequential dose groups (0.01, 0.1, 1.0, 3.0, 6.0 or 9.0 mg/kg). Within each group, four subjects received the indicated dose of the therapeutic and one subject received placebo. Final, unblinded safety and pharmacokinetic results for all subjects were completed in 2012.

In July 2012, we announced that AVI-7288 demonstrated up to 100% survival in a non-human primate study exploring the drug s effect when the initiation of treatment is delayed to various time points post-infection. This study showed a high degree of survival between 83% and 100% in each of four post-exposure cohorts that received daily treatments with AVI-7288 beginning one-, 24-, 48-, or 96-hours after infection, compared to 0% survival in the placebo-treated control group.

We plan to initiate a Phase I multiple ascending dose study in the first half of 2013, which is designed to characterize the safety, tolerability and pharmacokinetics of multiple doses of AVI-7288 in healthy adult volunteers. The randomized, double-blind placebo controlled studies will be overseen by an independent DSMB, which will review safety and clinical laboratory data after each dose cohort prior to enrolling the next higher dose cohort.

Influenza Program. Our infectious disease therapeutic programs are also focused on the development of our product candidates designed to treat pandemic influenza viruses. AVI-7100 is our lead product candidate for the treatment of influenza and employs our PMO*plus*® technology. In December 2012, we entered into a contract with NIAID which permits NIAID to conduct a Phase I single and multiple ascending dose study with AVI-7100. In June 2010, we were awarded a contract under DoD s Transformational Medical Technologies, or TMT, program, which funded our activities to develop AVI-7100 as a medical countermeasure against the pandemic H1N1 influenza virus. The period of performance for this contract ended in June 2011. See Management s Discussion and Analysis of Financial Condition and Results of Operations U.S. Government Contracts and Note 6 U.S. Government Contracts of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information.

Symptoms of H1N1 influenza include fever, cough, runny nose, headache, chills and fatigue. Many people infected with H1N1 also have respiratory symptoms without a fever. Severe illness and deaths have also occurred. The CDC estimated that between April 2009 and April 2010 there were up to 89 million cases of H1N1 infection in the United States. The CDC also estimated that there were up to 403,000 H1N1-related hospitalizations in the United States during the same time period.

Table of Contents

The TMT program established a contract with us to conduct a rapid response exercise against a real-world emerging threat like the pandemic H1N1 virus. The intent of the exercise was to demonstrate our capability to efficiently respond to a real-world emerging viral threat by rapidly designing and producing multiple therapeutic candidates and evaluating preclinical efficacy. Initially the exercise involved identifying target sequences against H1N1, designing several drug candidates utilizing proprietary derivatives of our PMO chemistry, and then manufacturing the candidates in sufficient quantity for limited preclinical testing. We successfully accomplished these steps in approximately one week, demonstrating our ability to rapidly respond to a real-world viral threat utilizing our RNA-based technology platforms.

Subsequently, we evaluated the preclinical activity of AVI-7100 and found that it showed a favorable safety profile in ferrets, rats and monkeys. In separate ferret studies, AVI-7100 demonstrated activity as a potentiator of Tamiflu and activity towards preventing transmission of Tamiflu-resistant H1N1.

In June 2011, we initiated dosing of AVI-7100 via intravenous infusion in single-ascending doses in up to 48 healthy adult volunteers. The first dose cohort in this Phase I, randomized, double-blind, placebo-controlled study was completed and received a favorable review from the DSMB to proceed to the next dose escalation. The period of performance under this DoD contract subsequently ended and, as a result, continued development was suspended until we entered into the clinical trial agreement with NIAID.

Under the December 2012 agreement with NIAID, NIAID researchers are allowed to proceed with a Phase I, double-blind, placebo-controlled, dose-escalating study to assess the safety, tolerability and pharmacokinetics of single and multiple doses of an intravenous formulation of AVI-7100 in healthy volunteers. Per the terms of the agreement, we will provide AVI-7100 to NIAID and in return, we will have the right to use the data from this clinical study to support future development of AVI-7100.

Discovery Stage Program Overview

Our PMO-chemistries are highly-differentiated from other RNA technologies, including antisense, siRNA and RNAi. Unlike these technologies, which are often used for down-regulation of gene expression, ours can be used to selectively up-regulate or down-regulate the expression of proteins involved in human diseases and disorders, or direct the production of novel proteins with clinically relevant properties.

In addition to our pan-exon strategy for DMD, our preclinical research efforts are focused on the creation of product candidates for the treatment of other neuromuscular, infectious and rare diseases.

Chemistry Technology

Our core chemistry is based on phosphorodiamidate-linked morpholino oligomers, or PMOs, and this core chemistry has been safely dosed in over 400 patients PMOs are synthetic molecules based on a fundamental redesign of the natural nucleic acid structure of DNA and RNA. PMOs bind to complementary sequences of RNA by standard Watson-Crick nucleic acid base-pairing and control gene expression by steric blockade of targeted RNA. Structurally, the key difference between PMOs and naturally occurring DNA and RNA is that while PMOs, like DNA and RNA, have nucleic acid bases, those bases are bound to synthetic morpholine rings instead of deoxyribose (in DNA) or ribose (in RNA) rings, and they are linked through phosphorodiamidate groups instead of phosphate groups. Replacement of anionic phosphates with the charge-neutral phosphorodiamidate groups eliminates ionization in the usual physiological pH range, thus PMOs in organisms or cells are uncharged molecules. Because of these modifications, PMOs are especially resistant to degradation by plasma and intracellular enzymes. Unlike some other RNA-based technologies, including siRNAs and other types of antisense, PMOs rely on steric blocking rather than cellular enzymatic activity for their biological effects. In this way, PMOs operate fundamentally differently from other well-known RNA-based technologies.

We have developed three new PMO-based chemistry platforms in addition to our original PMO-based technology. We believe that the novel, favorable characteristics intrinsic in these new platforms will allow for the development of drug candidates with superior delivery specificity, therapeutic windows and drug-like properties.

Table of Contents

PPMO. The first of these novel chemistries is based on peptide conjugated PMOs, or PPMOs, in which cellular uptake of the PMO component, as well as its potency and specificity of tissue targeting, may be significantly enhanced.

PMOplus®. The second of these chemistries, PMO*plus*®, includes the addition of selectively introduced positive charges to the PMO backbone. We believe that while PMO*plus*® has potentially broad therapeutic applications, it has thus far shown to be particularly effective in increasing the potency of PMO-based oligomers.

PMO-X. The third of these chemistries, PMO-X, involves novel, selective, and proprietary backbone chemistry modifications. We believe PMO-X may provide enhanced in vivo potency for our drug candidates, as well as greater flexibility in modulation of their tissue targeting, cellular delivery and uptake.

We intend to continue to support our internal research and development efforts in order to advance our proprietary chemistries and to develop new analogues that may provide additional benefits in key characteristics of drug performance.

Mechanisms of Action

Humans have far fewer genes than the number of unique proteins expressed in the human proteome. The genetic information stored in human DNA is not contiguous. Short DNA stretches, called exons that code for fragments of the protein are separated by long non-coding pieces of DNA called introns. During processing of precursor or pre-mRNA, which is copied from the DNA template, introns are removed and exons spliced together to create the mature mRNA, from which a functional protein can be made. Pre-mRNA copied from a gene can be spliced through alternative paths, such that different exons are combined, creating multiple mRNAs and, hence, generate multiple proteins from a single gene.

Our PMO-based molecules are designed to sterically block the access of cellular machinery to pre-mRNA and mRNA without degrading the RNA. Through this selective targeting, two distinct biologic mechanisms of action can be initiated: (1) modulation of pre-mRNA splicing (also commonly described as splice switching, exon skipping or directed alternative splicing) and (2) inhibition of mRNA translation (also commonly described as translation suppression). Through these mechanisms, steric-blocking oligonucleotides can repair defective RNA, up or down-regulate the production of selected proteins, or produce novel or remodeled proteins.

Material Agreements and Strategic Alliances

We believe that our RNA-based technology could be broadly applicable for the potential development of pharmaceutical products in many therapeutic areas. To further exploit our core technology, we have and may continue to enter into research, development or commercialization alliances with universities, hospitals, independent research centers, non-profit organizations and pharmaceutical and biotechnology companies for specific molecular targets or selected disease indications. We may also selectively pursue opportunities to access certain intellectual property rights that complement our internal portfolio through license agreements or other arrangements.

U.S. Department of Defense and DHHS Agreements

We currently have contracts with DoD and its agencies and DHHS and its agencies, funding and supporting our programs. For a more detailed description of our contracts with the U.S. government, see Management s Discussion and Analysis of Financial Condition and Results of Operations U.S. Government Contracts below and Note 6 U.S. Government Contracts of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K. Our contracts with the government may be subject to renegotiation or termination at the election of the government. For a description of the risks we face relating to such rights of the government see Risk Factors Risks Relating to Our Business

Table of Contents

University of Western Australia

In November 2008, we entered into an exclusive license with the University of Western Australia, or UWA, for certain patents and technical information relating to the use of certain antisense sequences for the treatment of DMD. The license grants us specific rights to the treatment of DMD by inducing the skipping of certain exons. Unless earlier terminated in accordance with the terms of the agreement, such agreement will expire on the expiration date of the last to expire patent within the patents licensed to us under the agreement. Our clinical candidate, eteplirsen, falls under the scope of this agreement. Any future drug candidates developed for the treatment of DMD by exon skipping may or may not fall under the scope of this agreement.

Under the agreement, we are required to meet certain performance diligence obligations related to development and commercialization of products developed under license. We believe we are currently in compliance with these obligations. We made an initial upfront payment to UWA on execution of the license. We may be required to make additional payments to UWA of up to a total of $150,000 based on successful achievement of certain regulatory-related milestones and also may be required to pay royalties ranging from a fraction of a percent to the low single digits on net sales of products covered by issued patents licensed from UWA during the term of the agreement. As of December 31, 2012, we have made milestone payments to UWA of approximately $10,000, but have not made, and are not under any current obligation to make, any royalty payments to UWA until a product candidate is approved for commercial sale.

Strategic Alliances

Isis Ercole Agreement

In May 2003, Ercole Biotechnology, Inc., or Ercole, and Isis Pharmaceuticals, or Isis, entered into a collaboration and license agreement related to RNA splicing. In March 2008, we acquired all of the stock of Ercole in exchange for 5,811,721 shares of our common stock, which was valued at approximately $8.4 million, and the assumption of approximately $1.8 million in liabilities of Ercole. We also issued warrants to purchase our common stock (also classified as equity), which were valued at $437,000, in exchange for certain outstanding warrants issued by Ercole. In connection with the March 2008 acquisition, we assumed Ercole s obligations under the Isis agreement. This agreement contains several cross-licenses between the parties granting each party certain exclusive and nonexclusive rights under a selected set of the other parties patents and patent applications for the research, development, and commercialization of antisense therapeutics using RNA splicing with respect to certain gene targets.

Subject to the satisfaction of certain milestones triggering the obligation to make any such payments, we may be obligated to make milestone payments to Isis of up to $23.4 million in the aggregate for each product developed under a licensed patent under this agreement.

As of December 31, 2012, we have not made, and are not under any current obligation to make, any such milestone payments, as the conditions triggering any such milestone payment obligations have not been satisfied. The range of percentage royalty payments required to be made by us under the terms of this agreement is from a fraction of a percent to mid single digits. We believe that our DMD, Ebola, Marburg and influenza programs will not fall under the scope of this agreement and therefore will not be subject to milestone or royalty obligations under its provisions.

Subject to the satisfaction of certain milestones triggering the obligation to make any such payments, Isis may be obligated to make milestone payments to us of up to $21.1 million in the aggregate for each product developed under a licensed patent under this agreement. As of December 31, 2012, Isis has not made any such milestone payments, as the conditions triggering any such milestone payment obligations have not been satisfied. The percentage royalty payments required to be made by Isis under the terms of this agreement is a fraction of a percent. As to any product commercialized under the agreement, the agreement will terminate on the expiration date of the last to expire licensed patent covering such product. Research collaboration activity defined in the agreement expired in 2006.

Table of Contents

Charley s Fund Agreement

In October 2007, Charley s Fund, Inc., or Charley s Fund, a nonprofit organization that funds drug development and discovery initiatives specific to DMD, awarded us a $2.45 million research grant and, in May 2009, the grant authorization was increased to a total of $5.0 million. Pursuant to the related sponsored research agreement, the grant was provided to support the development of product candidates related to exon 50 skipping using our proprietary exon skipping technologies. As of December 31, 2012, Charley s Fund has made payments of approximately $3.4 million to us. Revenue associated with this research and development arrangement is recognized based on the proportional performance method, using the payment received method. To date, we have recognized $60,000 as revenue, but did not recognize any revenue for the years ended December 31, 2012, 2011 and 2010. We do not expect to receive any incremental funding under the grant and have deferred $3.3 million of previous receipts which are anticipated to be recognized as revenue once we complete the remaining milestones.

Under the terms of the sponsored research agreement, as amended, if we and any of our strategic partners elect to discontinue the development and commercialization of any product containing any molecular candidate arising or derived from the research sponsored by Charley s Fund for reasons other than safety or efficacy, we must grant to Charley s Fund an exclusive, royalty-bearing, fully-paid, worldwide license, with right of sublicense, to any such product. Depending on whether and when Charley s Fund obtains a license to any such product, percentage royalty payments on net sales required to be made by Charley s Fund to us under the terms of the sponsored research agreement, as amended, would be in the mid single digits. Under the terms of the sponsored research agreement, as amended, if we are able to successfully commercialize any molecular candidate arising or derived from the research sponsored by Charley s Fund either through sales of products or through licensing or partnership arrangements with a third party that include rights for such third party to sell, distribute, promote or market such products or the underlying intellectual property, then we are obligated to repay the research funds paid to us by Charley s Fund, up to an amount equal to the total amount of funds provided by Charley s Fund to us. In connection with this repayment obligation, we agreed that we would pay a mid range single-digit percentage royalty on net sales of products containing any molecular candidate arising or derived from the research sponsored by Charley s Fund and a mid-teens amount of any upfront cash and/or milestone payments received from a licensing or partnership arrangement with a third party with respect to such products (in each case, up to an amount equal to the total amount of funds provided by Charley s Fund to us). This agreement will terminate by its own terms at the completion of the research being sponsored by Charley s Fund. The Sarepta technology upon which the agreement is based is covered by certain patents, the last of which expires following the termination of the agreement.

Previously, we noted unexpected toxicology findings in the kidney as part of our series of preclinical studies for AVI-5038, our PMO-based candidate designed for the treatment of individuals with DMD who have an error in the gene coding for dystrophin that can be treated by skipping exon 50. We have conducted additional preclinical studies and have not alleviated the toxicity problem. Pursuant to the terms of our agreement with Charley s Fund, the receipt of additional funds is tied to the satisfaction of certain clinical milestones. Because of the toxicity issues with AVI-5038, satisfaction of the additional milestones under the agreement is unlikely and we do not expect to receive any additional funds from Charley s Fund.

Manufacturing

We believe we have developed proprietary manufacturing techniques that allow synthesis and purification of our product candidates to support clinical development. We have entered into certain manufacturing and supply arrangements with third-party suppliers which will in part utilize these techniques to support production of certain of our product candidates and their components. We do not have, and do not intend to establish in the near term, any of our own internal mid-to-large scale manufacturing capabilities to support our product candidates.

For our current development programs we have entered into supply agreements with certain large pharmaceutical manufacturing firms for the production of the custom raw materials required for PMO production and the active pharmaceutical ingredients, or APIs, for our product candidates.

Table of Contents

For our DMD program, during the first half of this year, we are working to increase our API production capacity from small-scale to mid-scale with our existing manufacturers. During 2013, we will also evaluate whether to increase our API production capacity to a commercial scale. This decision will depend in significant part on our discussions with the FDA in 2013 as well as our expectations regarding if, and when, we would commence a pivotal trial for eteplirsen and potential commercialization.

There are a limited number of companies that can produce raw materials and APIs in the quantities and with the quality and purity that we require for our DMD development efforts. Due to their technical expertise, experience in manufacturing our product candidates and sophistication of their manufacturing facilities and quality systems, we are considering our existing manufacturers, as well as other manufacturers with relevant expertise, for the further scale-up of the production of raw materials and APIs for our DMD program. Establishing a relationship with alternative suppliers can be a lengthy process and might cause delays in our development efforts. If we are required to seek alternative supply arrangements, the resulting delays and potential inability to find a suitable replacement could materially and adversely impact our business.

Manufacturers and suppliers of product candidates are subject to the FDA s current Good Manufacturing Practices, or cGMP, requirements, and other rules and regulations prescribed by foreign regulatory authorities. We depend on our third-party suppliers and manufacturers for continued compliance with cGMP requirements and applicable foreign standards.

Sales and Marketing Strategy

We have not obtained regulatory approval for any of our product candidates and thus have not yet established a commercial organization or distribution capabilities. Due to the rare nature of DMD and the lack of disease-modifying treatments, patients suffering from DMD, together with their physicians, often have a high degree of organization and are well informed, which may simplify the identification of a target population for eteplirsen, our lead product candidate, if it is approved. We believe that, if approved for commercial sale, it will be possible to commercialize eteplirsen with a relatively small specialty sales force that calls on the physicians, foundations and other patient-advocacy groups focused on DMD. Our current expectation is to commercialize eteplirsen ourselves in the United States and plan to recruit a sales force and take other steps to establish the necessary commercial infrastructure at such time as we believe that eteplirsen is approaching marketing approval. We will continue to evaluate whether to market our DMD product candidates outside of the United States ourselves or enter into arrangements with other pharmaceutical or biotechnology companies for the marketing and sale of our products outside the United States either globally or on a country-by-country basis.

Patents and Proprietary Rights

Our success depends in part upon our ability to protect our core technology and intellectual property. To accomplish this, we rely on a combination of intellectual property rights, including patents, trade secrets, copyrights and trademarks, and contractual protections.

We seek appropriate patent protection for our proprietary technologies by filing patent applications in the United States and other countries. As of February 28, 2013, we owned or controlled approximately 290 U.S. and corresponding foreign patents and 185 U.S. and corresponding foreign patent applications. We intend to protect our proprietary technology with additional filings as appropriate.

Our patents and patent applications are directed to our product candidates as well as to our RNA-based technology platforms. Although we believe our patents and patent applications provide us with a competitive advantage, the patent positions of biotechnology and pharmaceutical companies can be uncertain and involve complex legal and factual questions. We and our collaborators may not be able to develop patentable products or

Table of Contents

processes or obtain patents from pending patent applications. Even if patent claims are allowed, the claims may not issue, or in the event of issuance, may not be sufficient to protect the technology owned by or licensed to us or our collaborators. For example, our competitor Prosensa has rights to European Patent No. EP 1619249. We opposed this patent in the Opposition Division of the European Patent Office, or the Opposition Division, and in November 2011, we announced that, although we succeeded in invalidating some of the patent s claims, the Opposition Division maintained in amended form certain claims of this patent relating to the treatment of DMD by skipping dystrophin exons 51 and 46. We and Prosensa both have the right to appeal this decision; however, pending final resolution of this matter and any appeal thereof, the patent at issue may provide the basis for Prosensa or other parties that have rights to such patent to assert that our drug eteplirsen infringes on such patent. The timing and outcome of an appeal, if pursued, cannot be predicted or determined as of the date of this report. We are also aware of certain claims that have issued to Prosensa in Japan that may provide the basis for Prosensa or other parties that have rights to these claims to assert that our drug eteplirsen infringes on such claims. We believe we have a basis to invalidate some or all of these claims and are evaluating the potential initiation of invalidation proceedings. Because we have not yet initiated an invalidation proceeding in Japan, the outcome and timing of such proceeding cannot be predicted or determined as of the date of this report. If as part of any appeal in the European Union we are unsuccessful in invalidating other of Prosensa s claims or if previously invalidated claims are restored on appeal, our ability to commercialize both eteplirsen and other therapeutic candidates for our pan-exon strategy could be materially impaired. We are also aware of certain claims that Prosensa has rights to in the United States that may provide the basis for Prosensa or other parties that have rights to these claims to assert that our drug eteplirsen infringes on such claims. We believe we have valid defenses to any such allegations or a basis to invalidate some or all of these claims and do not believe that Prosensa s patent seriously harms our ability to develop and commercialize our products; however, we cannot be certain of this. The DMD patent landscape is continually evolving and multiple parties, both commercial entities and academic institutions, may have rights to claims that could provide these parties a basis to assert that our product candidates infringe on these claims. Similarly, we may be able to assert that certain activities engaged in by these parties infringe on our patent rights. There has been, and we believe that there will continue to be, significant litigation in the biopharmaceutical and pharmaceutical industries regarding patent and other intellectual property rights. We also cannot be certain that other third parties will not assert patent infringement in the future with respect to any of our development programs.

Our clinical product candidates and our technology are protected by composition and use patents and patent applications. Patent protection afforded by the patents and patent applications covering our product candidates and out technology will expire over the following time frames:

Product Candidate / Technology	Expiration of Patent Protection
Eteplirsen	2025 (patents) 2030 (patents)
Other DMD exons	2025 (patent applications) 2030 (patents)
Exon-skipping	2013 (patents) 2023 (patents)
Antivirals (Ebola, Marburg, Dengue and Influenza)	2022 (patents) 2030 (patent applications)
Chemistry (PPMO, PMO*plus*® and PMO-X)	2024 (patents) 2032 (patent applications)
Antibacterials	2018 (patents) 2031 (patent applications)
Other rare diseases	2025 (patent applications) 2032 (patent applications)
Other targets and programs	2019 (patents) 2032 (patent applications)

Some of our patents on core technologies expired in 2008, including a patent for our basic PMO chemistry. However, as we continue to advance the research supporting our PMO-based technologies, we believe that the patented and likely patentable improvements we are developing will provide the necessary basis to develop and exclusively commercialize our products. We also rely on trade secrets and proprietary know-how, especially when we do not believe that patent protection is appropriate or can be obtained. Our policy is to require each of our employees, consultants and advisors to execute a confidentiality and inventions assignment agreement before beginning their employment, consulting or advisory relationship with us. These agreements provide that the individual must keep confidential and not disclose to other parties any confidential information developed or

Table of Contents

learned by the individual during the course of their relationship with us except in limited circumstances. These agreements also provide that we shall own all inventions conceived by the individual in the course of rendering services to us.

We are the owner of federal trademark registrations for four registered trademarks in the United States: AVI BioPharma®, Cytoporter®, PMO*plus*® and NeuGene®. We have pending trademark applications in the United States for PMO-X , Sarepta and Sarepta Therapeutics . We are the owner of international trademark registrations for Kepler Pharmaceuticals® in the European Community, Australia, New Zealand, Mexico, Norway and Switzerland; however, we have decided to let these registrations for Kepler Pharmaceuticals® expire at the end of their terms and will not seek to renew them. We have licensed certain technology to supplement and support certain of our core technologies. We have certain obligations and minimum royalties under those agreements, which costs are not material to our business and can be terminated at our discretion with minimal notice.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of the use, formulation and structure of our product candidates, and the methods used to manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to protect our product candidates from unauthorized making, using, selling, offering to sell or importing by third parties is dependent on the extent to which we have rights under valid and enforceable patents that cover these activities.

We do not have patents or patent applications in every jurisdiction where there is a potential commercial market for our product candidates. For each of our programs, our decision to seek patent protection in specific foreign markets, in addition to the United States, is based on many factors, including:

- our available resources;
- the number and types of patents already filed or pending;
- the likelihood of success of the product candidate;
- the size of the commercial market;
- the presence of a potential competitor in the market; and
- whether the legal authorities in the market effectively enforce patent rights.

We continually evaluate our patent portfolio and patent strategy and believe our owned and licensed patents and patent applications provide us with a competitive advantage; however, if markets where we do not have patents or patent applications become commercially important, our business may be adversely affected.

The patent positions of pharmaceutical, biotechnology and other life sciences companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date in the United States, and tests used for determining the patentability of patent claims in all technologies are in flux. In addition, there is no assurance as to the degree and range of protections any of our patents, if issued, may afford us or whether patents will be issued. For example, patents which may issue to us may be subjected to further governmental review that may ultimately result in the reduction of their scope of protection, and pending patent applications may have their requested breadth of protection significantly limited before being issued, if issued at all. The pharmaceutical, biotechnology and other life sciences patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in the patents that we own or have licensed or in third-party patents. Further, since publication of discoveries in scientific or patent literature often lags behind actual discoveries, there is no assurance that we were the first creator of inventions covered by our pending patent applications, or that we were the first to file patent applications for these inventions.

Table of Contents

Government Regulation

The testing, manufacturing, labeling, advertising, promotion, distribution, export and marketing of our products are subject to extensive regulation by governmental authorities in the United States and in other countries. In the United States, the FDA, under the Federal Food, Drug and Cosmetic Act and its implementing regulations, regulates pharmaceutical products. Failure to comply with applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, withdrawal of approval of approved products, warning letters, untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, civil penalties and/or criminal prosecution.

Drug Approval Process

To obtain FDA approval of a product candidate, we must, among other things, submit data providing substantial evidence of safety and efficacy of the product, as well as detailed information on the manufacture and composition of the product candidate and proposed labeling. The testing and collection of data and the preparation of necessary applications are expensive and time-consuming. The FDA may not act quickly or favorably in reviewing these applications, and we may encounter significant difficulties or costs in our efforts to obtain FDA approvals that could delay or preclude us from marketing our products.

The steps required before a drug may be approved for marketing in the United States generally include the following, with exceptions noted in the section captioned Government Regulation Animal Rule :

- preclinical laboratory tests and animal tests;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug product for each indication;
- the submission to the FDA of a NDA;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made to assess compliance with cGMP;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA.

Preclinical studies may include laboratory evaluations of the product chemistry, toxicity, and formulation, as well as animal studies to assess the potential safety and efficacy of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of the IND, which must become effective before clinical trials may be commenced. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the clinical trials as described in the protocol submitted as part of the IND prior to that time. In this case, the trials are placed on clinical hold, and the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed.

Clinical trials involve the administration of the product candidate to healthy volunteers or participants under the supervision of a qualified principal investigator. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted in accordance with the FDA s good clinical practices requirements and state subject rights laws. Further, each clinical trial must be

reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical

Table of Contents

trial design, participant informed consent, ethical factors, the safety of human subjects, and the possible liability of the institution. The FDA may order the partial, temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial subjects. The IRB may also require the clinical trial at that site to be halted, either temporarily or permanently, for failure to comply with the IRB s requirements, or may impose other conditions.

Clinical trials typically are conducted in three sequential phases prior to approval, but the phases may overlap. A fourth, or post-approval, phase may include additional clinical studies. These phases generally include the following; however, in the rare disease space, the number of subjects involved in each phase can be significantly less than the general parameters set forth below:

Phase I. Phase I clinical trials involve the initial introduction of the drug into human subjects. These studies are designed to determine the safety of usually single doses of the compound and determine any dose limiting intolerance, as well as evidence of the metabolism and pharmacokinetics of the drug in humans. Phase I studies usually involve less than 100 subjects and are most commonly conducted in healthy adult volunteers.

Phase II. Phase II clinical trials usually involve studies in a limited patient population to evaluate the efficacy of the drug for specific, targeted indications, to determine dosage tolerance and optimal dosage, and to identify possible adverse effects and safety risks. Phase II studies usually involve patients with the disease under investigation and numbers may vary from several dozen to several hundred.

Phase III. If a compound is found to be potentially effective and to have an acceptable safety profile in Phase II (or sometimes Phase I) studies, the clinical trial program will be expanded to further confirm clinical efficacy, optimal dosage and safety within an expanded patient population which may involve geographically dispersed clinical trial sites. Phase III studies usually include several hundred to several thousand patients. Generally, two adequate and well-controlled Phase III clinical trials are required by the FDA for approval of an NDA.

Phase IV. Phase IV clinical trials are studies required of or agreed to by a sponsor that are conducted after the FDA has approved a product for marketing. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase IV clinical trial requirement. Failure to promptly conduct Phase IV clinical trials could result in withdrawal of approval for products approved under accelerated approval regulations.

A company seeking marketing approval for a new drug in the United States must submit to the FDA the results of the preclinical and clinical trials, together with, among other things, detailed information on the manufacture and composition of the product candidate and proposed labeling, in the form of an NDA, including payment of a user fee. The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has ten months in which to complete its initial review of a standard NDA and respond to the applicant, and six months for a priority NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date. If the FDA s evaluations of the NDA and the clinical and manufacturing procedures and facilities are favorable, the FDA may issue an approval letter. If the FDA finds deficiencies in the NDA, it may issue a complete response letter, which contains the conditions that must be met in order to secure final approval

Table of Contents

of the NDA. If and when those conditions have been met to the FDA s satisfaction, the FDA will issue an approval letter, authorizing commercial marketing of the drug for certain indications. If the FDA s evaluation of the NDA submission and the clinical and manufacturing procedures and facilities is not favorable, the FDA may refuse to approve the NDA. Sponsors that receive a complete response letter may submit to the FDA information that represents a complete response to the issues identified by the FDA. Resubmissions by the NDA sponsor in response to a complete response letter trigger new review periods of varying length (typically two to six months) based on the content of the resubmission. The FDA may also refer an application to an appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee.

A sponsor may also seek approval of its drug candidates under programs designed to accelerate the FDA s review and approval of NDAs. For instance, a sponsor may seek FDA designation of a drug candidate as a fast track product. Fast track products are those products intended for the treatment of a serious or life-threatening disease or condition and which demonstrate the potential to address unmet medical needs for such disease or condition. If fast track designation is obtained, the FDA may initiate early, frequent, communication and begin reviewing sections of an NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the remaining information. We were granted fast track status for eteplirsen in 2007 and we announced in September 2012 that the FDA granted fast track status for the development of both AVI-7288 and AVI-7537.

The Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted and signed into law in 2012 amended the criteria for the fast track and accelerated approval pathways and, as a result, the pathways now shares many common eligibility criteria. FDASIA provides both sponsor companies and the FDA with greater flexibility with expedited regulatory mechanisms. The statute clarifies that a fast track product may be approved pursuant to an accelerated approval (Subpart H) or under the traditional approval process. In addition, FDASIA codified the accelerated approval pathway as separate and apart from fast track pathway, meaning that for drugs to be eligible for accelerated approval, they do not need to be designated under the fast track pathway. FDASIA reinforces FDA s authority to grant accelerated approval based on surrogate endpoints that are reasonably likely to predict clinical benefit, and provides for more expansive use of non-surrogate clinical endpoints by authorizing FDA to grant accelerated approval based on the use of clinical endpoints that can be measured earlier in the development process than irreversible morbidity or mortality, and that are reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. In determining whether to grant accelerated approval, the FDA must consider the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Approvals of this kind typically include requirements for appropriate post-approval Phase IV clinical trials. FDASIA retains this requirement and further requires those studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit. We are participating in an end of Phase II meeting with the FDA in the first quarter of 2013 to discuss the clinical results from our Phase IIb study of eteplirsen. Based on feedback from the meeting, we will make an initial determination regarding the most appropriate regulatory path for pursuing regulatory review and approval of eteplirsen. Our initial determination will be further informed by a subsequent Chemistry, Manufacturing and Controls, or CMC, meeting.

Additionally, FDASIA established a new, expedited regulatory mechanism referred to as breakthrough therapy designation. Breakthrough therapy designation, fast track, and accelerated approval are not mutually exclusive and are meant to serve different purposes. The breakthrough therapy designation is focused on expediting the development and review process and by itself does not create an alternate ground for product approval. A sponsor may seek FDA designation of a drug candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA is required to issue guidance to implement this provision and,

Table of Contents

if deemed necessary, is required to amend its regulations by the end of 2014. We will continue to evaluate, with input from the FDA, applying for breakthrough therapy designation as one aspect of our regulatory approach.

Finally, drug candidates, upon submission of an NDA, may also be eligible for priority review, or review within a six month timeframe from the date a complete NDA is accepted for filing, if a sponsor shows that its drug candidate provides a significant improvement compared to marketed drugs.

We cannot be sure that any of our drug candidates will qualify for any of these expedited development, review and approval programs, or that, if a drug does qualify, that the product candidates will be approved, will be accepted as part of any such program or that the review time will be shorter than a standard review.

Often, even after a drug has been approved by the FDA for sale, the FDA may require that certain post-approval requirements be satisfied, including the conduct of additional clinical studies. If such post-approval conditions are not satisfied, the FDA may withdraw its approval of the drug. In addition, holders of an approved NDA are required to:

- report certain adverse reactions to the FDA;
- submit annual and periodic reports summarizing product information and safety data;
- comply with certain requirements concerning advertising and promotional labeling for their products; and
- continue to have quality control and manufacturing procedures conform to cGMP after approval.

The FDA periodically inspects the sponsor s records related to safety reporting and/or manufacturing; this latter effort includes assessment of compliance with cGMP. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including withdrawal of the product from the market.

Many other countries and jurisdictions have similar drug development and regulatory review processes. We have conducted clinical trials in the United Kingdom and intend to submit for marketing approval in countries other than the United States. Therefore, we will have to comply with the legal and regulatory requirements in the countries where we conduct trials and submit for marketing approval.

Animal Rule

In the case of product candidates that are intended to treat rare life-threatening diseases, such as infection caused by exposure to various hemorrhagic fever viruses, conducting controlled clinical trials to determine efficacy may be unethical or unfeasible. Under regulations issued by the FDA in 2002, often referred to as the Animal Rule, the approval of such products can be based on clinical data from trials in healthy human subjects that demonstrate adequate safety, and immunogenicity and efficacy data from adequate and well-controlled animal studies. Among other requirements, the animal studies must establish that the drug or biological product is reasonably likely to produce clinical benefits in humans. Because the FDA must agree that data derived from animal studies may be extrapolated to establish safety and effectiveness in humans, seeking approval under the Animal Rule adds significant time, complexity and uncertainty to the testing and approval process. No animal model is established as predicting human outcomes in the prevention or treatment of any filovirus disease. We have yet to demonstrate the predictive value of our animal studies to the FDA s satisfaction. In addition, products approved under the Animal Rule are subject to additional requirements including post-marketing study requirements, restrictions imposed on marketing or distribution or requirements to provide information to patients. Only one novel medical countermeasures has been approved using this pathway to date. Three other countermeasures have been approved under the Animal Rule which were extensions of existing indications with

Table of Contents

human data to support efficacy. Additional clarity on animal rule requirements is not anticipated until later in 2013 when the FDA is expected to release an updated version of its draft guidance on the animal rule that was first published in January 2009.

Emergency Use Authorization

The Commissioner of the FDA, under delegated authority from the Secretary of DHHS may, under certain circumstances, issue an Emergency Use Authorization, or EUA, that would permit the use of an unapproved drug product or unapproved use of an approved drug product. Before an EUA may be issued, the Secretary must declare an emergency based on one of the following grounds:

- a determination by the Secretary of Department of Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a specified biological, chemical, radiological or nuclear agent or agents;
- a determination by the Secretary of DoD that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces of attack with a specified biological, chemical, radiological, or nuclear agent of agents; or
- a determination by the Secretary of DHHS of a public health emergency that effects or has the significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such agent or agent.

In order to be the subject of an EUA, the FDA Commissioner must conclude that, based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing a disease attributable to the agents described above; that the product s potential benefits outweigh its potential risks; and that there is no adequate, approved alternative to the product.

Although an EUA cannot be issued until after an emergency has been declared by the Secretary of DHHS, the Agency strongly encourages an entity with a possible candidate product, particularly one at an advanced stage of development, to contact the FDA Center responsible for the candidate product before a determination of actual or potential emergency. Such an entity may submit a request for consideration that includes data to demonstrate that, based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing the serious or life-threatening disease or condition. This is called a pre-EUA submission and its purpose is to allow FDA review considering that during an emergency, the time available for the submission and review of an EUA request may be severely limited. We intend to work with DoD in the future on pre-EUA submissions with respect to our product candidates intended to treat Marburg and Ebola in order to inform and expedite the FDA s issuance of an EUA, should one become necessary in the event of an emergency.

Orphan Drug Designation and Exclusivity

Some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. In the United States, orphan drug designation must be requested before submitting an application for marketing approval. An orphan drug designation does not shorten the duration of the regulatory review and approval process. The approval of an orphan designation request does not alter the standard regulatory requirements and process for obtaining marketing approval. Safety and efficacy of a compound must be established through adequate and well-controlled studies. If a product which has an orphan

Table of Contents

drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to an orphan drug exclusivity period, which means the FDA may not grant approval to any other application to market a different drug for the same indication for a period of seven years, except in limited circumstances, such as where an alternative product demonstrates clinical superiority to the product with orphan exclusivity. In addition, holders of exclusivity for orphan drugs are expected to assure the availability of sufficient quantities of their orphan drugs to meet the needs of patients. Failure to do so could result in the withdrawal of marketing exclusivity for the drug. An additional six months of exclusivity may be granted to a sponsor of an NDA, if the sponsor conducted a pediatric study or studies of such product. This process is initiated by the FDA as a written request for pediatric studies that applies to sponsor s product. If the sponsor conducts qualifying studies and the studies are accepted by the FDA, then an additional six months of pediatric exclusivity will attach to any other regulatory exclusivity or patent protection applicable to any drug product containing the same active moiety as the drug studied and for which the party submitting the studies holds the NDA. Competitors may receive approval of different drugs or biologics for the indications for which the orphan product has exclusivity. We have been granted orphan drug designation for eteplirsen and AVI-5038 in the United States and European Union.

The European Orphan Drug Regulation is considered for drugs intended to diagnose, prevent or treat a life-threatening or very serious condition afflicting five or fewer out of 10,000 people in the EU, including compounds that for serious and chronic conditions would likely not be marketed without incentives due to low market return on the sponsor s development investment. The medicinal product considered should be of significant benefit to those affected by the condition. Benefits of being granted orphan drug designation are significant, including eight years of data exclusivity, two years of marketing exclusivity and a potential one year extension of both. The EU Community and Member States may not accept or grant for ten years a new marketing authorization or application for another drug for the same therapeutic indication as the orphan drug, although the ten year period can be reduced to six years if, at the end of the fifth year, available evidence establishes that the product is sufficiently profitable not to justify maintenance of market exclusivity. A supplementary protection certificate may extend the protection six months beyond patent expiration if that is later than the orphan drug exclusivity period. To apply for the supplementary protection, a pediatric investigation plan, or PIP, must be included in the market application. In Europe all drugs now seeking a marketing authorization need to have a PIP agreed with the EMA before it can be approved, even if it is a drug being developed specifically for a pediatric indication. If a product is developed solely for use in the pediatric population, then a Pediatric Use Marketing Authorization, or PUMA, may provide eight years of data exclusivity and ten years of marketing exclusivity. This PUMA applies to our DMD compounds, eteplirsen and AVI-5038.

Other Regulatory Requirements

In addition to regulation by the FDA and certain state regulatory agencies, we are also subject to a variety of foreign regulations governing clinical trials and the marketing of other products. Outside of the United States, our ability to market a product depends upon receiving a marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from country to country. In any country, however, we will only be permitted to commercialize our products if the appropriate regulatory authority is satisfied that we have presented adequate evidence of safety, quality and efficacy. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must be obtained prior to the commencement of marketing of the product in those countries. The time needed to secure approval may be longer or shorter than that required for FDA approval. The regulatory approval and oversight process in other countries includes all of the risks associated with regulation by the FDA and certain state regulatory agencies as described above.

Pharmaceutical Pricing and Reimbursement

In both U.S. and foreign markets, our ability to commercialize our products successfully, and to attract commercialization partners for our products, depends in significant part on the availability of adequate financial coverage and reimbursement from third-party payers, including, in the United States, governmental payers such

Table of Contents

as the Medicare and Medicaid programs, managed care organizations, and private health insurers. Third-party payers are increasingly challenging the prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost effectiveness of our products. Even with the availability of such studies, our products may be considered less safe, less effective or less cost-effective than alternative products, and third-party payers may not provide coverage and reimbursement for our product candidates, in whole or in part.

Political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could significantly affect our business, including the Patient Protection and Affordable Care Act of 2010. We anticipate that the U.S. Congress, state legislatures and the private sector will continue to consider and may adopt healthcare policies intended to curb rising healthcare costs. These cost containment measures include:

- controls on government funded reimbursement for drugs;
- mandatory discounts under certain government sponsored programs;
- controls on healthcare providers;
- challenges to the pricing of drugs or limits or prohibitions on reimbursement for specific products through other means;
- reform of drug importation laws; and
- expansion of use of managed care systems in which healthcare providers contract to provide comprehensive healthcare for a fixed cost per person.

We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted could have a material adverse effect on our business prospects.

Competition

The pharmaceutical and biotechnology industries are intensely competitive, and any product candidate developed by us would likely compete with existing drugs and therapies. There are many pharmaceutical companies, biotechnology companies, public and private universities, government agencies and research organizations that compete with us in developing various approaches to the treatment of rare and infectious diseases. Many of these organizations have substantially greater financial, technical, manufacturing and marketing resources than we have. Several of them have developed or are developing therapies that could be used for treatment of the same diseases that we are targeting. In addition, many of these competitors have significantly greater commercial infrastructures than we have. Our ability to compete successfully will depend largely on:

- our ability to complete clinical development and obtain regulatory approvals for our product candidates;
- the efficacy, safety and reliability of our product candidates;

the timing and scope of regulatory approvals;

product acceptance by physicians and other health care providers;

protection of our proprietary rights and the level of generic competition;

the speed at which we develop product candidates;

our ability to supply commercial quantities of a product to the market;

Table of Contents

obtaining reimbursement for product use in approved indications;

our ability to recruit and retain skilled employees; and

the availability of substantial capital resources to fund development and commercialization activities, including the availability of funding from the U.S. Government.

DMD Program Competition. Currently, no product has been approved for the treatment of DMD. Companies including, but not limited to, Prosensa in collaboration with GlaxoSmithKline plc, or GSK, have product candidates in development for the treatment of DMD.

The Prosensa / GSK program commenced treatment in December 2010 in a Phase III clinical study in ambulant individuals with DMD who have a dystrophin gene mutation amenable to treatment by skipping exon 51. Prosensa s candidate for skipping exon 51, GSK2402968, utilizes a different chemistry, 2 O-methyl-phosphorothioate, which has the potential for different performance, safety and tolerability characteristics than eteplirsen. This randomized, placebo controlled study is fully enrolled, with approximately 180 participants who are being dosed for 48 weeks. The primary efficacy endpoint is a measure of muscle function using the 6MWT. Results for this Phase III study are anticipated by the end of 2013. In September 2010, the Prosensa / GSK program commenced a Phase II double-blind, placebo-controlled study. This study is designed to assess the efficacy of two different dosing regimens of GSK2402968 administered over 24 weeks in DMD patients, and then to continue observing the patients over a second 24 week interval for a total study time frame of 48 weeks. This study completed enrollment with 54 DMD patients in October 2011 and has since concluded with results expected after the Phase III clinical study is complete. Another study using GSK2402968 in non-ambulatory DMD patients has been initiated using a 6 mg/kg dose and is anticipated to enroll 20 patients. These studies may or may not prove that GSK2402968 is safer and more efficacious than eteplirsen; however, data obtained from these studies could aid Prosensa / GSK in obtaining marketing approval before our lead DMD product candidate eteplirsen.

Hemorrhagic Fever Virus Programs. No specific treatment has been proven effective, and no approved vaccine currently exists for either Ebola or Marburg. Investigational compounds cannot be tested for efficacy on humans except in outbreak environments so these agents must be tested extensively in animals and meet strict government regulations. Vaccine development is in the early stages in both the biotech industry and by U.S. government agencies (*e.g.*, the National Institute of Allergy and Infectious Diseases and the Centers for Disease Control and Prevention). The government is also supporting early stage research on broad-spectrum therapeutics effective against hemorrhagic fever viruses. With respect to therapeutics in advanced development, February 2012, Tekmira Pharmaceuticals Corp. initiated a Phase I trial for TKM-Ebola, a systemically delivered RNAi therapeutic for the treatment of Ebola virus infection. We commenced initial human safety studies of our therapeutic candidates against Marburg and Ebola viruses in May 2011.

Influenza Program. Currently, there are two therapeutic products for influenza that have received market approval from the FDA and are recommended for use in the United States. These are: (1) oseltamivir (Tamiflu), a Roche Holding and Gilead product; and (2) zanamivir (Relenza), a GSK product. In addition to these products, Daiichi Sankyo s laninamivir and BioCryst s peramivir were launched in 2010 in Japan. Currently, DHHS funding is helping support clinical trials of Biota s laninamivir. In addition, other companies including, Toyama Chemical (a subsidiary of Fujifilm), have influenza therapeutic compounds in development. Toyama Chemical s favipiravir is in a Phase II clinical trial in the United States and has completed a Phase III trial in Japan. DHHS is currently seeking additional antiviral therapeutics for the treatment and/or prophylaxis of influenza A and B infections.

In addition to therapeutic products, other companies are focusing development efforts on universal influenza vaccines, including BiondVax Pharmaceuticals Ltd., which initiated a Phase IIa trial of its universal influenza vaccine candidate in October 2010. Successful development of a universal influenza vaccine could lead to a reduction in the number of influenza cases and, therefore, the market size.

Table of Contents

Platform Technology. We believe that other biotechnology and pharmaceutical companies share a focus on RNA-based drug discovery and development. Competitors with respect to our RNA-based technologies include, but are not limited to, Alnylam Pharmaceuticals, Inc., Tekmira Pharmaceuticals Corp., Isis Pharmaceuticals, Inc., Prosensa, Sanofi Aventis, and Santaris Pharma A/S. We are unaware of any other commercial organization that is developing therapeutics based on a PMO chemistry platform.

Research and Development

We devote a substantial portion of our resources to developing new product candidates. During 2012, 2011 and 2010, we expended approximately $52.4 million, $66.9 million and $36.0 million, respectively, on research and development activities.

Employees

As of December 31, 2012, we had 103 employees, 39 of which hold advanced degrees. Of these employees, 64 are engaged directly in research and development activities and 39 are in administration. None of our employees are covered by collective bargaining agreements and we consider relations with our employees to be good.

Item 1A. Risk Factors.

Factors That Could Affect Future Results

Set forth below and elsewhere in this Annual Report on Form 10-K and in other documents we file with the SEC are descriptions of risks and uncertainties that could cause actual results to differ materially from the results contemplated by the forward-looking statements contained in this Annual Report on Form 10-K. Because of the following factors, as well as other variables affecting our operating results, past financial performance should not be considered a reliable indicator of future performance and investors should not use historical trends to anticipate results or trends in future periods. The risks and uncertainties described below are not the only ones facing us. Other events that we do not currently anticipate or that we currently deem immaterial also affect our results of operations and financial condition.

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, AVI-7288 in Marburg and AVI-7100 in influenza 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 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, our infectious disease candidates, our proprietary chemistry, and other potential therapeutic areas that provide long-term market opportunities. With current resources, we may be restricted or delayed in our ability to develop these and 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 FDA under Subpart H Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) or any other designations that will expedite the review or approval process for any of our

Table of Contents

product candidates, based on an inability to adequately demonstrate the safety and effectiveness of our product candidates, failure to meet other regulatory requirements, lack of funding, changes in the regulatory landscape, manufacturing or other reasons. If we are unable to obtain approval for any of our product candidates it could delay or eliminate any potential product revenue by delaying or terminating the potential commercialization of our product candidates.

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;
- sufficient commercial supply of the product;
- 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;
- 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-7537 for the treatment of Ebola virus 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 (assuming no exceptions to the grant of orphan drug status to additional product candidates were to apply). 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 designation 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 may 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

Table of Contents

product candidates. Obtaining marketing approval is a lengthy, expensive and uncertain process and approval is never assured. As of the date of this report, 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 authorities have substantial discretion in the approval process, and determining when or whether regulatory approval, of any type, 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 and our CMC and related manufacturing processes are satisfactory, the FDA or foreign authorities may disagree with our interpretations and determine such data is not sufficient to accept out application or support approval. Furthermore, regulatory agencies may approve a product candidate for fewer indications or for a more narrowly defined indication 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 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 occur that require additional studies that were not originally planned. Other factors may also impact our ability to obtain approval and commercialize our product candidates, including, for example, the fact that a therapeutic commercial product utilizing our RNA-based technologies and the manufacturing techniques necessary to produce them at commercial scale have never been approved or validated by any regulatory authority. Due to these factors, among others, 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 eliminate any potential product revenue by delaying or terminating the potential commercialization of our product candidates.

For example, we are pursuing FDA approval of eteplirsen, our lead product candidate, and recently reported results from a U.S. based Phase IIb 12-patient clinical trial for eteplirsen at 30 mg/kg and 50 mg/kg. Based on feedback from an end of Phase II meeting with the FDA, we will make an initial determination regarding the most appropriate path for pursuing regulatory review and approval of eteplirsen. Our initial decision will be further informed by a subsequent CMC, meeting. There can be no assurance that after our evaluation of the feedback and minutes from the end of Phase II meetings with the FDA that we will decide to pursue or submit an NDA under Subpart H accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback and CMC meetings that we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation (*e.g.*, breakthrough therapy designation), there can be no assurance that such submission or application will be accepted (*e.g.*, refusal to file) or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other foreign authorities could also require us conduct further studies or CMC related work (*e.g.*, a complete response letter) prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for eteplirsen or any of our other product candidates (i) would result in a longer time period for commercialization of such product candidate, (ii) could potentially increase the cost of development of such product candidate and (iii) could harm our competitive position in the marketplace.

Additionally, even if we receive regulatory approval for our product candidates, we will be subject to ongoing FDA obligations and oversight, including adverse event reporting requirements, marketing restrictions and, potentially, other post-marketing obligations such as confirmatory studies, 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

Table of Contents

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 also need to obtain regulatory approval from regulatory authorities in foreign countries to market our product candidates in those countries. We have not submitted an application 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.

In 2012 we completed Study 201, a U.S. based Phase IIb 12 person clinical trial for eteplirsen at 30 mg/kg and 50 mg/kg. Following completion of this study, we initiated Study 202, an ongoing open label extension study with the same participants from Study 201. These trials were initiated, in part, to further demonstrate efficacy and safety, including the production of dystrophin, and explore and identify a more consistently effective dose that may be more appropriate for future clinical trials. While Studies 201 and 202 met their primary endpoints at weeks 24 and 48 respectively, we cannot assure you that data from these studies will be sufficient for regulatory approval or that Study 202 extension study results will continue to be positive through the remaining study period. If these data are not sufficient to demonstrate safety and efficacy to regulators, do not continue to demonstrate safety and efficacy through the remainder of Study 202, or are insufficient to identify a consistently effective dose, we expect we will need 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. 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), additional placebo-controlled pivotal study or studies, or additional trials before conducting a pivotal trial or trials of the product. Any additional studies required by regulatory authorities would increase our costs and delay commercialization of eteplirsen and any of our other product candidates. Even if we conform to any guidance regulatory authorities provide it does not guarantee receipt of marketing approval, even if we believe our preclinical and clinical trials are successful.

Furthermore, success in preclinical and early clinical trials does not ensure that the ongoing Study 202 and later larger-scale trials will be successful nor does it predict final results. Acceptable results in early trials may not be reproduced in the remainder of the Study 202 extension study or later trials. For example, pivotal trials for eteplirsen will likely involve a larger number of patients to achieve 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.

We currently rely on certain 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 in the quantities that we need to conduct our clinical trials and we rely upon a limited number of manufacturers to supply our product

Table of Contents

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 product candidates and their components, fill vials, and store sufficient quantities of our product candidates for research and development programs, clinical trials and potential commercial supply. For each of our eteplirsen, Marburg and other development programs, based on limited capacity for our specialized manufacturing needs we have had to enter into limited or, at times, sole-source agreements with multinational manufacturing firms for the production of the APIs for eteplirsen, Marburg and other therapeutics. There are a limited number of companies that can produce APIs in the quantities and with the quality and purity that we require. Establishing a relationship with alternative suppliers can be a lengthy process and might cause delays in our development efforts. If we are required to seek alternative supply arrangements, the resulting delays and potential inability to find a suitable replacement 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, clinical use or potential commercial supply 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, commercial supply or otherwise discontinue development and production of our product candidates. In addition, we currently depend on certain third-party vendors, which in some cases may be sole sources, 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 sufficient quantities of quality raw materials and we are unable to contract on acceptable terms for these raw materials with alternative suppliers, if any, our ability to have our product candidates manufactured in sufficient quantities for preclinical testing, clinical trials, and potential commercial use would be adversely affected.

We do not yet have all of the agreements necessary for the supply of APIs and raw materials for the production of any 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 and their components 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 development or operation of those facilities due to events such as order delays for equipment or materials, 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 or materials.

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

Table of Contents

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. As we prepare for later stage clinical trials in eteplirsen and potential commercialization, we are working to increase the scale of production of our drug product and planning for mid-scale production in the first half of 2013. In 2013, we will also evaluate whether to increase API production capacity to a commercial scale which will depend in significant part on feedback from the FDA and our expectations regarding if and when we would commence a pivotal trial for eteplirsen and potential commercialization. In order to conduct larger or late-stage scale clinical trials for a product candidate and supply sufficient commercial quantities of the resulting drug product and its components, 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 processes, technologies and validation studies, which are costly, may not be successful 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 manufacture of any of our product candidates in sufficient quality and quantity, the development of that product candidate and regulatory approval or commercial launch for any resulting drug products may be delayed or there may be a shortage in supply, which could significantly harm our business.

In addition, in order to release product and demonstrate stability of product candidates for use in late stage clinical trials (and any resulting drug products for commercial use), our analytical methods must be validated in accordance with regulatory guidelines. We may not be able to successfully validate our analytical methods or demonstrate adequate stability of the product candidates in a timely or cost-effective manner or at all. If we are unable to successfully validate our analytical methods or to demonstrate adequate stability, the development of our product candidates and regulatory approval or commercial launch for any resulting drug products may be delayed, which could significantly harm our business.

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 and support 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 as was the case in 2012 with regards to the Ebola portion of our July 2010 Agreement for the development of therapeutics against the Ebola and Marburg viruses,

Table of Contents

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 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. Currently DOD is operating under a Continuing Resolution for FY 2013. Additionally, on March 1, 2013, a sequestration went into effect which implements across-the-board cuts to government agencies, totaling $1.2 trillion over 10 years. These cuts are to be split 50-50 between domestic and defense discretionary spending. DoD must make $47 billion in cuts before September 30, 2013. These cuts could have widespread ramifications including on DoD s procurement and research and development programs. Sequestration may result in a reduction of funds available for new procurements, but also existing contracts may also be reduced in scope, terminated, or partially terminated. 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 and sequestration, but the $5.6 billion advanced appropriation is rapidly depleting and will expire at the end of FY 2013. Thus, the viability of DHHS and its agencies as a continuing partner and 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 or renegotiate 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 or reduces 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 and influenza product candidates, 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 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

Table of Contents

successfully meet these requirements. If it does not, DoD may choose to terminate the contract. With respect to the civilian sector, Marburg and influenza viruses are among the top chemical, biological, radiological and nuclear threats to national security, yet DHHS has not defined the civilian requirements, making the broader demand for our drug candidates 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.

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 for the periods presented in this report 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.

Table of Contents

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 and 62-week results on December 7, 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 trials may be subject to significant delays relating to various causes, including scheduling conflicts with participating clinicians and clinical institutions, discussions with regulatory authorities regarding the trial design and implementation, 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 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;

Table of Contents

our inability to produce or obtain sufficient quantities of the product candidate to complete the trials;

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 therapies 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 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.

The Animal Rule is a 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. Only one novel product has been approved using the Animal Rule. It has thus far been used to extend the indicated use of three previously licensed products which

Table of Contents

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 GLP requirements given the requirement for BSL-4 containment.

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

We had an operating loss of $29.7 million for the year ended December 31, 2012, and incurred an operating loss of $35.9 million for the year ended December 31, 2011. As of December 31, 2012, our accumulated deficit was $431.3 million and substantially all of our revenue has been derived from research and development contracts with the U.S. government. We have not yet generated any material revenue from product sales and have incurred expenses related to research and development of our technology and product candidates, from general and administrative expenses that we have incurred while building our business infrastructure 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.

We will likely 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 likely require additional capital from time to time in the future in order to continue the development of product candidates in our pipeline and to expand our product portfolio. The actual amount of funds that we may need will be determined by many factors, some of which are beyond our control. These factors include the success of our research and development efforts, the status of our preclinical and clinical testing, costs and timing 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 it 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, in 2012, we sold approximately 6.9 million shares of our common stock in connection with our September 2012 at-the-market equity offering program and December 2012 public financing.

Table of Contents

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 government entities for the development of additional exon-skipping drug candidates for the treatment of DMD and a drug candidate for the treatment of influenza, we currently do not have a strategic relationship with a third party to perform research or development using our 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.

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

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

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

Our RNA-based platforms, utilizing proprietary PMO-based technology, have not been incorporated into a therapeutic commercial product and are still at a relatively early stage of development. This technology is used in all of our therapeutic candidates, including eteplirsen. We are conducting toxicology, pharmacology, pharmacokinetics and other preclinical studies and, although we have conducted Phase I clinical trials for AVI-6003 (we are now pursuing development of AVI-7288, one of the two component oligomers in AVI-6003) and AVI-7100 and conducted a Phase IIb clinical trial in eteplirsen, additional preclinical studies may be required for these product candidates and before other product candidates enter human clinical trials. In addition, preclinical models to study participant toxicity and activity of compounds are not necessarily predictive of toxicity or efficacy of these compounds in the treatment of human disease and there may be substantially different results in clinical trials from the results obtained in preclinical studies. Any failures or setbacks in utilizing our PMO-based technology, including adverse effects resulting from the use of this technology in humans, could have a detrimental impact on our internal product candidate pipeline and our ability to maintain and/or enter into new corporate collaborations regarding these technologies, which would negatively affect our business and financial position.

The relocation of our corporate headquarters and selected research and development activities may create unintended negative consequences, including increased costs and loss of personnel.

We recently moved our corporate headquarters from Bothell, Washington to Cambridge, Massachusetts. We also moved selected research and development activities from Bothell to our existing site in Corvallis, Oregon and will develop additional research and development activities at a future site in Cambridge. We expect the transition will continue through 2013. While we believe the relocation will improve our business operations and enhance our ability to attract and retain industry talent, this relocation may result in the following negative consequences:

- increased costs associated with the closing of our existing facility in Bothell, Washington including the moving of lab equipment to Cambridge and Corvallis;

- increased costs associated with the relocation of personnel, including reimbursement of relocation expenses and cost of living adjustments to base salaries;

Table of Contents

employee turnover due to relocation;

increased costs associated with retention and/or severance packages for Bothell-based personnel;

business disruptions resulting from the relocation; and

increased long-term lease costs.

If any of these consequences occur, the negative impact may outweigh any benefits related to the relocation, which could have an adverse effect on our business.

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

We are highly dependent on the efforts and abilities of the principal members of our senior management. Additionally, we have scientific personnel with significant and unique expertise in RNA-based therapeutics and related technologies and personnel with experience overseeing compliance with and execution of the terms of our U.S. government contracts. The loss of the services of any one of the principal members of our managerial, scientific or government contract compliance staff may prevent us from achieving our business objectives.

The competition for qualified personnel in the biotechnology field and for qualified personnel with government contracting experience is intense, and our future success depends upon our ability to attract, retain and motivate such personnel. In order to develop and commercialize our products successfully, we will be required to retain key managerial, scientific and government contract compliance staff. In certain instances, we may also need to expand our workforce and our management ranks. We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, as well as academic and other research institutions. If we are unable to attract, assimilate or retain such key personnel, our ability to advance our proprietary programs and perform our U.S. government contracts would be adversely affected. Any failure to perform under our U.S. government contracts could result in a termination of the agreement, which would harm our business.

Recent changes in our executive leadership and any similar changes in the future may serve as a significant distraction for our management and employees.

In January 2011, Christopher Garabedian, a member of our board of directors, was hired to serve as our president and chief executive officer. Since the beginning of 2011, there have been a number of changes to our executive leadership team. Most recently, in November 2012, we hired our senior vice president, chief financial officer, Sandesh Mahatme and our senior vice president, general counsel and corporate secretary, David Tyronne Howton. In June 2012, our former senior vice president and chief scientific officer, Peter Linsley, resigned from his employment with us and in February 2012 our former senior vice president and general counsel, Effie Toshav, resigned from her employment with us. Such changes, or any other future changes in our executive leadership, may disrupt our operations as we adjust to the reallocation of responsibilities and assimilate new leadership and, potentially, differing perspectives on our strategic direction. If the transition in executive leadership is not smooth, the resulting disruption could negatively affect our operations and impede our ability to execute our strategic plan.

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

We actively evaluate various strategic transactions on an ongoing basis, including licensing or acquiring complementary products, technologies or businesses. Any potential acquisitions may entail numerous risks, including increased operating expenses and cash requirements, assimilation of operations and products, retention of key employees, diversion of our management s attention and uncertainties in our ability to maintain key business relationships of the acquired entities. In addition, if we undertake acquisitions, we may issue dilutive

Table of Contents

securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

Asserting, defending and maintaining our intellectual property rights could be challenging and costly, and our failure to do so could harm our ability to compete and impair the outcome of our operations. The pharmaceutical, biotechnology and academic environments are highly competitive and competing intellectual property could limit our ability to protect our products.

Our success will depend in significant part on our existing intellectually property rights and our ability to obtain additional patents and licenses in the future. As of February 28, 2013, we owned or controlled approximately 290 U.S. and corresponding foreign patents and 185 U.S. and corresponding foreign patent applications. We license patents from other parties for certain complementary technologies. We cannot be certain that pending patent applications will result in patents being issued in the United States or foreign countries. We cannot be certain that we were the first to make the inventions covered by any of our patents, if issued, or our pending patent applications. In addition, the patents that have been or will be issued may not afford meaningful protection for our technology and products. Competitors may develop products similar to ours that do not conflict with our patents. To protect our rights to any of our patents, if issued, and proprietary information, we may need to litigate against infringing third parties, or avail ourselves of the courts or participate in hearings to determine the scope and validity of those patents or other proprietary rights. These types of proceedings are often costly and could be very time-consuming to us, and we cannot assure you that the deciding authorities will rule in our favor. An unfavorable decision could allow third parties to use our technology without being required to pay us licensing fees or may compel us to license needed technologies to avoid infringing third-party patent and proprietary rights.

Pharmaceutical research and development is highly competitive; others may file patents first that cover our products or technology. For example, our competitor Prosensa has rights to patent families corresponding to WO2002/024906 and WO2004/083432, including issued US 7,973,015, US 7,534,879, and granted European Patent No. EP 1619249. We opposed EP 1619249 in the Opposition Division of the European Patent Office, or the Opposition Division, and in November 2011, we announced that, although we succeeded in invalidating some of the patent s claims, the Opposition Division maintained in amended form certain claims of this patent relating to the treatment of DMD by skipping dystrophin exons 51 and 46. We and Prosensa both have the right to appeal this decision; however, pending final resolution of this matter and any appeal thereof, the patent at issue may provide the basis for Prosensa or other parties that have rights to such patent to assert that our drug eteplirsen infringes on such patent. The timing and outcome of an appeal, if pursued, cannot be predicted or determined as of the date of this report. We are also aware of certain claims that have issued to Prosensa in Japan (JP 4846965) that may provide the basis for Prosensa or other parties that have rights to these claims to assert that eteplirsen infringes on such claims. We believe we have a basis to invalidate some or all of these claims and are evaluating the potential initiation of invalidation proceedings. Because we have not yet initiated an invalidation proceeding in Japan, the outcome and timing of such proceeding cannot be predicted or determined as of the date of this report. We are also aware of certain claims that Prosensa has rights to in the United States that may provide the basis for Prosensa or other parties that have rights to these claims to assert that our drug eteplirsen infringes on such claims. We believe we have valid defenses to any such allegations or a basis to invalidate some or all of these claims and do not believe that Prosensa s patent seriously harms our ability to develop and commercialize eteplirsen; however, we cannot be certain of this. If we are unsuccessful in invalidating certain of Prosensa s claims, if previously invalidated claims are restored on appeal, or if Prosensa prevails on claims they may assert in the United States, our ability to commercialize both eteplirsen and other therapeutic candidates for our pan-exon strategy could be materially impaired.

Our success will also depend partly on our ability to operate without infringing upon the proprietary rights of others as well as our ability to prevent others from infringing on our proprietary rights. We may be required at times to take legal action to protect our proprietary rights and, despite our best efforts, we may be sued for infringing on the patent rights of others. We have not received any communications or other indications from

Table of Contents

owners of related patents or others that such persons believe our products or technology may infringe on their patents. Patent litigation can involve complex factual and legal questions and its outcome is uncertain. Patent litigation is costly and, even if we prevail, the cost of such litigation could adversely affect our financial condition. If we do not prevail, in addition to any damages we might have to pay, we could be required to stop the infringing activity or obtain a license. If any patent related to our products or technology issues, and if our activities are determined to be covered by such a patent, we cannot assure you that we will be able to obtain or maintain a license, which could have a material adverse effect on our business, financial condition, ability to sell our products, operating results and ability to obtain and/or maintain our strategic business relationships.

Others may challenge our patents and, as a result, our patents could be narrowed or invalidated. The patent position of pharmaceutical and biotechnology firms, as well as academia, is generally highly uncertain, involves complex legal and factual questions, and has recently been the subject of much litigation. No consistent policy has emerged from the U.S. Patent and Trademark Office, or USPTO, or the courts regarding the breadth of claims allowed or the degree of protection afforded under biotechnology patents. In addition, there is a substantial backlog of pharmaceutical and biotechnology patent applications at the USPTO and the approval or rejection of patents may take several years.

To help protect our proprietary rights in unpatented proprietary information, trade secrets and know-how, we require our employees, consultants and advisors to execute confidentiality agreements and invention assignment agreements. However, such agreements may not provide us with adequate protection if confidential information is used or disclosed improperly. In addition, in some situations these agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants or advisors have prior employment or consulting relationships. Further, others may independently develop substantially equivalent proprietary information and techniques, or otherwise gain access to our trade secrets.

Our research collaborators may publish data and information to which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information may be impaired.

We face intense competition and rapid technological change, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

The biotechnology and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. We are aware of many pharmaceutical and biotechnology companies that are actively engaged in research and development in areas related to antisense technology and other RNA technologies or that are developing alternative approaches to or therapeutics for the disease indications on which we are focused. Some of these competitors are developing or testing product candidates that now, or may in the future, compete directly with our product candidates. For example, we believe that companies including Alnylam Pharmaceuticals, Isis Pharmaceuticals and Santaris share a focus on RNA-based drug discovery and development. Competitors with respect to our exon-skipping DMD program, or eteplirsen, include Prosensa and GSK and other companies such as PTC Therapeutics and Summit plc have also been working on DMD programs.

Clinical trials evaluating the systemic administration of the Prosensa/GSK lead DMD drug candidate are currently ongoing, including a placebo-controlled global Phase III clinical trial. Two placebo-controlled Phase II clinical trials, one based in the United States and one based outside the United States have now concluded, but results are not anticipated until the Phase III clinical trial is complete. The Prosensa/GSK drug candidate may, or may not, prove to be safer or more efficacious than our product candidate and it could gain marketing approval before our product candidate. This might affect our ability to successfully complete a clinical development program or market eteplirsen once approved. This competition may also extend to other exon-skipping drugs for DMD limiting our ability to gain market share.

Table of Contents

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

develop safer or more effective products;

implement more effective approaches to sales and marketing;

develop less costly products;

obtain quicker regulatory approval;

have access to more manufacturing capacity;

develop products that are more convenient and easier to administer;

form more advantageous strategic alliances; or

establish superior proprietary positions.

We may be subject to clinical trial claims and our insurance may not be adequate to cover damages.

We currently have no products that have been approved for commercial sale; however, the current and future use of our product candidates by us and our corporate collaborators in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made directly by consumers or healthcare providers or indirectly by pharmaceutical companies, our corporate collaborators or others selling such products. We may experience financial losses in the future due to product liability claims. We have obtained limited general commercial liability insurance coverage for our clinical trials. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for any of our product candidates. However, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against all losses. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

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

Our research and development activities involve the use of hazardous materials, including organic and inorganic solvents and reagents. Accordingly, we are subject to federal, state, and local laws and regulations governing the use, storage, handling, manufacturing, exposure to, and disposal of these hazardous materials. In addition, we are subject to environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens, and the handling of biohazardous materials. Although we believe that our activities conform in all material respects with such environmental laws, there can be no assurance that violations of these laws will not occur in the future as a result of human error, accident, equipment failure, or other causes. Liability under environmental, health and safety laws can be joint and several and without regard to fault or negligence. The failure to comply with past, present or future laws could result in the imposition of substantial fines and penalties, remediation costs, property damage and personal injury claims, loss of permits or a cessation

of operations, and any of these events could harm our business and financial conditions. We expect that our operations will be affected by other new environmental and health and workplace safety laws on an ongoing basis, and although we cannot predict the ultimate impact of any such new laws, they may impose greater compliance costs or result in increased risks or penalties, which could harm our business.

Table of Contents

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

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

Risks Related to Our Common Stock

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

The market prices for, and trading volumes of, securities of biotechnology companies, including our securities, have been historically volatile. For example, during 2012, our stock has traded from a low of $3.30 per share to a high of $45.00 per share. The market has from time to time experienced significant price and volume fluctuations unrelated to the operating performance of particular companies. The market price of our common stock may fluctuate significantly due to a variety of factors, including:

- our ability to obtain and any decision to pursue Subpart H accelerated approval for eteplirsen;
- positive or negative results of testing and clinical trials by ourselves, strategic partners, or competitors;
- delays in entering or failing to enter into strategic relationships with respect to development and/or commercialization of our product candidates or entry into strategic relationships on terms that are not deemed to be favorable to our company;
- technological innovations or commercial product introductions by ourselves or competitors;
- changes in government regulations;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of any of our products;
- financing, through the issuance of equity or equity-linked securities or incurrence of debt, or other corporate transactions;
- comments by securities analysts;
- litigation; or

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

In addition, the stock market has recently experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of individual companies. Broad market and industry factors may seriously affect the market price of companies stock, including ours, regardless of actual operating performance. In addition, in the past, following periods of volatility in the overall market and the market price of a particular company s securities, securities class action litigation has often been instigated against these companies. Such litigation, if instigated against us, could result in substantial costs and a diversion of our management s attention and resources.

Table of Contents

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

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

- classification of our board of directors into two classes, with one class elected each year;
- prohibition of cumulative voting of shares in the election of directors;
- prohibition of shareholder actions by less than unanimous written consent;
- express authorization of the board of directors to make, alter or repeal our bylaws;
- advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by shareholders at shareholder meetings; and
- the ability of our board of directors to authorize the issuance of undesignated preferred stock, the terms and rights of which may be established and shares of which may be issued without shareholder approval, including rights superior to the rights of the holders of common stock.

In addition, the Oregon Control Share Act and Business Combination Act may limit parties that acquire a significant amount of voting shares from exercising control over us for specific periods of time. These provisions could discourage, delay or prevent a transaction involving a change of control, even if doing so would benefit our shareholders. These provisions also could discourage proxy contests and make it more difficult for shareholders to elect directors of their choosing or cause us to take other corporate actions, such as replacing or removing management or members of our board of directors.

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

Our quarterly operating results have fluctuated in the past, and we believe they will continue to do so in the future. Some of these fluctuations may be very pronounced as a result of the issuance of warrants to purchase approximately 5.0 million shares of our common stock by us in December 2007 and January and August 2009 of which 3.1 million remain outstanding and exercisable as of December 31, 2012. Each of these warrants is classified as a derivative liability and accordingly, the fair value of the warrants is recorded on our consolidated balance sheet as a liability, and such fair value is adjusted at each financial reporting date with the adjustment to fair value reflected in our consolidated statement of operations. For example, for the year ended December 31, 2012, the impact of the change in fair value of these warrants resulted in a $91.9 million charge to our Consolidated Statement of Operations and Comprehensive Loss. The fair value of the warrants is determined using the Black-Scholes option valuation model. Fluctuations in the assumptions and factors used in the Black-Scholes model can result in adjustments to the fair value of the warrants reflected on our balance sheet and, therefore, our statement of operations. Due to the classification of such warrants and other factors, quarterly results of operations are difficult to forecast, and period-to-period comparisons of our operating results may not be predictive of future performance. Additionally, our quarterly operating results may fluctuate due to the variable nature of our revenue and research and development expenses. Specifically, a change in the timing of activities performed in support of our U.S. government research contracts could either accelerate or defer anticipated revenue from period to period. Likewise, our research and development expenses may experience fluctuations as a result of the timing of activities performed in support of our U.S. government research contracts and the timing and magnitude of expenditures incurred in support of our DMD and other proprietary drug development programs. In one or more future quarters, our results of operations may fall below the expectations of securities analysts and investors. In that event, the market price of our common stock could decline. In addition, the market price of our common stock may fluctuate or decline regardless of our operating performance.

Table of Contents

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

As of December 31, 2012, there were 31.7 million shares of common stock outstanding, outstanding awards to purchase 2.7 million shares of common stock under various incentive stock plans and outstanding warrants to purchase up to 3.1 million shares of common stock. Additionally, as of December 31, 2012, there were 1.2 million shares of common stock available for future issuance under our 2011 Equity Incentive Plan. In addition, we may issue additional common stock and warrants from time to time to finance our operations. We may also issue additional shares to fund potential acquisitions or in connection with additional stock options or other equity awards granted to our employees, officers, directors and consultants under our 2011 Equity Incentive Plan. The issuance of additional shares of common stock or warrants to purchase common stock, perception that such issuances may occur, or exercise of outstanding warrants or options may have a dilutive impact on other shareholders and could have a material negative effect on the market price of our common stock.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

A description of the facilities we own and/or occupy is included in the following table. We are transitioning our corporate headquarters from Bothell, Washington to Cambridge, Massachusetts and, as part of this transition, we are moving our administrative and research activities from Washington to our existing facilities in Corvallis, Oregon and to our newly leased space in Massachusetts**.** We believe that our current facilities in Oregon and additional administrative and laboratory space that is readily available near our Cambridge facility is suitable and will provide sufficient capacity to meet the projected needs of our business for the next 12 months. Except as noted below, all of our properties are currently being used in the operation of our business.

Location of Property	Square Footage	Lease Expiration Date	Purpose	Other Information
215 First Street, Suite 7, Cambridge, MA 02142	7,087	February 2014	Office space	Temporary corporate headquarters
3450 Monte Villa Parkway, Suite 101, Bothell, WA 98021	19,108	April 2013	Laboratory and office space	Former corporate headquarters and lab space
4575 SW Research Way, Suite 200, Corvallis, OR 97333	53,000	December 2020	Laboratory and office space	Primarily lab space
245 First Street, Riverview II, Suite 1800, Cambridge, MA 02142	1,742	June 30, 2013	Office space	Administrative office
1749 SW Airport Avenue, Corvallis, OR 97333	36,150	N/A facility is owned; land lease expires February 2042	Acquired with intention of providing future expansion space for the manufacture of potential products and components;	Approximately 25,000 square feet leased and the remaining space unoccupied**

Table of Contents

* Our offices in Cambridge are governed by the terms of service agreements, which do not create a tenancy interest, leasehold estate or other real property interest in our favor.

** In November 2011, the tenant, Perpetua Power Source Technologies, Inc., or Perpetua, agreed to lease approximately 25,000 square feet of the building until March 2017. Perpetua may terminate the lease at the end of the 36th month upon 180 days prior written notice, together with delivery of a termination fee. Perpetua has the option to extend the lease for an additional year if notice is provided no less than 12 months prior to the expiration date. Perpetua also has a right of first refusal relating to the lease of the remaining space at the building and was granted an option to purchase the building during the term of the lease, provided there is no uncured default by Perpetua at the time of exercise. If the purchase option is exercised, the price for the building is $2.0 million until February 2015, $2.1 from March 2015 until February 2016 and $2.2 million from March 2016 through the remainder of the initial lease term. If Perpetua exercises its extension option, the purchase price will be $2.3 million during the term of the extension.

Item 3. Legal Proceedings.

As of the date hereof, we are not a party to any material legal proceedings with respect to us, our subsidiaries, or any of our material properties. In the normal course of business, we may from time to time be named as a party to various legal claims, actions and complaints, including matters involving employment, intellectual property, effects from the use of therapeutics utilizing our technology, or other topics. It is impossible to predict with certainty whether any resulting liability would have a material adverse effect on our financial position, results of operations or cash flows.

Item 4. Mine Safety Disclosures.

Not applicable.

Table of Contents

PART II

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

Market Information

Our Common Stock is quoted on The NASDAQ Global Market under the symbol SRPT. The following table sets forth the high and low sales prices as reported by The NASDAQ Global Market for each quarterly period in the two most recent years:

	High	Low
Year Ended December 31, 2011		
First Quarter	$ 16.44	$ 10.26
Second Quarter	11.28	7.98
Third Quarter	10.20	6.12
Fourth Quarter	6.66	3.00
Year Ended December 31, 2012		
First Quarter	$ 9.84	$ 4.20
Second Quarter	7.80	3.48
Third Quarter	16.44	3.30
Fourth Quarter	45.00	14.84

Holders

As of February 28, 2013, we had 195 shareholders of record of our common stock.

Dividends

We have neither declared nor paid cash dividends on our common stock in 2012 or 2011. 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.

Table of Contents

Performance Graph

The following graph compares the performance of our Common Stock for the periods indicated with the performance of the NASDAQ Composite Index and the Amex Biotech Index. This graph assumes an investment of $100 on December 31, 2007 in each of our common stock, the NASDAQ Composite Index and the Amex Biotech Index, and assumes reinvestment of dividends, if any. The stock price performance shown on the graph below is not necessarily indicative of future stock price performance. This graph is not soliciting material, is not deemed filed with the SEC and is not to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

	SRPT	NASDAQ Composite Index	Amex Biotech Index
End of Fiscal 2007	100.00	100.00	100.00
End of Fiscal 2008	46.81	59.46	82.28
End of Fiscal 2009	103.55	85.55	119.79
End of Fiscal 2010	150.35	100.02	164.99
End of Fiscal 2011	53.19	98.22	138.77
End of Fiscal 2012	304.96	113.85	196.70

Recent Sales of Unregistered Securities.

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers.

None.

Table of Contents

Item 6. Selected Financial Data.

The following selected financial data is derived from our audited financial statements and should be read in conjunction with, and is qualified in its entirety by, Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operation, and Item 8, Financial Statements and Supplementary Data.

	Year Ended December 31,				
	2012	2011	2010	2009	2008
			(in thousands)		
Operations data:					
Revenues	$ 37,329	$ 46,990	$ 29,420	$ 17,585	$ 21,258
Research and development	52,402	66,862	35,972	24,396	27,331
General and administrative	14,630	16,055	14,382	8,696	11,469
Acquired in-process research and development					9,916
Operating loss	(29,703)	(35,927)	(20,934)	(15,507)	(27,458)
Interest income and other net	354	587	259	(454)	344
Gain (Loss) on change in warrant valuation	(91,938)	33,022	(11,502)	(9,198)	3,161
Net loss	$ (121,287)	$ (2,318)	$ (32,177)	$ (25,159)	$ (23,953)
Net loss per share basic and diluted	$ (5.14)	$ (0.11)	$ (1.74)	$ (1.69)	$ (2.07)
Balance sheet data:					
Cash and cash equivalents	$ 187,661	$ 39,904	$ 33,589	$ 48,446	$ 11,474
Working capital	115,022	24,583	(8,019)	17,803	9,756
Total assets	204,993	54,368	45,976	60,027	25,536
Shareholders equity (deficit)	123,679	31,017	(2,817)	23,630	15,732

Table of Contents

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below, and those discussed in the section titled Risk Factors included elsewhere in this Annual Report on Form 10-K. Throughout this discussion, unless the context specifies or implies otherwise, the terms Sarepta , we , us and our refer to Sarepta Therapeutics, Inc. and its subsidiaries.

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 Duchenne muscular dystrophy drug candidates, including our lead product candidate, eteplirsen, which is currently in a Phase IIb trial. We are also focused on developing therapeutics for the treatment of infectious diseases and leveraging our RNA-based technology platforms to identify additional product candidates and explore various strategic opportunities.

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. Eteplirsen is our lead therapeutic candidate for DMD. If we are successful in our development efforts, eteplirsen will address a severe unmet medical need. Restoration of dystrophin expression and dystrophin positive fibers is believed to be critical for successful disease-modifying treatment of individuals with DMD. We initiated a Phase IIb trial for eteplirsen in August 2011 and in April 2012, we announced this trial met the primary efficacy endpoint of increasing novel dystrophin at 24 weeks, when compared to placebo/delayed treatment cohort. At the end of the Phase IIb trial, we initiated an open label extension trial with the same participants where we demonstrated a statistically significant benefit over the placebo/delayed treatment cohort in the 6-minute walk test after 48 and 62 weeks of treatment with eteplirsen. We are currently expecting to initiate a pivotal clinical trial for eteplirsen by the end of 2013 and commencing dosing in this trial by early 2014. We are also in the early stages of identifying additional exon skipping drug candidates for the treatment of DMD which addresses different genetic imperfections than eteplirsen.

We are also leveraging the capabilities of our RNA-based technology platforms to develop therapeutics for the treatment of infectious diseases. Our primary program for infectious diseases is for the treatment of Marburg virus, a severe and fatal disease which is characterized as a Category A bioterrorism agent by the Centers for Disease Control and Prevention and a material threat to national security by the Department of Homeland Security. Currently, there are no treatments beyond supportive care. Our lead therapeutic candidate against the Marburg virus, AVI-7288, has shown positive safety results when administered intravenously to healthy human volunteers and a survival rate in non-human primates of 83% to 100% when daily treatments were begun between 1 and 96 hours after infection compared to 0% survival in the placebo group. In addition, we recently completed a study administering AVI-7288 via intramuscular injection and the results indicated the drug was well tolerated and achieved high survival rates similar to previous studies where AVI-7288 was administered intravenously. The U.S. Department of Defense, or DoD, has provided significant financial support for the development of therapeutics against Ebola, Marburg, Dengue and influenza viruses.

The basis for our novel RNA-based therapeutics is our phosphorodiamidate-linked morpholino oligomer, or PMO, chemistries. Unlike other RNA-based therapeutics, which are often used to down-regulate gene expression, our technologies can be used to selectively up-regulate or down-regulate the production of a target protein, or direct the expression of novel proteins involved in human diseases and disorders. Further, we believe

Table of Contents

the charge-neutral nature of our PMO-based molecules may have the potential to reduce off-target effects, such as immune stimulatory effects often seen in alternative RNA-based technologies. We believe that our highly-differentiated, novel proprietary and innovative RNA-based technology platforms, based on charge neutral morpholino oligomers, may represent a significant improvement over traditional RNA-based technologies. As of February 28, 2013, we owned or controlled approximately 290 U.S. and corresponding foreign patents and 185 U.S. and corresponding foreign patent applications.

Since our inception in 1980, we have incurred losses of approximately $431.3 million and substantially all of our revenue has been derived from research and development contracts with the U.S. government. We have not yet generated any material revenue from product sales and we have incurred expenses related to research and development, general and administrative charges and acquired in-process research and development resulting from two acquisitions. We expect to continue to incur losses in the future as we continue our research and development efforts and seek approval from various regulatory agencies for our product candidates, but there can be no assurance that we will obtain approval for our product candidates and achieve revenues from product sales.

As of December 31, 2012, we had cash and cash equivalents of $187.7 million which, we believe is sufficient to fund operations for more than the next twelve months. Should our funding from the U.S. government cease or be delayed, we would likely curtail certain of our infectious disease research and development efforts unless additional funding was obtained. We are also likely to pursue securing additional cash resources through public or private financings, seeking additional government contracts, and from establishing collaborations or licensing our technology to other companies.

The likelihood of our long-term success must be considered in light of the expenses, difficulties and delays frequently encountered in the development and commercialization of new pharmaceutical products, competitive factors in the marketplace, the risks associated with U.S. government sponsored programs, and the complex regulatory environment in which we operate. There can be no assurance that we will ever achieve significant revenues or profitable operations.

U.S. Government Contracts

In the periods presented, nearly all of the revenue we generated was derived from research contracts with and grants from the U.S. government. As of December 31, 2012, we had substantially completed all of our contracts with the U.S. government except for the Marburg portion of the July 2010 agreement for the development of therapeutics against Ebola and Marburg viruses and the August 2012 agreement for the intramuscular administration of our drug candidate against the Marburg virus.

The following table sets forth the revenue from each of our contracts with the U.S. government and other revenue for the years ended December 31, 2012, 2011 and 2010:

	Year Ended December 31,		
	2012	2011	2010
		(in thousands)	
July 2010 Agreement (*Ebola and Marburg*)	$ 36,557	$ 42,875	$ 9,822
August 2012 Agreement *(Intramuscular administration)*	673		
June 2010 Agreement (*H1N1*)		3,490	8,809
May 2009 Agreement (*H1N1*)		516	5,171
November 2006 Agreement (*Ebola, Marburg and Junín Viruses*)			3,204
Grants			1,622
Other Agreements	99	109	792
Total	$ 37,329	$ 46,990	$ 29,420

The following is a description of each of our significant U.S. government contracts and grants.

Table of Contents

July 2010 Agreement (Ebola and Marburg)

On July 14, 2010, we were awarded a contract with the DoD Chemical and Biological Defense Program through the U.S. Army Space and Missile Defense Command for the advanced development of our hemorrhagic fever virus therapeutic candidates, AVI-6002 and AVI-6003, against the Ebola and Marburg viruses, respectively. In February 2012, we announced that we received permission from the FDA to proceed with a single oligomer from AVI-6003, AVI-7288, as the lead product candidate against Marburg virus infection.

On August 2, 2012, we received a stop-work-order related to the Ebola virus portion of the contract and, on October 2, 2012, the U.S. government terminated the Ebola portion of the contract for convenience of the government due to government funding constraints. The remaining Marburg portion of the contract is structured into four segments and has an aggregate remaining period of performance spanning approximately four years if DoD exercises its options for all segments. Our activities under the first segment began in July 2010 and include Phase I studies in healthy volunteers as well as preclinical studies. The first segment is scheduled to be completed in the first half of 2014 subject to agreement with DoD. The remaining funding for the current Marburg segment of the contract is approximately $15.9 million.

After completion of the first segment, and each successive segment, DoD has the option to proceed to the next segment. If DoD exercises its options for segments II, III and IV, our contract activities would include all clinical and licensure activities necessary to obtain FDA regulatory approval for our therapeutic candidate against the Marburg virus. The funding for segments II, III and IV of the Marburg virus portion of the contract is estimated to be approximately $84.4 million.

August 2012 Agreement (Intramuscular administration)

On August 29, 2012, we were awarded a contract from the U.S. Department of Defense s Joint Project Manager Transformational Medical Technologies (JPM-TMT) program, a component of the U.S. Department of Defense s Joint Program Executive Office for Chemical and Biological Defense. The contract is for approximately $3.9 million to evaluate the feasibility of an intramuscular (IM) route of administration using AVI-7288, our candidate for treatment of Marburg virus. The period of performance of this contract is scheduled to conclude in the second half of 2013. Under the July 2010 Agreement (Ebola and Marburg) described above, we are developing AVI-7288 as an intravenous formulation.

June 2010 Agreement (H1N1/Influenza)

On June 4, 2010, we entered into a contract with the Defense Threat Reduction Agency (DTRA) to advance the development of AVI-7100 as a medical countermeasure against the pandemic H1N1 influenza virus in cooperation with the Transformational Medical Technologies program, or TMT, of the U.S. Department of Defense, or DoD. The period of performance for this contract ended on June 3, 2011.

May 2009 Agreement (H1N1/Influenza)

In May 2009, we entered into a contract with DTRA to develop swine flu drugs using our proprietary PMO and PMO*plus*® antisense chemistry. In March 2010, the contract was amended to include testing against additional influenza strains. We have agreed with DTRA that the key activities under this contract were completed in 2011.

November 2006 Agreement (Ebola, Marburg and Junín Viruses)

In November 2006, we entered into a research contract with DTRA to fund the development of our antisense therapeutic candidates against Ebola, Marburg and Junín hemorrhagic viruses. In November 2010, we and DTRA agreed that the key activities under this contract had been completed.

Table of Contents

2010 Qualifying Therapeutic Discovery Project

In October 2010, we were awarded five cash grants for our DMD program and infectious disease programs totaling approximately $1.2 million under the U.S. government s Qualifying Therapeutic Discovery Project, or QTDP, and recognized the entire amount as revenue in 2010. We will not receive any further funding under the QTDP grants.

Key Financial Metrics

Revenue

Government Research Contract and Grant Revenue. Substantially all of our revenue is generated from U.S. government research contracts and grants. See Note 6 U.S. Government Contracts of the financial statements included elsewhere in this Annual Report on Form 10-K. We recognize revenue from U.S. government research contracts and grants during the period in which the related expenses are incurred and present such revenues and related expenses gross in the consolidated financial statements.

License Arrangements. Our license arrangements may consist of non-refundable upfront license fees, data transfer fees, research reimbursement payments, exclusive licensed rights to patented or patent pending compounds, technology access fees, various performance or sales milestones and future product royalty payments. Some of these arrangements are multiple element arrangements.

We defer recognition of non-refundable upfront fees if we have continuing performance obligations when the technology, right, product or service conveyed in conjunction with the non-refundable fee has no utility to the licensee that is separate and independent of our performance under the other elements of the arrangement. In addition, if we have continuing involvement through research and development services that are required because of our know-how or because the services can only be performed by us, then such up-front fees are deferred and recognized over the period of continuing involvement. As of December 31, 2012, we had deferred revenue of $3.3 million, which represents up-front fees which we will recognize as revenue as we satisfy the outstanding performance obligations.

Expenses

Research and Development. Research and development expense consists of costs associated with research activities as well as costs associated with our product development efforts, conducting preclinical studies, and clinical trial and manufacturing costs.

Direct research and development expenses associated with our programs include clinical trial site costs, clinical manufacturing costs, costs incurred for consultants and other outside services, such as data management and statistical analysis support, and materials and supplies used in support of the clinical programs. Indirect costs of our clinical program include salaries, stock based compensation, and an allocation of our facility costs.

The amount and timing of future research and development expense will depend in part on our ability to obtain U.S. government awards to fund the advanced development of our infectious disease therapeutic candidates. Without such funding, we would likely significantly reduce our spending in these areas. Future research and development expenses may also increase as our internal projects, such as eteplirsen for DMD, enter later stage clinical development. Our research and development programs are in Phase IIb clinical trials or earlier and may not result in any approved products. Product candidates that appear promising at early stages of development may not reach the market for a variety of reasons. Similarly, any of our product candidates may be found to be ineffective during clinical trials, may take longer to complete clinical trials than we have anticipated, may fail to receive necessary regulatory approvals, or may prove impracticable to manufacture in commercial quantities at reasonable cost and with acceptable quality.

Table of Contents

As a result of these uncertainties and the other risks inherent in the drug development process, we cannot determine the duration and completion costs of current or future clinical stages of any of our product candidates. Similarly, we cannot determine when, if, or to what extent we may generate revenue from the commercialization and sale of any product candidate. The timeframe for development of any product candidate, associated development costs, and the probability of regulatory and commercial success vary widely.

General and Administrative. General and administrative expense consists principally of salaries, benefits, stock-based compensation expense, and related costs for personnel in our executive, finance, legal, information technology, business development and human resource functions. Other general and administrative expenses include an allocation of our facility costs and professional fees for legal, consulting and accounting services.

Interest Income and Other, Net. Interest income and other, net, primarily consists of interest on our cash and cash equivalents, interest expense, and rental income. Our cash equivalents consist of money market investments. Interest expense includes interest paid on our mortgage loan related to the Corvallis property, the substantial portion of which we leased in November 2011. Rental income is from subleasing excess space in some of our facilities.

Gain (Loss) on Change in Warrant Valuation. Warrants issued in connection with our December 2007 and January and August 2009 financings are classified as liabilities as opposed to equity due to their settlement terms. These warrants are non-cash liabilities; we are not required to expend any cash to settle these liabilities. The fair market value of these warrants was recorded on the balance sheet at issuance and the warrants are marked to market each financial reporting period, with changes in the fair value recorded as a gain or loss in our statement of operations. The fair value of the warrants is determined using the Black-Scholes option-pricing model, which requires the use of significant judgment and estimates related to the inputs used in the model and can result in significant swings in the fair market valuation primarily due to changes in our stock price. For more information, see Note 8 Warrants of the financial statements included elsewhere in this Annual Report on Form 10-K.

Critical Accounting Policies and Estimates

The discussion and analysis of our financial condition and results of operations are based upon our financial statements included elsewhere in this Annual Report on Form 10-K. The preparation of our financial statements in accordance with accounting principles generally accepted in the United States, or GAAP, requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosure of contingent assets and liabilities for the periods presented. Some of these judgments can be subjective and complex, and, consequently, actual results may differ from these estimates. For any given individual estimate or assumption we make, there may also be other estimates or assumptions that are reasonable. We believe that the estimates and judgments upon which we rely are reasonable based upon historical experience and information available to us at the time that we make these estimates and judgments. To the extent there are material differences between these estimates and actual results, our financial statements will be affected. Although we believe that our judgments and estimates are appropriate, actual results may differ from these estimates.

The policies that we believe are the most critical to aid the understanding of our financial results include:

- revenue recognition;
- stock-based compensation; and
- accounting for and valuation of warrants classified as liabilities.

Revenue Recognition

We have historically generated revenue from our U.S. government research contracts and grants and other license arrangements. For a more detailed description of our revenue recognition policies, see Key Financial

Table of Contents

Metrics above and Note 2 Summary of Significant Accounting Policies of the financial statements included elsewhere in this Annual Report on Form 10-K.

Stock Compensation Expense

To determine stock-based compensation costs, we apply the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, Share-Based Payments. We use the Black-Scholes option pricing model for determining the estimated fair value for stock-based awards on the date of grant, which requires the use of subjective and complex assumptions to determine the fair value of stock-based awards, including the award s expected term and the price volatility of the underlying stock. We recognize the value of the portion of the awards that is ultimately expected to vest as expense over the requisite vesting periods on a straight-line basis for the entire award. Stock awards granted to employees are service-based and prior to December 31, 2010 typically vest over a three year period, with one-third of the underlying shares vesting on each anniversary of grant, and have a ten year term. Beginning in January 2011, newly granted stock awards have a ten year term and typically vest over a four year period, with one fourth of the underlying shares vesting on the first anniversary of the grant and 1/48th of the underlying shares vesting monthly thereafter, such that the underlying shares will be fully vested on the fourth anniversary of the grant. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The following table summarizes the weighted average assumptions used in determining the fair value of stock options granted:

	Year Ended December 31,		
	2012	**2011**	**2010**
Risk-free interest rate	0.6% - 1.1%	0.9% - 2.4%	1.4% - 3.8%
Expected dividend yield	%	%	%
Expected lives	4.8 - 5.3 years	5.2 - 8.9 years	5.3 - 8.0 years
Expected volatility	79.7% - 108.6%	78.2% - 81.6%	82.5% - 90.3%

The risk free interest rate is estimated using an average of U.S. Treasury bill interest rates over a historical period commensurate with the expected life of the option that correlates to the prevailing interest rates at the time of grant. The expected dividend yield is zero as we have not paid any dividends to date and do not expect to pay dividends in the future. The expected lives are estimated using expected and historical exercise behavior. The expected volatility is estimated using calculated volatility of our common stock over a historical period commensurate with the expected life of the option. The amounts estimated according to the Black-Scholes option pricing model may not be indicative of the actual values realized upon the exercise of these options by the holders.

The assumptions used in calculating the fair value of stock-based compensation expense represent management s best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and we use different assumptions, our stock-based compensation expense could be materially different in the future. See Note 3 Stock Compensation of the audited financial statements included elsewhere in this Annual Report on Form 10-K for a further discussion of stock-based compensation.

Warrant Liability

In December 2007 and January and August of 2009, we issued warrants to purchase an aggregate of 5.0 million shares of our common stock in connection with offerings of our common stock. These warrants are classified as a liability due to their settlement terms. These warrants are non-cash liabilities; we are not required to expend any cash to settle these liabilities.

Table of Contents

The fair value of the warrants is recorded on our consolidated balance sheet as a liability, and fair value is adjusted at each financial reporting period with the adjustment reflected in our consolidated statement of operations. The fair value of the warrants is determined using the Black-Scholes option pricing model, which requires the use of significant judgment and estimates related to the inputs used in the model. The following reflects the weighted-average assumptions for each of the periods indicated:

	Year Ended December 31,		
	2012	2011	2010
Risk-free interest rate	0.2% - 0.3%	0.1% - 0.4%	0.6% - 1.0%
Expected dividend yield	%	%	%
Expected lives	1.1 - 1.6 years	1.0 - 2.7 years	2.0 - 3.7 years
Expected volatility	139.2% - 164.1%	71.8% - 75.6%	84.7% - 90.1%

Fluctuations in the assumptions and factors used in the Black-Scholes model can result in adjustments to the fair value of the warrants reflected on our balance sheet and, therefore, our statement of operations. If, for example, the market value of our common stock or its volatility at December 31, 2012 were 10% higher or lower than what we used in the valuation of the warrants, our valuation of the warrants would have increased or decreased by $7.5 million due to the change in market price, and our valuation would have increased or decreased by $ 2.0 million due to the change in volatility, with the differences being reflected in our statement of operations. See Note 8 Warrants of the audited financial statements included elsewhere in this Annual Report on Form 10-K for a further discussion of warrants.

Results of Operations for the years ended December 31, 2012, 2011 and 2010

The following table sets forth selected consolidated statements of operations data for each of the periods indicated:

Summary of Results for Fiscal Years 2012, 2011 and 2010

	Year Ended December 31,		
	2012	2011	2010
	(in thousands, except per share amounts)		
Operations data:			
Revenues	$ 37,329	$ 46,990	$ 29,420
Research and development	52,402	66,862	35,972
General and administrative	14,630	16,055	14,382
Operating loss	(29,703)	(35,927)	(20,934)
Interest income and other, net	354	587	259
Gain (Loss) on change in warrant valuation	(91,938)	33,022	(11,502)
Net loss	$ (121,287)	$ (2,318)	$ (32,177)
Net loss per share basic and diluted	$ (5.14)	$ (0.11)	$ (1.74)

Revenue

Revenue for 2012 decreased by $9.7 million, or 21%, compared to 2011. The decrease was due to $4.0 million less revenue from the May 2009 and June 2010 H1N1 agreements which ended in 2011 and $6.3 million less revenue from the 2010 Ebola and Marburg contract. Of the $6.3 million from the 2010 Ebola and Marburg contract, $5.6 million was due to the Ebola portion of the contract being terminated for convenience by the U.S. government due to lack of funding in the third quarter of 2012. These decreases in 2012 revenue were partially offset by initial revenue from the IM contract of $0.7 million.

Table of Contents

Revenue for 2011 increased by $17.6 million, or 60%, compared to 2010. The increase was primarily due to the 2010 Ebola and Marburg contract we received in July 2010, which contributed revenue of $42.9 million in 2011, an increase of $33.1 million over the prior year. This increase was partially offset by decreases in revenue on contracts we completed during 2011, including $10.0 million from the May 2009 and June 2010 H1N1 agreements, $1.2 million from the QTDP grants and a $3.7 million decrease for the 2006 Ebola, Marburg and Junín contracts.

Research and Development Expenses

Research and development expenses for 2012 decreased by $14.5 million, or 22%, compared to 2011. The decrease was due primarily to a $ 6.4 million decrease in non DMD proprietary research and a $4.1 million reduction in costs related to the Ebola portion of the July 2010 Ebola and Marburg contract which the U.S. government terminated due to a lack of funding in the third quarter of 2012, a $2.0 million reduction in costs resulting from the completion of the May 2009 and June 2010 H1N1 government contracts in 2011, a $1.0 million reduction due to the timing of various activities in both the Marburg portion of the July 2011 contract and the DMD program.

Research and development expenses for 2011 increased by $30.9 million, or 86%, compared to 2010 due primarily to a $22.8 million increase in costs related to the July 2010 Ebola and Marburg contract, a $6.4 million increase in costs for our proprietary DMD program that is in Phase II clinical trials, a $4.8 million increase for proprietary research and development and a $3.9 million increase from manufacturing activities. These increases were partially offset by a $5.0 million decrease in costs related to the May 2009 and June 2010 H1N1 contracts completed in 2011 and a $2.0 million decrease related to the 2006 Ebola, Marburg and Junín contract, which was completed in 2010.

General and Administrative Expenses

General and administrative expenses for 2012 decreased by $1.4 million, or 9%, compared to 2011. The decrease was primarily due to a decrease of $1.2 million in professional consulting services and $0.7 million in severance costs. These decreases were partially offset by $0.3 million of higher personnel costs due to filling vacant senior level positions.

General and administrative expenses for 2011 increased by $1.7 million, or 12%, compared to 2010. This increase was due primarily to an increase of $1.4 million in personnel related costs and $1.1 million in professional consulting costs. Legal fees and employee severance costs decreased by approximately $0.5 million each while facility costs also increased by $0.2 million.

Gain (Loss) on Change in Warrant Valuation

In 2012, we recognized $91.9 million of expense due to the increase in the fair value of our outstanding warrants that are classified as liabilities on our December 31, 2012 consolidated balance sheet and warrants exercised during 2012. In 2011, we recognized $33.0 million of income due to the reduction in the fair value of our outstanding warrants that are classified as liabilities on our December 31, 2011 consolidated balance sheet. The change in fair value of our warrant liability is primarily attributable to the change in our stock price.

Net Loss

The increase in our net loss of $119.0 million for 2012 compared to 2011 was primarily attributable to a $125.0 million increase in other non operating income (loss) resulting from an increase in the fair value of warrants accounted for as liabilities partially offset by a $ 6.2 million decrease in our operating loss.

The decrease in our net loss of $29.9 million, or 93%, for 2011 compared to 2010 was primarily attributable to a $44.9 million increase in non operating income (loss) resulting from a decrease in the fair value of our outstanding warrants offset by an increase in operating loss of $15.0 million.

Table of Contents

Liquidity and Capital Resources

At December 31, 2012, our cash and cash equivalents were $187.7 million, compared to $39.9 million at December 31, 2011. The significant increase is due primarily to public offerings of our common stock and the exercise of outstanding warrants for the purchase of our common stock. Based on the factors described below, we believe that our currently available cash and cash equivalents is more than sufficient to finance our operations for the next 12 months.

Our principal sources of liquidity are revenue from our U.S. government research contracts and grants and equity transactions. Our principal uses of cash are research and development expenses, general and administrative expenses and other working capital requirements.

Our primary source of revenue is from development of product candidates pursuant to our contracts with the U.S. government. Government funding is subject to the U.S. government s appropriations process and the U.S. government has the right under our contracts with them to terminate such contracts for convenience as was done regarding the Ebola portion of the 2010 Ebola Marburg contract. If U.S. government funding is not received or is delayed, we would likely curtail certain of our infectious disease research and development efforts unless additional funding was obtained. Currently, we do not generate any revenue from the commercial sale of our pharmaceutical product candidates.

Our future expenditures and capital requirements depend on numerous factors, most of which are difficult to project beyond the short term. These requirements include the progress of our research and development programs and our pre-clinical and clinical trials, our ability to meet the requirements of our U.S. government research projects, the time and costs involved in obtaining regulatory approvals, the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights, competing technological and market developments, our ability to establish collaborative arrangements and the terms of any such arrangements, and the costs associated with manufacturing and commercialization of our products.

Our cash requirements are expected to continue to increase as we advance our research, development and commercialization programs and we expect to seek additional financing primarily from, but not limited to, the sale and issuance of equity, debt securities or the licensing or sale of our technology. We cannot assure you that financing will be available when and as needed or that, if available, the financings will be on favorable or acceptable terms. If we are unable to obtain additional financing when and if we require, it would have a material adverse effect on our business and results of operations. To the extent we issue additional equity securities, our existing shareholders could experience substantial dilution.

Historical Trends

The following table sets forth sources and uses of funds activity for the period shown:

	Year Ended December 31,		
	2012	2011	2010
		(in thousands)	
Cash provided by (used in):			
Operating activities	$ (29,694)	$ (23,679)	$ (15,209)
Investing activities	(1,145)	(2,305)	(1,961)
Financing activities	178,596	32,299	2,484
Increase (decrease) in cash and equivalents	$ 147,757	$ 6,315	$ (14,686)

Table of Contents

Operating Activities.

We used $29.7 million of cash in operating activities for the year ended December 31, 2012, an increase of $6.0 million, or 25%, compared to $23.7 million of cash used in operating activities for the year ended December 31, 2011. In 2012, if the non-cash income effects associated with th