

Sarepta Therapeutics Announces Eteplirsen Demonstrates Stability on Pulmonary Function Tests through 120 Weeks in Phase IIb Study in Duchenne Muscular Dystrophy

February 5, 2014 8:30 AM ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 5, 2014-- Sarepta Therapeutics, Inc. (NASDAQ: SRPT), a developer of innovative RNA-based therapeutics, today announced new pulmonary function data through Week 120 from Study 202, a Phase IIb open-label extension study of eteplirsen in patients with Duchenne muscular dystrophy (DMD). Results through more than two years of treatment showed stable pulmonary function in the Intent-to-Treat (ITT) study population (N=12). These data are consistent with previously reported 120-week clinical data showing a general stabilization of walking ability in eteplirsen-treated patients evaluable on the 6-minute walk test (6MWT).

Respiratory muscle function from baseline through Week 120, as measured by maximum inspiratory and expiratory pressure (MIP and MEP), showed a 14.6 percent mean increase in MIP and a 15.0 percent mean increase in MEP. Analyses of MIP percent predicted (MIP adjusted for weight) and MEP percent predicted (MEP adjusted for age) demonstrated a mean increase from 90.2 percent at baseline to 95.2 percent at Week 120 in MIP percent predicted, and a slight mean increase from 79.3 percent at baseline to 79.6 percent at Week 120 in MEP percent predicted. In addition, there was a mean increase in forced vital capacity (FVC), a measure of lung volume, of 8.7 percent from baseline to Week 120, and FVC percent predicted (FVC adjusted for age and height) was maintained above a mean of 90 percent through Week 120, with 101 percent at baseline and 93 percent at Week 120.

“We now have pulmonary function clinical outcome measures demonstrating general stability over a time period and in an age group where we would expect to see decline,” said Edward Kaye, M.D., senior vice president and chief medical officer of Sarepta Therapeutics. “While we will continue to monitor these patients on pulmonary function tests, the 120-week data potentially provide early evidence towards achieving a key treatment goal, the delay or avoidance of pulmonary ventilation assistance in DMD patients.”

“The first sign of respiratory muscle weakness in DMD is often deterioration in MIP and MEP as patients approach and enter their early teen years,” said Jerry Mendell, M.D., director of the Centers for Gene Therapy and Muscular Dystrophy at Nationwide Children's Hospital and principal investigator of the Phase IIb study. “As the muscles continue to weaken over the course of the disease, respiratory dysfunction requiring ventilation support can severely impact quality of life and respiratory failure is often a significant factor in patient mortality in the later stages of disease progression.”

Results through Week 120 for other exploratory efficacy endpoints, including timed function tests (e.g., Gowers' maneuver and timed 4-step test) and the North Star Ambulatory Assessment have shown declines compared to baseline, though at potentially slower rates as compared to the limited available natural history data. These endpoints are less well characterized in DMD patients than the 6MWT and pulmonary function tests and have more inter- and intra-patient variability, although they may be predictors of decline at various stages of this disease. All patients evaluable on measures of ambulation (modified Intent-to-Treat, or mITT population) are still able to perform these tests with the exception of one patient who is no longer able to perform the Gowers' maneuver.

As previously reported, eteplirsen was well tolerated through Week 120 and there were no reported clinically significant treatment-related adverse events and no treatment-related serious adverse events. In addition, there were no hospitalizations or discontinuations.

Summary of Pulmonary Function Test Results for Two Patients Excluded from the Modified Intent-to-Treat Population

Previously reported analyses of the 6MWT results for the mITT population excluded two non-ambulatory patients in the 30 mg/kg cohort. The two patients, who are identical twin boys, continue to be evaluated on pulmonary function tests and were included in the ITT analyses for these measures. Pulmonary function results for these patients are notable because non-ambulatory patients are more likely to experience major respiratory complications.¹

Both patients showed rapid disease progression upon enrollment and lost ambulation proximate to the Week 24 visit, the time point at which increases in dystrophin protein were first confirmed in their respective muscle biopsies. Consistent with this result, both patients demonstrated a mild decline on pulmonary function tests from baseline to Week 24. From Week 24 to Week 120, these

patients showed general stability on these measures, with both showing increases in MEP and FVC, and one of them showing an increase in MIP. Over this time period, there was stability or limited declines in MIP percent predicted, MEP percent predicted, and FVC percent predicted in these patients.

Summary of Pulmonary Function Tests: Week 120 Treatment Results

Pulmonary Function Test (PFT)†	Mean Baseline PFT Value	Mean Week 120 Value	% Change from Baseline*
Maximum Inspiratory Pressure	63.1 cm H ₂ O	72.3 cm H ₂ O	14.6%
Maximum Expiratory Pressure	68.1 cm H ₂ O	78.3 cm H ₂ O	15.0%
Forced Vital Capacity	1.73 liters	1.88 liters	8.7%
Forced Vital Capacity % Predicted	101.3%	93.2%	-8.0%
Maximum Inspiratory Pressure % Predicted	90.2%	95.2%	5.5%
Maximum Expiratory Pressure % Predicted	79.3%	79.6%	0.4%

† All PFT analyses include the ITT population (N=12)

* All Week 120 data were not statistically significantly different from baseline, except for a statistically significant increase in MEP (using one-sample t-test).

About the Phase IIb Eteplirsen Program (Studies 201 and 202)

Study 201 was a randomized, double-blind, placebo-controlled clinical study conducted at Nationwide Children's Hospital in Columbus, Ohio. Twelve boys aged 7 to 13 years with a confirmed genotype amenable to treatment with an exon-51 skipping drug were randomized to one of three cohorts: 30 mg/kg (n=4), 50 mg/kg (n=4), and placebo/delayed treatment (n=4). Eteplirsen and placebo were administered weekly by intravenous infusion.

At Week 25, all patients rolled over to Study 202, a long-term open-label extension study, and placebo-treated patients initiated eteplirsen treatment at 30 mg/kg (n=2) or 50 mg/kg (n=2).

The primary efficacy endpoint in Study 201 and Study 202 was the increase in novel dystrophin as assessed by muscle biopsy at Weeks 12 and 24 and at Week 48, respectively. The primary clinical endpoint was the 6MWT, a well-accepted measure of ambulation and clinical function in DMD. Long-term follow up in Study 202 continues to evaluate safety and clinical outcomes including the 6MWT.

About the Pulmonary Function Tests (PFTs)

Progressive respiratory muscle dysfunction in patients with DMD typically leads to ventilation assistance and respiratory failure, and may ultimately be a significant factor in patient mortality.² Measurements of respiratory function are important for tracking the course of the disease, as well as the evaluation of potential therapeutic interventions. Maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP) and forced vital capacity (FVC) were included in the Phase IIb clinical studies of eteplirsen as exploratory clinical outcome measures.

MIP and MEP measure the highest level of pressure a person can generate during inhalation and exhalation, respectively, and are the most sensitive measures of respiratory muscle strength.³ Specifically, MIP is a sensitive measure of diaphragm muscle weakness. In addition, DMD natural history studies have shown a decline in MEP before changes in other pulmonary function tests, including MIP and FVC, suggesting MEP is an early indicator of respiratory dysfunction.⁴ FVC measures the total volume of air expelled during forced exhalation after maximum inspiration. In DMD, FVC increases concomitantly with physical growth until the early teens. However, as growth slows or is stunted by disease progression, and muscle weakness progresses, the vital capacity enters a descending phase and declines at an average rate of about 8 to 8.5 percent per year after 10 to 12 years of age.^{4,5} MIP percent predicted (MIP adjusted for weight), MEP percent predicted (MEP adjusted for age) and FVC percent predicted (FVC adjusted for age and height) are supportive analyses.

About Duchenne Muscular Dystrophy

DMD is an X-linked rare degenerative neuromuscular disorder causing severe progressive muscle loss and premature death. One of the most common fatal genetic disorders, DMD affects approximately one in every 3,500 boys born worldwide. A devastating and incurable muscle-wasting disease, DMD is associated with specific errors in the gene that codes for dystrophin, a protein that plays a key structural role in muscle fiber function. Progressive muscle weakness in the lower limbs spreads to the arms, neck and other areas. Eventually, increasing difficulty in breathing due to respiratory muscle dysfunction requires ventilation support, and cardiac dysfunction can lead to heart failure. The condition is universally fatal, and death usually occurs before the age of 30.

About Sarepta's Proprietary Exon-Skipping Platform Technology

Eteplirsen is Sarepta's lead drug candidate and is designed to address the underlying cause of DMD by enabling the production of a functional dystrophin protein. Data from clinical studies of eteplirsen in DMD patients have demonstrated a broadly favorable safety and tolerability profile and restoration of dystrophin protein expression.

Eteplirsen uses Sarepta's novel phosphorodiamidate morpholino oligomer (PMO)-based chemistry and proprietary exon-skipping technology to skip exon 51 of the dystrophin gene enabling the repair of specific genetic mutations that affect approximately 13 percent of the total DMD population. By skipping exon 51, eteplirsen may restore the gene's ability to make a shorter, but still functional, form of dystrophin from messenger RNA, or mRNA. Promoting the synthesis of a truncated dystrophin protein is intended to stabilize or significantly slow the disease process and prolong and improve the quality of life for patients with DMD.

Sarepta is also developing other PMO-based exon-skipping drug candidates intended to treat additional patients with DMD.

About Sarepta Therapeutics

Sarepta Therapeutics is focused on developing first-in-class RNA-based therapeutics to improve and save the lives of people affected by serious and life-threatening rare and infectious diseases. The Company's diverse pipeline includes its lead program eteplirsen, for Duchenne muscular dystrophy, as well as potential treatments for some of the world's most lethal infectious diseases. Sarepta aims to build a leading, independent biotech company dedicated to translating its RNA-based science into transformational therapeutics for patients who face significant unmet medical needs. For more information, please visit us at www.sarepta.com.

Forward-Looking Statements and Information

This press release contains forward-looking statements. These forward-looking statements generally can be identified by use of words such as "believes or belief," "anticipates," "plans," "expects," "will," "intends," "potential," "possible," "advance" and similar expressions. These forward-looking statements include statements about the development of eteplirsen and its efficacy, potency and utility as a potential treatment for DMD, the potential for the creation of ongoing novel dystrophin and its ability to lead to significant clinical benefit, including as measured by the 6MWT and exploratory measures such as pulmonary function tests, over a longer course of treatment.

Each forward-looking statement contained in this press release is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statement. Applicable risks and uncertainties include, among others: subsequent clinical trials may fail to demonstrate the safety and efficacy of eteplirsen or replicate results; treatment of patients with DMD using eteplirsen over a longer duration may not lead to significant clinical benefit, including as measured by the 6MWT and exploratory measures such as pulmonary function tests; any of Sarepta's drug candidates, including eteplirsen, may fail in development, may not receive required regulatory approvals (including Subpart H accelerated approval), or may not become commercially viable during projected time frames or at all due to delays or other reasons; and those identified under the heading "Risk Factors" in Sarepta's Annual Report on Form 10-K for the full year ended December 31, 2012 and as updated by our 2013 third quarter 10-Q, and filed with the Securities and Exchange Commission (SEC).

Any of the foregoing risks could materially and adversely affect Sarepta's business, results of operations and the trading price of Sarepta's common stock. For a detailed description of risks and uncertainties Sarepta faces, you are encouraged to review the Company's filings with the SEC. We caution investors not to place considerable reliance on the forward-looking statements contained in this press release. Sarepta does not undertake any obligation to publicly update its forward-looking statements based on events or circumstances after the date hereof.

References:

- ¹ Bushby K. , R. Finkel, D. Birkrant, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. *Lancet Neurol.* 2010 Feb; 9(2): 177-89.
- ² Finder J.D., D. Birnkrant, J. Carl, et al. Respiratory care of the patient with Duchenne muscular dystrophy: an official ATS consensus statement. *Am J Respir Crit Care Med.* 2004; 170: 456–65.
- ³ Lynn, D. J., R. P. Woda and J. R. Mendell. Respiratory dysfunction in muscular dystrophy and other myopathies. *Clin Chest Med.* 1994; 15(4): 661-674.
- ⁴ Hahn, A., J. R. Bach, A. Delaubier, et al. Clinical implications of maximal respiratory pressure determinations for individuals with Duchenne muscular dystrophy. *Arch Phys Med Rehabil.* 1997; 78(1): 1-6.
- ⁵ McDonald, C. M., R. T. Abresch, G. T. Carter, et al. Profiles of neuromuscular diseases. Duchenne muscular dystrophy. *Am J Phys Med Rehabil.* 1995; 74(5 Suppl): S70-92.

Source: Sarepta Therapeutics

Sarepta

Investor Contact:

Erin Cox, 857-242-3714

ecox@sarepta.com

or

Media Contact:

Jim Baker, 857-242-3710

jbaker@sarepta.com