Sarepta Therapeutics Announces Eteplirsen Demonstrates Sustained Benefit on Walking Test Through 74 Weeks in Phase IIb Study in Duchenne Muscular Dystrophy

April 5, 2013 8:30 AM ET

Data to Be Presented at the Muscular Dystrophy Association Scientific Conference

CAMBRIDGE, MA -- (Marketwired) -- 04/05/13 -- Sarepta Therapeutics, Inc. (NASDAQ: SRPT), a developer of innovative RNA-based therapeutics, today announced updated data from Study 202, a Phase IIb open-label extension study of eteplirsen in patients with Duchenne muscular dystrophy (DMD). Results at 74 weeks showed a continued stabilization of walking ability in eteplirsen-treated patients evaluable on the 6-minute walk test (6MWT). As previously reported, Study 202 met its primary endpoint of increased novel dystrophin as assessed by muscle biopsy at week 48 and is now in the long-term extension phase in which patients continue to be followed for safety and clinical outcomes. Eteplirsen is Sarepta's lead exon-skipping compound in development for the treatment of patients with DMD who have a genotype amenable to skipping of exon 51.

After 74 weeks, patients in the 30 mg/kg and 50 mg/kg dose cohorts who were able to perform the 6MWT (modified Intent-to-Treat or mITT population; n=6) showed a statistically significant treatment benefit of 65.2 meters ($p \leq 0.004$) when compared to the placebo/delayed-treatment cohort (n=4). The eteplirsen-treated patients in the mITT population demonstrated less than a 5 percent decline (13.4 meters) from baseline in walking ability. After experiencing a substantial decline earlier in the study, the placebo/delayed-treatment cohort also demonstrated stabilization in walking ability from week 36 through 74, the period in which meaningful levels of dystrophin were likely produced, with a less than 10 meter decline over this timeframe.

"We are encouraged to see a continued stabilization of walking ability in patients treated with eteplirsen for nearly one and a half years," said Chris Garabedian, president and chief executive officer of Sarepta Therapeutics. "These data are particularly compelling when viewed in the context of published natural history studies, which showed substantial declines on the 6-minute walk test over this timeframe in a similar ambulatory DMD population. These results continue to support the potential of eteplirsen to be a major advance in the treatment of DMD in altering the course of this progressive and irreversible disease."

Through 74 weeks, eteplirsen was well tolerated and there were no clinically significant treatment-related adverse events, serious adverse events, hospitalizations or discontinuations. As previously reported at 62 weeks, one patient had a transient elevation of urine protein on a laboratory urine dipstick test, which resolved and resulted in no clinical symptoms. The patient continued treatment without interruption and remained free of proteinuria through week 74.

Across both the eteplirsen (mITT) and placebo/delayed-treatment cohorts, there is evidence of continued stabilization on clinical laboratory tests, echocardiogram, pulmonary function tests and muscle strength.

Summary of Additional 6MWT Analyses

Patients performed two 6MWT evaluations on consecutive days at time points coinciding with a muscle biopsy procedure at baseline and weeks 12, 24 and 48. All other evaluations were a single 6MWT. The pre-specified primary analysis included the maximum distance walked at those clinic visits where repeated tests were taken. Other analyses of the repeated 6MWT results assessed mean, minimum, and day 1 (first measure) scores. Results from these additional 6MWT analyses confirm the robust treatment effect observed in the primary analysis.

Summary of 6MWT: Eteplirsen (mITT) versus Placebo/Delayed-Treatment to Week 74*

Analysis of Repeated 6MWT Values	Baseline 6MWT (meters)	Adjusted Mean 6MWT Change from Baseline (meters)	Estimated Treatment Benefit (Eteplirsen Minus Placebo/delayed-Tx)	P-Value

Maximum Score Eteplirsen (n=6)	399.7	-13.4	65.2 m	≤ 0.004
Maximum Score Placebo/delayed-Tx (n=4)	394.5	-78.6		
Mean Score Eteplirsen (n=6)	388.6	-2.2	62.4 m	≤ 0.007
Mean Score Placebo/delayed-Tx (n=4)	380.3	-64.6		
Minimum Score Eteplirsen (n=6)	377.5	+9.0	59.6 m	≤ 0.015
Minimum Score Placebo/delayed-Tx (n=4)	366.0	-50.6		
Day 1 Score Eteplirsen (n=6)	379.7	+6.6	62.2 m	≤ 0.013
Day 1 Score Placebo/delayed-Tx (n=4)	371.5	-55.6		

**All analyses are based on a Mixed Model Repeated Measures test.*

Jerry R. 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, will present these data in an oral presentation at the Muscular Dystrophy Association Scientific Conference on Tuesday, April 23 at 4:05 p.m. EDT in Washington, D.C. Dr. Mendell's presentation will be posted on the Sarepta website in the "Events & Presentations" section after the session is completed.

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 7-13 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 every 12 weeks.

About the 6-Minute Walk Test (6MWT)

The 6-minute walk test (6MWT) was developed as an integrated assessment of cardiac, respiratory, circulatory, and muscular capacity (American Thoracic Society 2002) for use in clinical trials of various cardiac and pulmonary conditions. In recent years the 6MWT has been adapted to evaluate functional capacity in neuromuscular diseases and has served as the basis for regulatory approval of a number of drugs for rare diseases, with mean changes in the 6MWT ranging from 28 to 44 meters (Rubin 2002, Wraith 2004, Muenzer 2006). Additionally, published data from longitudinal natural history studies assessing dystrophinopathy, a disease continuum comprised of DMD and Becker muscular dystrophy, support the utility of the 6MWT as a clinically meaningful endpoint (McDonald 2010) in DMD. These data show that boys with DMD experience a significant decline in walking ability compared to healthy boys over one year, suggesting that slowing the loss of walking ability is a major treatment goal.

About the Statistical Methodology and the Modified Intent-to-Treat (mITT) Population

The Mixed Model Repeated Measures (MMRM) test was used for all statistical analyses of the 6MWT results, including for all subgroups. Analysis of Covariance (ANCOVA) for ranked data was used when the assumptions of normality of the dependent

variable (the change in 6MWT distance from baseline) were violated. Baseline 6MWT scores and duration since DMD diagnosis were included as covariates.

The mITT population used in the 6MWT analyses consisted of 10 of the 12 enrolled patients, including 4 patients in the 50 mg/kg cohort, 2 patients in the 30 mg/kg cohort and 4 patients in the placebo/delayed-treatment cohort. Two patients in the 30 mg/kg cohort showed rapid disease progression upon enrollment and lost ambulation by week 24, and thus were excluded.

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 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 eventually spreads to the arms, neck and other areas. Eventually, this progresses to complete paralysis and increasing difficulty in breathing due to respiratory muscle dysfunction requiring ventilation support, as well as cardiac dysfunction leading to heart failure. The condition is terminal, and death usually occurs before the age of 30.

About Sarepta's Proprietary Exon-Skipping Platform Technology

Eteplirsen is Sarepta's lead drug candidate that 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 improve, 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.sareptatherapeutics.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 in the treatment of DMD and the potential for the creation of novel dystrophin to lead to significant clinical benefit 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; any of Sarepta's drug candidates, including eteplirsen, may fail in development, may not receive required regulatory approvals, or may not become commercially viable 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

filed with the Securities and Exchange Commission.

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 Securities and Exchange Commission. 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.

"Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995: The statements that are not historical facts contained in this release are forward-looking statements that involve risks and uncertainties, including, but not limited to, the results of research and development efforts, the results of preclinical and clinical testing, the effect of regulation by the FDA and other agencies, the impact of competitive products, product development, commercialization and technological difficulties, and other risks detailed in the company's Securities and Exchange Commission filings.

Sarepta Investor Contact:
Erin Cox
857.242.3714

Sarepta Media Contact:
Jim Baker
857.242.3710

Source: Sarepta Therapeutics, Inc.