Sarepta Therapeutics Reports Long-Term Outcomes through 168 Weeks from Phase IIb Study of Eteplirsen in Duchenne Muscular Dystrophy

CAMBRIDGE, Mass. --Jan 12, 2015-- Sarepta Therapeutics, Inc. (NASDAQ: SRPT), a developer of innovative RNA-based therapeutics, today announced data through Week 168 from Study 202, a Phase IIb open-label extension study of eteplirsen in patients with Duchenne muscular dystrophy (DMD). After more than three years of treatment, results of the 6-minute walk test (6MWT) at 168 weeks showed continued ambulation across all patients evaluable on the test, however all patients showed a decline in distance walked on this measure since the week 144 timepoint. In addition, a continued stability of respiratory muscle function was observed, as assessed by pulmonary function tests. As previously reported, Study 202 met its primary endpoint of increased novel dystrophin as assessed by muscle biopsy at Week 48.

At Week 168, the six patients in the modified Intent-to-Treat or mITT population in the 30 and 50 mg/kg eteplirsen cohorts who were able to perform the 6MWT experienced a decline of 76.7 meters, or about 19.5 percent, from baseline in walking ability. A statistically significant treatment benefit of 65.4 meters ($p \leq 0.017$) was observed compared with the placebo/delayed-treatment cohort (n=4), which initiated treatment at Week 25 following 24 weeks of placebo. This cohort, after experiencing a substantial decline of 68.4 meters from baseline to Week 36, demonstrated a decline of 73 meters in walking ability from Week 36 through Week 168, the period from which meaningful levels of dystrophin were likely produced. These analyses were based on the maximum 6MWT score when the test was performed on two consecutive days.

''With greater than three years of eteplirsen experience, the clinical outcomes that our team has demonstrated in the testing of these boys exhibit greater stability in function than anticipated at a time when we often observe a more significant decline without treatment. Based on my many years of caring for patients with this devastating disease, I view these more than 3 years of data as very encouraging," said Jerry Mendell, M.D., director of the Centers for Gene Therapy and Muscular Dystrophy at Nationwide Children's Hospital and principal investigator of Study 202. "The safety profile of eteplirsen continues to impress me. We have not witnessed any clinically meaningful treatment-related adverse events during the 168 weeks of eteplirsen treatment."

Respiratory muscle function from baseline through Week 168 in the Intent-to-Treat population (n=12), as measured by maximum inspiratory and expiratory pressure (MIP and MEP), continued to show a 11.1 percent mean increase in MIP and a 14.7 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 change from 91.7 percent at baseline to 89.5 percent at Week 168 in MIP percent predicted, and a mean change from 79.3 percent at baseline to 74.3 percent at Week 168 in MEP percent predicted. In addition, there was a mean increase in forced vital capacity (FVC), a measure of lung volume, of 11.6 percent. FVC percent predicted (FVC adjusted for age and height) was maintained above a mean of 90 percent at Week 168, with 101.3 percent at Baseline and 91.9 percent at Week 168.

"PPMD's benefit-risk pilot data demonstrated that parents' highest priority is to slow DMD progression. With this priority in mind, these Phase II data have exceeded our expectations" said Pat Furlong, Founding President and CEO of Parent Project Muscular Dystrophy (PPMD), a nonprofit organization focused on finding a cure for Duchenne muscular dystrophy. "In practical terms, continued ambulation and preservation of respiratory function have immense benefit for individuals with Duchenne. It is important to keep in mind, that individuals participating in this study lived with Duchenne for over 9 years on average prior to receiving eteplirsen, an age when the pathological process that occurs based on the absence of dystrophin is typically well underway. Understanding this, in the eyes of the community these Phase II data are significant and represent an important step toward changing the landscape."

Sarepta announced last year that the 168 week results are one of several datasets the FDA has requested be included in, or at the time of, the NDA application. Sarepta's plan for a mid-year 2015 NDA submission remains unchanged and will continue to be evaluated based on FDA discussions and as additional data become available.

"While these older boys showed a continued decline in walking distance at the week 168 timepoint, we continue to be encouraged by those who have maintained their walking ability over this long-term extension study. We look forward to sharing the 168 results with the FDA, along with the additional datasets that will be collected in the coming months, as part of our ongoing discussions with the Agency," said Chris Garabedian, president and chief executive officer of Sarepta Therapeutics. "We are actively working towards the ongoing development of eteplirsen and future exon-skipping candidates which includes multiple clinical studies with eteplirsen across a broad spectrum of DMD patients and the initiation of a placebo-controlled study that will evaluate our follow-on exon-skipping drugs for DMD targeting exons 45 and 53 later this year."

Through 168 weeks, eteplirsen was well tolerated and there were no reported clinically significant treatment-related adverse events and no treatment-related serious adverse events. In addition, there were no treatment-related hospitalizations or discontinuations.

Summary of 6MWT: Week 168 Treatment Results*

Patients performed two 6MWT evaluations on consecutive days at time points coinciding with a muscle biopsy procedure at baseline and at Weeks 12, 24 and 48. Two 6MWT evaluations were also performed at Weeks 120, 144, and 168, and will be performed at all future functional assessment visits. 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 data observations in the primary analysis.

Analysis of Repeated 6MWT Values†	Baseline 6MWT (meters)	Adjusted Mean 6MWT Change from Baseline (meters) at Week 168	Estimated Treatment Benefit (Eteplirsen Minus Placebo/delayed-Tx)	P-Value
Maximum Score Eteplirsen (n=6)	399.7	-75.8	65.4	0.017
Maximum Score Placebo/delayed-Tx (n=4)	394.5	-141.2		
Mean Score Eteplirsen (n=6)	388.6	-72.9	63.0	0.023
Mean Score Placebo/delayed-Tx (n=4)	380.3	-135.9		
Minimum Score Eteplirsen (n=6)	377.5	-70.2	60.2	0.034
Minimum Score Placebo/delayed-Tx (n=4)	366.0	-130.4		
Day 1 Score Eteplirsen (n=6)	379.7	-64.1	67.3	0.025
Day 1 Score Placebo/delayed-Tx (n=4)	371.5	-131.3		

** All 6MWT analyses are based on a Mixed Model Repeated Measures test.*
† All 6MWT analyses include the mITT population

Summary of Pulmonary Function Tests: Week 168 Treatment Results

Pulmonary Function Test (PFT)*	Mean Baseline PFT Value	Mean Week 168 Value	% Change from Baseline†
Maximum Inspiratory Pressure	63.1 cm H_2O	70.1 cm H_2O	+11.1%
Maximum Expiratory Pressure	68.1 cm H_2O	77.3 cm H_2O	+13.5%
Forced Vital Capacity	1.73 liters	1.93 liters	+11.6%
Forced Vital Capacity % Predicted	101.3%	91.9%	-9.3%
Maximum Inspiratory Pressure % Predicted	91.7%	89.5%	-2.4%
Maximum Expiratory Pressure % Predicted	79.3%	74.3%	-6.3%

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

† All Week 168 data were not statistically significantly different from baseline, except for a statistically significant increase & decrease in FVC & FVC % Predicted, respectively (using one-sample t-test).

Summary of Additional Exploratory Efficacy Endpoints

Results through Week 168 for other exploratory efficacy endpoints, including timed function tests (e.g., Gowers' maneuver, 10 meter run/walk and timed 4-step test) and the North Star Ambulatory Assessment have shown continued 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 including the 10 meter run/walk and 4-step test, with the exception of three patients who are no longer able to perform the Gowers' maneuver.

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 6-Minute Walk Test (6MWT)

The 6-minute walk test (6MWT) was developed as an integrated assessment of cardiac, respiratory, circulatory, and muscular capacity for use in clinical trials of various cardiac and pulmonary conditions.[1] 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.[2,3,4] 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 in DMD.[5] 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 6MWT 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. 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 since they were no longer evaluable for the 6MWT. All other data were analyzed for all 12 patients.

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.[6] 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.[7] 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.[8] 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.[8,9] 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 internally deleted 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 an internally deleted 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 the 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 Sarepta's plans for a mid-year 2015 NDA submission, including its plans to produce and include additional data and information requested by the FDA as part of or at the time of the submission, such as the 168 week data; Sarepta's continuing evaluation of its planned NDA submission based on FDA ongoing discussions and additional data; the ongoing development of eteplirsen and follow-on product candidates, including the ongoing and planned additional clinical trials involving eteplirsen and exon skipping product candidates for exons 45 and 53; the potential safety, efficacy, and utility of eteplirsen as a potential treatment for DMD, including any potential eteplirsen benefit as compared to patients who receive current standard of care or no treatment; and the potential regulatory acceptance of a submission and approval of eteplirsen and other follow-on exon-skipping candidates.

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: We may not have sufficient funds to execute our business plans; ongoing or subsequent clinical trials may fail to demonstrate safety and efficacy of eteplirsen, replicate results or provide positive 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 and as compared to patients that receive standard of care or no treatment; any of Sarepta's drug candidates, including eteplirsen, may fail in development, may not receive required regulatory approvals, or may not become commercially viable during projected time frames or at all due to delays or other reasons; the FDA may determine that substantial additional data is required for accelerated or other approval of eteplirsen or that our NDA submission for eteplirsen does not qualify for filing, even if Sarepta complies with requests for additional data and information; there may be delays in timelines relating to an NDA submission or we may not make an NDA submission; there may be delays in initiating or we may not be able to successfully complete our ongoing or planned clinical trials; we may not be able to manufacture sufficient drug supply for clinical trials or commercialization; agency or court decisions with respect to our patents may negatively impact our business; and those risks identified under the heading "Risk Factors" in Sarepta's Quarterly Report on Form 10-Q for the quarter ended September 30, 2014 filed with the Securities and Exchange Commission (SEC), and Sarepta's other filings with the SEC. Investors and potential investors are encouraged to read our filings with the SEC, available at www.sec.gov, for a discussion of these and other risks and uncertainties.

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. 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.

Internet Posting of Information

We routinely post information that may be important to investors in the 'For Investors' section of our web site at www.sarepta.com*. We encourage investors and potential investors to consult our website regularly for important information about us.*

References:

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