Sarepta Therapeutics Announces Significant Clinical Benefit With Eteplirsen After 36 Weeks in Phase IIb Study for the Treatment of Duchenne Muscular Dystrophy

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Jul 24, 2012 (Marketwire via COMTEX) --Sarepta Therapeutics (NASDAQ: SRPT), a developer of innovative RNA-based therapeutics, today announced that treatment with its exon-skipping compound, eteplirsen, achieved a significant clinical benefit on the primary clinical outcome, the 6-minute walk test (6MWT), over a placebo/delayed treatment cohort in a Phase IIb trial in Duchenne muscular dystrophy (DMD) patients. 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 open-label extension. In the predefined prospective analysis of the study's intent-to-treat (ITT) 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 (n=4) 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 (n=4) 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 ($p \leq 0.019$).

"The magnitude of this clinical benefit is an unprecedented treatment effect in DMD. This result represents a major advance in the pursuit of a disease modifying treatment for this severe, progressive and life-threatening disease," 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. Dr. Mendell added, "The 6-minute walk test results with eteplirsen, combined with its safety profile to date, make eteplirsen the most promising advance to treat the underlying cause of muscular dystrophy I've seen in my more than 30 years in the field."

The clinical benefit observed in the 50mg/kg treatment cohort compared to placebo was also significant at week 32 with a benefit of 59.9 meters ($p \leq 0.045$). The safety profile of eteplirsen was evaluated across all subjects through 36 weeks 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.

"These data suggest that the previously reported levels of dystrophin we observed in muscle biopsies after 24 weeks of treatment are translating to a clinical benefit on the standard measure of ambulation in DMD patients," said Chris Garabedian, President and CEO of Sarepta Therapeutics. "The magnitude of this 69.4-meter difference after 36 weeks of treatment and the robustness of the statistical analysis is encouraging, especially given the average benefit in the 6-minute walk test for several approved drugs in other diseases has been 30 to 40 meters."

There was no statistically significant difference between the cohort of patients who received 30mg/kg weekly of eteplirsen and the placebo/delayed treatment cohort.

Modified Intent-to-Treat and Subgroup Analyses

A modified intent-to-treat (mITT) population was evaluated that excluded two patients who were randomized to the 30mg/kg weekly eteplirsen cohort who showed signs of rapid disease progression within weeks after enrollment and were unable to perform measures of ambulation beyond 24 weeks. This mITT population consisting of 10 patients (4 eteplirsen-treated patients receiving 50mg/kg weekly, 2 eteplirsen-treated patients receiving 30mg/kg weekly, and 4 placebo/delayed-treatment patients) was further analyzed.

Summary of 6MWT: Eteplirsen versus Placebo/Delayed-treatment through Week 36*

Treatment Arm	Mean 6MWT Change from Baseline (meters)	Estimated Treatment Effect (Eteplirsen minus Placebo/Delayed-Tx)	p-value
Placebo/Delayed-Tx (n=4)	-70.9		
Eteplirsen 50 mg/kg (n=4)	-5.2	65.8 meters	0.0002
Eteplirsen Both Doses (n=6)	-14.6	56.2 meters	0.0004
Eteplirsen 30 mg/kg (n=2)	-33.3	37.6 meters	ns

**Note: Analysis based on Mixed Model Repeated Measures test*

Summary of Additional Sub-Group Analyses at Week 36**

Subset	Mean 6MWT Change from Baseline (meters)	Estimated Treatment Benefit (Eteplirsen minus Placebo/delayed-Tx)	p-value
Placebo/delayed Tx: < 9.5 yrs at baseline (n=2; mean=7.6 yrs)	-60.6	63.6 meters	0.0040
Eteplirsen: < 9.5 yrs at baseline (n=3; mean=8.4 yrs)	+3.1		
Placebo/delayed Tx: ≥9.5 yrs at baseline (n=2; mean=10.1 yrs)	-73.4	36.0 meters	ns
Eteplirsen: ≥9.5 yrs at baseline (n=3; mean=10.4 yrs)	-37.4		
Placebo/delayed Tx: Higher 6MWT baseline (n=2; mean=422m)	-75.5	82.5 meters	0.0001
Eteplirsen: Higher 6MWT baseline (n=3; mean=424m)	+7.0		
Placebo/delayed Tx: Lower 6MWT baseline (n=2; mean=367m)	-72.1	39.9 meters	ns
Eteplirsen: Lower 6MWT baseline (n=3; mean=375m)	-32.3		
Placebo/delayed Tx: Genotype 49-50 deletion (n=3; age mean=9.2 yrs, 6MWT BL mean=397m)	-67.6	68.5 meters	0.0001
Eteplirsen: Genotype 49-50 deletion (n=2; age mean=9.1 yrs, 6MWT BL mean=383m)	+0.9		

*** Note: Analysis based on Mixed Model Repeated Measures test*

About Study 201 and Study 202 (Phase IIb Eteplirsen Study)

Study 4658-US-201 was conducted at Nationwide Children's Hospital in Columbus, Ohio. Twelve boys meeting the inclusion criteria being between 7 and 13 years of age with appropriate deletions of the dystrophin gene that confirm eligibility for treatment with an exon-51 skipping drug, received double-blind IV infusions of placebo (n=4), 30 mg/kg of eteplirsen (n=4), or 50 mg/kg of eteplirsen once weekly for 24 weeks (n=4). Muscle biopsies for evaluation of dystrophin were obtained at baseline for all subjects, and after 12 weeks for patients in the 50 mg/kg cohort and after 24 weeks for patients in the 30 mg/kg cohort. Two placebo patients were randomized to the 30 mg/kg cohort and two placebo patients were randomized to the 50 mg/kg cohort. This study design allowed Sarepta to investigate the relationship of dose and duration of eteplirsen treatment on the production of dystrophin over the course of the 24-week study.

Study 4658-US-202 is the extension study to 201 and continues to assess the long-term safety and efficacy of open-label eteplirsen. The four placebo patients were rolled over to open-label eteplirsen at week 24, with six patients on 30 mgs/kg, and six patients on 50 mgs/kg. Third biopsies will occur at 48 weeks in the original study 201 treated patients, and at 24 weeks, the same time point, in the original placebo patients. 6MWT was performed at 32 weeks and 36 weeks, and will continue to be performed every 12 weeks going forward.

About the 6-Minute Walk Test

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 Duchenne and Becker muscular dystrophy, support the utility of the 6MWT as a clinically meaningful endpoint (McDonald C, et al, Muscle & Nerve, December 2010) in Duchenne muscular dystrophy (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

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. The inclusion of the two patients with extreme scores due to rapid progression in the ITT population (n=12) resulted in a violation of the normality assumptions of the Change from Baseline in 6MWT data, and thus required the use of ANCOVA for ranked data. The exclusion of these two patients from the mITT population (n=10) resulted in the 6MWT data becoming normally distributed and the MMRM statistics exhibiting much improved residuals and fit statistics as compared to the ITT population. As such, the estimated mean values and their associated p-values for the mITT population were slightly different from those for the ITT population.

Conference Call and Slide Show

The Company will hold a conference call and broadcast a slide show today at 8:00 a.m. EDT (5:00 a.m. PDT) to discuss these results. The audio conference call may be accessed by dialing 866.783.2139 for domestic callers and 857.350.1598 for international callers. The passcode for the call is 77518015. Please specify to the operator that you would like to join the "Sarepta Therapeutics 36-Week Clinical Results Call." To view the slide show while using the audio dial-in please go to the events section of Sarepta's website at www.sareptatherapeutics.com. The call and slide show will also be webcast live under the events section and will be archived there following the call for 90 days. Please connect to Sarepta's website several minutes prior to the start of the broadcast to ensure adequate time for any software download that may be necessary. An audio replay will be available through July 31, 2012 by calling 888.286.8010 or 617.801.6888 and entering access code 44234182.

About Duchenne Muscular Dystrophy and Eteplirsen

Duchenne muscular dystrophy (DMD) is an X-linked rare, degenerative neuromuscular disorder causing severe, progressive muscle loss and a 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 inborn 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 ventilatory support, as well as cardiac muscle dysfunction leading to heart failure. The condition is terminal, and death usually occurs before the age of 30.

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 -- formerly AVI BioPharma -- 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

In order to provide Sarepta's investors with an understanding of its current results and future prospects, this press release contains statements that are forward-looking. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "will," "intends," "potential," "possible" and similar expressions are intended to identify forward-looking statements. 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.

These forward-looking statements involve risks and uncertainties, many of which are beyond Sarepta's control. Known risk factors include, among others: clinical trials may not demonstrate the safety and efficacy of eteplirsen and/or Sarepta's antisense-based technology platform; treatment of patients with DMD using eteplirsen over a longer duration may not lead to significant clinical benefit; and any of Sarepta's drug candidates, including eteplirsen, may fail in development, may not receive required regulatory approvals, or be delayed to a point where they do not become commercially viable.

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. Sarepta does not undertake any obligation to publicly update its forward-looking statements based on events or circumstances after the date hereof.

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