Sarepta Therapeutics, Inc.
Form 8-K
October 04, 2012

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the

Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 3, 2012

Sarepta Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Oregon	**001-14895**	**93-0797222**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

3450 Monte Villa Parkway, Suite 101

Bothell, WA 98021

(Address of principal executive offices, including zip code)

(425) 354-5038

(Registrant s telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

¨ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

¨ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

¨ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

¨ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 8.01 Other Events

On October 3, 2012, Sarepta Therapeutics, Inc. announced that treatment with its lead exon-skipping compound, eteplirsen, met the primary efficacy endpoint, increase in novel dystrophin, and achieved a significant clinical benefit on the primary clinical outcome, the 6-minute walk test (6MWT) over the placebo/delayed treatment cohort in a Phase IIb extension trial in Duchenne muscular dystrophy (DMD) patients.

Eteplirsen administered once weekly at either 30 mg/kg or 50 mg/kg for 48 weeks (n=8) resulted in a statistically significant increase ($p \leq 0.001$) 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 ($p \leq 0.009$).

Eteplirsen administered once weekly at 50 mg/kg over 48 weeks resulted in an 89.4 meter benefit compared to patients who received placebo for 24 weeks followed by 24 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 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 ANCOVA 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.

Summary of Dystrophin: Eteplirsen-Treated Patients in All Dose Groups through Week 48*

Treatment Arm	Mean Change from Baseline in % Dystrophin-Positive Fibers	p-value
Eterplirsen (both doses): 48 wks of Tx (n=8)	47.0	≤0.001
Eteplirsen 50 mg/kg (n=4)	41.7	≤0.008
Eteplirsen 30 mg/kg (n=4)	52.1	≤0.001
Placebo/Delayed Tx: 24 wks of Tx (n=4)	38.3	≤0.009
Placebo/50 mg/kg Delayed-Tx (n=2)	42.9	ns
Placebo/30 mg/kg Delayed-Tx (n=2)	34.2	ns

* ***Values based on Immunofluorescence using anti-dystrophin antibody MANDYS106***

Modified Intent-to-Treat (mITT)

The 6MWT results were further analyzed using the mITT population which excluded two patients who were randomized to the 30 mg/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 consisted of 10 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).

Summary of 6MWT: Eteplirsen versus Placebo/Delayed-Treatment to Week 48*

Treatment Arm	Mean Change from Baseline in 6MWT (meters)	Estimated Treatment Effect (Eteplirsen minus Placebo/Delayed-Tx)	p-value
Placebo/Delayed-Tx (n=4)	-60.3		
Eteplirsen 50 mg/kg (n=4)	+27.1	87.4 m	≤0.001
Eteplirsen Both Doses (n=6)	+7.3	67.3 m	≤0.001
Eteplirsen 30 mg/kg (n=2)	-31.5	28.8 m	ns

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

Summary of Additional Sub-Group Analyses at Week 48*

Subset	Mean 6MWT Change from Baseline (meters)	Estimated Treatment Benefit (Eteplirsen minus Placebo/delayed-Tx)	p-value
Placebo/delayed Tx:	-42.3	58.9 m	≤0.038
<9.5 yrs at baseline			
(n=2; mean=7.6 yrs)			
Eteplirsen:	+16.5		
<9.5 yrs at baseline			
(n=3; mean=8.4 yrs)			
Placebo/delayed Tx:	-63.5	52.1 m	ns
≥9.5 yrs at baseline			
(n=2; mean=10.1 yrs)			
Eteplirsen:	-11.3		
≥9.5 yrs at baseline			
(n=3; mean=10.4 yrs)			
Placebo/delayed Tx:	-53.5	93.8 m	≤0.001
Higher 6MWT baseline			
(n=2; mean=422m)			
Eteplirsen:	+40.3		
Higher 6MWT baseline			
(n=3; mean=424m)			
Placebo/delayed Tx: Lower	-65.8	39.6 m	ns
6MWT baseline			

(n=2; mean=367m)			
Eteplirsen:	-26.2		
Lower 6MWT baseline			
(n=3; mean=375m)			
Placebo/delayed Tx:	-69.0	83.4 m	≤0.001
Genotype 49-50 deletion			
(n=3; age mean=9.2 yrs,			
6MWT BL mean=397m)			
Eteplirsen:	+14.4		
Genotype 49-50 deletion			
(n=2; age mean=9.1 yrs,			
6MWT BL mean=383m)			

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

An abstract describing the results from this Phase IIb extension study has been accepted as part of the World Muscle Society (WMS) Congress s Late-Breaking Science program in Perth, Australia during October 9 to October 13, 2012. Principal investigator, Jerry R. Mendell, M.D. of Nationwide Children s Hospital, will present the data via an oral presentation of the abstract titled, Results at 48 Weeks of a Phase IIb Extension Study of the Exon-Skipping Drug Eteplirsen in Patients with Duchenne muscular dystrophy (DMD). Dr. Mendell will present on October 13 at 4:00 p.m. WST UTC +8 hours/4:00 a.m. EDT. Dr. Mendell s presentation will be posted on the Sarepta website in the Events & Presentations section after the session is completed. In addition, Sarepta is sponsoring an educational symposium at WMS chaired by Professor Steve Wilton, PhD, Head of the Molecular Genetic Therapy Group and Director of Translational Research and Development, Australian Neuromuscular Research Institute at the University of Western Australia. Professor Wilton is a long-time collaborator of Sarepta s whose groundbreaking research has extended the use of antisense oligomers to DMD.

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 occurred 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, 36 weeks, 48 weeks and will continue to be performed every 12 weeks going forward.

About Dystrophin

Dystrophin, a large structural protein, is critical to the stability of myofiber membranes in skeletal, diaphragmatic and cardiac muscle, protecting muscle fibers from contraction-induced damage. Loss of functional dystrophin destabilizes the dystroglycan protein complex, impairing its localization to the muscle membrane, and compromising the integrity of the membrane structure. The absence of functional dystrophin results in muscle membrane breakdown with muscle fibers being replaced by adipose and fibrotic tissue.

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

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.

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Forward-looking statements are identified by such words as anticipate, believe, expect, will and words of similar import and are based on current expectations that involve risks and uncertainties, such as the Company s plans, objectives, expectations and intentions. All statements other than historical or current facts are forward-looking statements, including, without limitation, 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 are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. The Company does not undertake any obligation to publicly update its forward-looking statements based on events or circumstances after the date hereof.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Sarepta Therapeutics, Inc.

By: /s/ Michael A. Jacobsen
Michael A. Jacobsen
Vice President, Finance and Secretary

Date: October 3, 2012