Sarepta Therapeutics Announces FDA Considers NDA Filing for Eteplirsen Premature in Light of Recent Competitive Drug Failure and Recent DMD Natural History Data

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FDA Questions Dystrophin as a Biomarker Due to Failed Studies of Other Investigational Drugs for DMD; FDA Questions 6-Minute Walk Test Results for Eteplirsen, Suggesting Study Population Should Be Stable Over Two-Year Timeframe Due to Recent Natural History Data; FDA Requests Further Discussion on Endpoints, Design of Confirmatory Clinical Study

CAMBRIDGE, MA -- (Marketwired) -- 11/12/13 -- Sarepta Therapeutics, Inc. (NASDAQ: SRPT) today provided an update on its discussions with the U.S. Food and Drug Administration (FDA) regarding its planned New Drug Application (NDA) submission and confirmatory clinical study with eteplirsen for the treatment of Duchenne muscular dystrophy (DMD). Citing recent developments since Sarepta's last meeting with the agency, including a failed study with a competitive product and recent natural history data in DMD, the FDA indicated the new data raise "considerable doubt" about both the dystrophin biomarker and the supportive clinical efficacy assessed on the 6-minute walk test (6MWT) in the Phase IIb clinical study of eteplirsen. As a result of these recent data, the FDA stated that they "currently consider an NDA filing for eteplirsen as premature."

"We are very disappointed with the FDA's decision to reconsider their openness to a potential NDA filing based on our current data and the resultant impact this change may have on our efforts to achieve an earlier approval of eteplirsen," said Chris Garabedian, president and chief executive officer of Sarepta Therapeutics. "We strongly believe in the potential of eteplirsen to address a serious unmet medical need in DMD and we are committed to its development. Our team at Sarepta recognizes the urgency of families who are seeking new treatments, and we will continue to work with the FDA on an acceptable confirmatory study design and, in parallel, seek to address their concerns regarding a potential NDA filing based on our current dataset."

The FDA provided the feedback in pre-meeting comments and clarified them in a meeting with Sarepta that took place late last week to discuss the eteplirsen clinical program.

Excerpts from the FDA's pre-meeting comments on reconsidering an NDA filing included:

"Since our last meeting, a large phase 3 trial of drisapersen, a drug with a similar mechanism of action, was reported to be negative, despite increased expression of dystrophin. The disconnect between increased expression of dystrophin and clinical efficacy for drisapersen, combined with previous negative reports for PTC124, another drug thought to act by increasing dystrophin, raises considerable doubt about the biomarker, and consequentially, its ability to reasonably likely predict clinical benefit."

"...the quantity of dystrophin that might be necessary to be considered reasonably likely to predict clinical benefit is even less clear; small or perhaps even moderate increases are seemingly not enough, at least in the subpopulation of boys studied so far. An adequately validated quantitative assay for dystrophin now seems a prerequisite to further consideration of the biomarker as supportive of approval. Since our last meeting, our concern about the shortcomings of your current quantification methods has grown."

"Recent natural history data in DMD indicate that a baseline 6-Minute Walk Test (6MWT) ≥350 meters predicts continued general stability for such patients, not the 75- to 83-meter yearly decline you suggest in the meeting package. Thus, considerable doubt is also cast on the efficacy support provided by your ongoing open-label study (4658-us-202, 96-week data submitted), in which baseline 6MWT was >350 m for all patients."

"...the expected variability of 6MWT values appears sufficient to explain differences between arms on which the post-hoc analysis was based. Because of this, together with our lack of confidence in the capacity of your dystrophin biomarker to predict clinical benefit, we currently consider an NDA filing for eteplirsen as premature."

Additional excerpts from the FDA's pre-meeting comments on the eteplirsen confirmatory study design included:

"Recent trial failures in DMD suggest it may be productive to re-examine study enrollment criteria and endpoints."

"...it seems worthwhile to consider selection of other endpoints and/or populations for the next trial of eteplirsen. We

stress that we would still accept 6MWT in an appropriately powered study; however, because 6MWT excludes both younger boys who cannot perform such a demanding test, and older boys who are no longer ambulatory, we are concerned that seemingly avoidable limitations on enrollment could undermine study feasibility. Many possible combinations of endpoints and subpopulations appear possible. Motor scales that measure a broader range of function and demand less sustained effort than 6MWT could be appropriate for a much wider range of boys, perhaps including non-ambulatory boys. To allow inclusion of a broader range of patients, a study could also be designed that mathematically combined findings from, for example, an ambulation endpoint in less advanced patients with findings from an upper-limb or respiratory endpoint in more advanced patients. We remain open to consideration of endpoints and populations you may suggest."

"...we believe that a placebo-controlled trial would be the most likely method for developing interpretable evidence of efficacy for eteplirsen, because efficacy endpoints in DMD are effort-dependent and susceptible to bias, and the natural history is highly variable and has recently improved with steroid use and advances in ancillary care. We would like to discuss the perceived barriers to conducting such a trial with you."

The FDA's request to discuss different clinical endpoints, combined endpoints, and different DMD subpopulations for a confirmatory clinical study, along with their questions about dystrophin as a biomarker and the need for a placebo-controlled study, will delay the initiation of dosing in the eteplirsen confirmatory study until at least the second quarter of 2014. A follow up meeting with FDA has been scheduled to take place this month to discuss the confirmatory study design.

Conference Call Information

Sarepta will hold a conference call to discuss this update in addition to the Company's third quarter financial results today at 8:00 a.m. EST (5:00 a.m. PST). The conference call may be accessed by dialing 888.895.5271 for domestic callers and 847.619.6547 for international callers. The passcode for the call is 35957586. Please specify to the operator that you would like to join the "Sarepta Third Quarter Earnings Call." The conference call will be webcast live under the investor relations section of Sarepta's website at www.sarepta.com 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 November 26, 2013 by calling 888.843.7419 or 630.652.3042 and entering access code 35957586.

About Duchenne Muscular Dystrophy

DMD is an X-linked rare degenerative neuromuscular disorder causing severe progressive muscle loss and premature death. 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 Eteplirsen

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 use of dystrophin to predict significant clinical benefit, the clinical significance of our 6mwt results to date, the timing of clinical studies and the timing and potential for regulatory submissions and meetings.

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 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 (including Subpart H accelerated approval), 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 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.

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