



## **Sarepta Therapeutics Announces Positive Expression Results from the Casimersen (SRP-4045) Arm of the ESSENCE Study**

-- Interim analysis found statistically significant increase in dystrophin production as measured by western blot in casimersen-treated participants compared to baseline and placebo --

-- Based on positive results, Company intends to schedule a pre-NDA meeting with FDA and plans to submit an NDA for casimersen in the middle of 2019 --

-- Results once again validate the Company's exon-skipping platform for the treatment of DMD --

CAMBRIDGE, Mass., March 28, 2019 (GLOBE NEWSWIRE) -- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today announced results from its interim analysis of muscle biopsy endpoints comparing casimersen treatment to placebo in the ESSENCE study, also known as study 4045-301. ESSENCE is a global, randomized double-blind, placebo-controlled Phase 3 study evaluating the efficacy and safety of casimersen and golodirsen in patients amenable to skipping exons 45 or 53, respectively.

After soliciting feedback from the FDA, Sarepta conducted an interim analysis for levels of dystrophin protein expression in those patients who are amenable to exon 45 skipping to determine the potential for a New Drug Application (NDA) filing based on dystrophin as a surrogate endpoint. With these results, the Company intends to work toward submission of an NDA for casimersen in the middle of 2019.

Patients amenable to exon 45 skipping were randomized to receive a once-weekly intravenous (IV) infusion of casimersen dosed at 30mg/kg (N=27) or placebo (N=16) for 96 weeks. The interim analysis was performed on data from biopsies of the bicep muscle at baseline and on-treatment at Week 48.

Key findings from the interim analysis include:

- In the casimersen arm, mean dystrophin protein (% normal dystrophin as measured by western blot) increased to 1.736% of normal compared to a mean baseline of 0.925% of normal ( $p < 0.001$ ).
- A statistically significant difference in the mean change from baseline to week 48 in dystrophin protein was observed between the casimersen-treated arm compared to the placebo arm ( $p = 0.009$ ).

- Of the 22 patients receiving casimersen who have been tested for increased exon-skipping mRNA using reverse transcription polymerase chain reaction (RT-PCR), all have displayed an increase in skipping exon 45 ( $p < 0.001$ ) over their baseline levels, representing a 100% response rate.
- A statistically significant positive correlation between exon 45 skipping and dystrophin production was observed (Spearman rank correlation = 0.635,  $p < 0.001$ ).
- The study is ongoing and remains blinded to collect additional efficacy and safety data.

“We are pleased to see that the anticipated exon skipping after treatment resulted in a statistically significant mean increase of dystrophin protein, as measured by western blot,” said Professor Francesco Muntoni, University College London. “This is the third exon-skipping agent to have shown a statistically significant increase in dystrophin production, and reinforces our confidence in the exon-skipping approach for treating Duchenne patients with amenable mutations.”

“The casimersen results and submission of our application for golodirsen earlier this year further validate our RNA research engine,” said Doug Ingram, Sarepta Therapeutics’ president and chief executive officer. “If golodirsen and casimersen are approved, nearly a third of the boys and young men living with DMD in the United States could benefit from our RNA therapies. We continue to advance toward our ultimate goal of profoundly improving the lives of as many patients around the world with DMD as possible.”

Dystrophin is a protein found in muscle cells that, while present in extremely small amounts (about 0.002 percent of total muscle protein), is crucial in strengthening and protecting muscle fibers. 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 of the body. The condition is universally fatal, and death usually occurs before the age of 30 generally due to respiratory or cardiac failure.

Casimersen uses Sarepta Therapeutics’ proprietary phosphorodiamidate morpholino oligomer (PMO) chemistry and exon-skipping technology to skip exon 45 of the DMD gene. Casimersen is designed to bind to exon 45 of dystrophin pre-mRNA, resulting in exclusion, or “skipping”, of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 45 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein.

### **About the ESSENCE Study**

The ESSENCE study is a double-blind, placebo-controlled, multi-center study to evaluate the efficacy and safety of casimersen (SRP-4045) and golodirsen (SRP-4053). Eligible patients with out-of-frame deletion mutations amenable to exon 45 or 53 skipping are randomized to receive once weekly intravenous (IV)

infusions of 30 mg/kg SRP-4045 or 30 mg/kg SRP-4053 respectively (combined-active group) or placebo for up to 96 weeks. This is followed by an open label extension period in which all patients will receive open-label active treatment for 48 weeks, up to Week 144 of study.

Clinical efficacy is being assessed at regularly scheduled study visits, including functional tests such as the six-minute walk test (6MWT). All patients undergo a muscle biopsy at baseline and will undergo a second muscle biopsy either at Week 48 or Week 96.

Safety is being assessed through the collection of adverse events, laboratory tests, electrocardiograms (ECGs), echocardiograms (ECHOs), vital signs, and physical examinations throughout the study.

The study is titled, "A Double-Blind, Placebo-Controlled, Multi-Center Study With an Open-Label Extension to Evaluate the Efficacy and Safety of SRP-4045 and SRP-4053 in Patients With Duchenne Muscular Dystrophy."

### **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 - 5,000 male births worldwide.

### **About Sarepta Therapeutics**

Sarepta is at the forefront of precision genetic medicine, having built an impressive and competitive position in Duchenne muscular dystrophy (DMD) and more recently in gene therapies for 5 Limb-girdle muscular dystrophy diseases (LGMD), Charcot-Marie-Tooth (CMT), MPS IIIA, Pompe and other CNS-related disorders, totaling over 20 therapies in various stages of development. The Company's programs and research focus span several therapeutic modalities, including RNA, gene therapy and gene editing. Sarepta is fueled by an audacious but important mission: to profoundly improve and extend the lives of patients with rare genetic-based diseases. For more information, please visit [www.sarepta.com](http://www.sarepta.com).

### **Forward-Looking Statements**

*This press release contains "forward-looking statements." 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 regarding Sarepta's intention to schedule a pre-NDA meeting with FDA and to submit an NDA for casimersen in the middle of 2019; the potential of Sarepta's exon-skipping platform for the treatment*

*of DMD; the potential of golodirsén and casimersén, if approved, to treat nearly a third of the boys and young men living with DMD in the United States; Sarepta's goal of profoundly improving the lives of as many patients around the world with DMD as possible; Casimersén's potential to skip exon 45 of the DMD gene; Casimersén's potential to bind to exon 45 of dystrophin pre-mRNA, resulting in exclusion, or "skipping", of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 45 skipping; and the potential of exon skipping to allow for production of an internally truncated dystrophin protein.*

*These forward-looking statements involve risks and uncertainties, many of which are beyond Sarepta's control. Known risk factors include, among others: success in preclinical testing and early clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful, and results from an interim analysis do not necessarily predict final results; the data presented in this release may not be consistent with the final data set and analysis thereof or result in a safe or effective treatment benefit; there may be delays in Sarepta's projected development or regulatory timelines for casimersén (SRP-4045) and its other products candidates for various reasons, some of which may be outside of Sarepta's control; Sarepta's ongoing research and development efforts may not result in any viable treatments suitable for clinical research or commercialization due to a variety of reasons, some of which may be outside of Sarepta's control, including possible limitations of company financial and other resources, manufacturing limitations that may not be anticipated or resolved for in a timely manner, and regulatory, court or agency decisions, such as decisions by the United States Patent and Trademark Office with respect to patents that cover our product candidates; and even if Sarepta's programs result in new commercialized products, Sarepta may not achieve any significant revenues from the sale of such products; and those risks identified under the heading "Risk Factors" in Sarepta's most recent Annual Report on Form 10-K for the year ended December 31, 2018, and most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) as well as other SEC filings made by the Company which you are encouraged to review.*

*Any of the foregoing risks could materially and adversely affect the Company'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 SEC filings made by Sarepta. 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 website at [www.sarepta.com](http://www.sarepta.com). We encourage investors and potential investors to consult our website regularly for important information about us.*

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