Sarepta Therapeutics Announces Positive Clinical Results from MOMENTUM, a Phase 2 Clinical Trial of SRP-5051 in Patients with Duchenne Muscular Dystrophy Amenable to Skipping Exon 51

12/7/20

-- Results from the multiple-ascending dose trial demonstrate proof-of-concept for SRP-5051 and support continued dose escalation --

-- At a total dose exposure approximately 10x lower than eteplirsen, SRP-5051 at 20 mgs/kg showed enhanced tissue exposure, greater exon skipping, and greater dystrophin production with no negative renal or other laboratory findings --

-- These are the first clinical results from the Company's peptide phosphorodiamidate morpholino oligomer (PPMO) technology, its next-generation chemistry platform --

CAMBRIDGE, Mass., Dec. 07, 2020 (GLOBE NEWSWIRE) -- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today announced results from the ongoing MOMENTUM study (Study 5051-201), a global Phase 2 clinical trial, of SRP-5051, its next-generation treatment for patients with Duchenne muscular dystrophy who are amenable to exon 51 skipping. This is the first clinical data from SRP-5051, an investigational treatment that uses Sarepta's peptide phosphorodiamidate morpholino oligomer (PPMO) technology. PPMO technology includes a proprietary cell-penetrating peptide that is conjugated to Sarepta's PMO backbone with the goal of increasing cellular uptake of drug in the muscle tissue.

Results from Part A of the multi-ascending dose MOMENTUM study found consistently higher tissue exposure, exon-skipping and dystrophin production in patients taking a monthly dose of SRP-5051 compared to baseline. SRP-5051 was generally well-tolerated across all doses studied, with no clinical or laboratory findings reported. The results support continued dose escalation of SRP-5051 and further clinical development.

"Sarepta's PMO RNA technology is a vital platform on which we design therapies to treat those with Duchenne muscular dystrophy. Our next-generation PPMO technology is designed to increase cell penetration with the goal of offering significantly improved efficacy with more convenient dosing in Duchenne patients amenable to exon skipping," said Doug Ingram, president and chief executive officer, Sarepta. "While patient numbers in each dose arm are small, the higher tissue concentration, exon skipping and dystrophin production in the 20 mg/kg dosing group were observed at an early 12-week timepoint and with far less cumulative drug exposure when compared to our current PMO technology. We know from our experience with PMOs that exon-skipping and dystrophin increase over time, and these results along with our preclinical experience, give us confidence as we dose escalate and continue to advance our PPMO exon-skipping therapies for Duchenne, including another five potential therapies that have already been designed, and explore the utility of the PPMO RNA platform for new disease indications."

When compared to a control group of Duchenne patients from the PROMOVI study who received biopsies at 24 weeks after taking a weekly 30 mg/kg dose of eteplirsen, once-monthly dosing of SRP-5051 resulted in higher muscle concentration, increased exon-skipping and dystrophin at 12 weeks. A dose-dependent increase in exon-skipping and dystrophin was observed, with patients in the 20 mg/kg dose group of SRP-5051 seeing a 1.6-fold increase in exon skipping (n=4) and a 5-fold increase in the % of normal dystrophin (n=2) when compared to the group taking eteplirsen at 24 weeks.

The incidence of adverse events in the MOMENTUM study was similar across all dosed cohorts and does not suggest dose dependency. One treatment-emergent event, unrelated to study drug, occurred in the 4 mg/kg dose group. No clinical or laboratory findings were observed. Full results will be presented at a future medical meeting.

About MOMENTUM (SRP-5051-201)
MOMENTUM is a multi-arm, ascending dose study designed to identify the maximum tolerated dose of SRP-5051. Informed by Study 5051-101, a single-ascending dose study of SRP-5051, patients in the MOMENTUM study will receive monthly intravenous (IV) infusions of SRP-5051, starting at 4 mg/kg and ascending to 40 mg/kg. The study will enroll up to 70 patients, both ambulant and non-ambulant, between the ages of 7 to 21 at sites in the U.S., Canada and European Union. The primary endpoint is safety, and secondary and exploratory endpoints include exon-skipping, dystrophin expression and tissue concentration. All patients will undergo a muscle biopsy at baseline and 12 weeks in Part A and at baseline and 24 weeks in Part B. More information can be found on www.clinicaltrials.gov.

About SRP-5051
SRP-5051 uses Sarepta's PPMO chemistry and exon-skipping technology to skip exon 51 of the dystrophin gene. SRP-5051 is designed to bind to exon 51 of dystrophin pre-mRNA, resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 51 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein. PPMO is Sarepta's next-generation chemistry platform designed around a proprietary cell-penetrating peptide conjugated to the PMO backbone, with the goal of increasing tissue penetration, increasing exon skipping and significantly increasing dystrophin production. Around 13% of DMD patients have mutations which make them amenable to skipping exon 51. If successful, the PPMO offers the potential for improved efficacy and less frequent dosing for patients.

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. 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 due to respiratory or cardiac failure.

About EXONDYS 51
EXONDYS 51 (eteplirsen) uses Sarepta's proprietary phosphorodiamidate morpholino oligomer (PMO) chemistry and exon-skipping technology to bind to exon 51 of dystrophin pre-mRNA, resulting in "skipping" of this exon during mRNA processing in patients with genetic mutations that are

amenable to exon 51 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein.

EXONDYS 51 is indicated for the treatment of Duchenne muscular dystrophy in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping.

This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in some patients treated with EXONDYS 51. Continued approval may be contingent upon verification of a clinical benefit in confirmatory trials.

EXONDYS 51 has met the full statutory standards for safety and effectiveness and as such is not considered investigational or experimental.

Important Safety Information About EXONDYS 51
Hypersensitivity reactions, including rash and urticaria, pyrexia, flushing, cough, dyspnea, bronchospasm, and hypotension, have occurred in patients who were treated with EXONDYS 51. If a hypersensitivity reaction occurs, institute appropriate medical treatment and consider slowing the infusion or interrupting the EXONDYS 51 therapy.

Adverse reactions in DMD patients (N=8) treated with EXONDYS 51 30 mg or 50 mg/kg/week by intravenous (IV) infusion with an incidence of at least 25% more than placebo (N=4) (Study 1, 24 weeks) were (EXONDYS 51, placebo): balance disorder (38%, 0%), vomiting (38%, 0%) and contact dermatitis (25%, 0%). The most common adverse reactions were balance disorder and vomiting. Because of the small numbers of patients, these represent crude frequencies that may not reflect the frequencies observed in practice. The 50 mg/kg once weekly dosing regimen of EXONDYS 51 is not recommended.

In the 88 patients who received ≥30 mg/kg/week of EXONDYS 51 for up to 208 weeks in clinical studies, the following events were reported in ≥10% of patients and occurred more frequently than on the same dose in Study 1: vomiting, contusion, excoriation, arthralgia, rash, catheter site pain, and upper respiratory tract infection.

For further information, please see the full **Prescribing Information**.

About Sarepta Therapeutics
At Sarepta, we are leading a revolution in precision genetic medicine and every day is an opportunity to change the lives of people living with rare disease. The Company has built an impressive position in Duchenne muscular dystrophy (DMD) and in gene therapies for limb-girdle muscular dystrophies (LGMDs), mucopolysaccharidosis type IIIA, Charcot-Marie-Tooth (CMT), and other CNS-related disorders, with more than 40 programs in various stages of development. The Company's programs and research focus span several therapeutic modalities, including RNA, gene therapy and gene editing. For more information, please visit www.sarepta.com or follow us on Twitter, LinkedIn, Instagram and Facebook.

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 the potential benefits of PPMO, including increasing cellular uptake of drug in the muscle tissue and offering significantly improved efficacy with less frequent dosing; our plan to continue to dose escalate and advance our PPMO exon-skipping therapies for Duchenne, including another five potential therapies that have already been designed, and to explore the utility of the PPMO RNA platform for new disease indications; and potential market opportunities.

These forward-looking statements involve risks and uncertainties, many of which are beyond our control. Known risk factors include, among others: success in preclinical trials and clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful; 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; different methodologies, assumptions and applications we utilize to assess particular safety or efficacy parameters may yield different statistical results, and even if we believe the data collected from clinical trials of our product candidates are positive, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities; if the actual number of patients suffering from DMD is smaller than estimated, our revenue and ability to achieve profitability may be adversely affected; we may not be able to execute on our business plans and goals, including meeting our expected or planned regulatory milestones and timelines, clinical development plans, and bringing our product candidates to market, due to a variety of reasons, some of which may be outside of our control, including possible limitations of company financial and other resources, manufacturing limitations that may not be anticipated or resolved for in a timely manner, 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 the COVID-19 pandemic; and even if Sarepta's programs result in new commercialized products, Sarepta may not achieve the expected 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, 2019, 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. We encourage investors and potential investors to consult our website regularly for important information about us.

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