Sarepta Therapeutics' SRP-9001 Shows Sustained Functional Improvements in Multiple Studies of Patients with Duchenne

10/11/21

- ***Results presented at 'Micro-dystrophin Day' highlight breadth, depth and strength of the clinical evidence to date for SRP-9001 in treating Duchenne muscular dystrophy; tolerability profile remains consistent across treated patients***

- ***Results from Study SRP-9001-101 found that SRP-9001-treated participants (n=4, ages 4 to 7 years) improved 8.6 points on the North Star Ambulatory Assessment (NSAA) compared to a matched natural history cohort three years after treatment***

- ***Results from Study SRP-9001-102 found that SRP-9001-treated participants (n=12, ages 6 to 7) had a positive 2.9-point difference on NSAA compared to a matched natural history cohort one year after treatment***

- ***Functional results from Study SRP-9001-103 Cohort 1 (n=11, ages 4-7) found participants improved 3.0 points on NSAA six months after treatment***

- ***EMBARK, the first global Phase 3 pivotal double-blind gene therapy trial in Duchenne to enroll 120 patients in the US, Europe and Asia, conducted in partnership with Roche***

CAMBRIDGE, Mass., Oct. 11, 2021 (GLOBE NEWSWIRE) -- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today shared new analyses and functional data from its SRP-9001 (rAAVrh74.MHCK7.micro-dystrophin) development program and details of Study SRP-9001-301, known as EMBARK, its global pivotal Phase 3 trial of SRP-9001 for the treatment of Duchenne muscular dystrophy. SRP-9001, being developed in partnership with Roche, is an investigational gene transfer therapy intended to deliver its micro-dystrophin-encoding gene to muscle tissue for the targeted production of the micro-dystrophin protein.

In new analyses presented at "SRP-9001 Micro-dystrophin Day," results from participants treated with SRP-9001 in Study SRP-9001-101 (n=4, ages 4 to 7) found that participants in Study 101 improved 8.6 points on the North Star Ambulatory Assessment (NSAA)* compared to a matched natural history cohort three years following a single administration of SRP-9001 ($p<0.0001$). In Study SRP-9001-102, SRP-9001-treated participants ages 6 to 7 (n=12) had a positive 2.9-point difference on NSAA change from baseline compared to a matched natural history control ($p=0.0129$).

In addition, the first functional results were presented from Study SRP-9001-103 (ENDEAVOR), which uses commercially representative SRP-9001 material. Results from the first 11 participants in Cohort 1, ages 4 to 7, demonstrated a 3.0-point improvement from baseline on NSAA six months after treatment.

"With 77 patients treated to date, the multi-study development program for SRP-9001 represents the most comprehensive and long-term dataset for a Duchenne muscular dystrophy gene therapy in existence. The totality of evidence shows that SRP-9001 is a significantly differentiated gene therapy product candidate with one-time dosing and a stable tolerability profile, results in robust expression and evidence of sustained functional benefits across our various studies," said Doug Ingram, president and chief executive officer, Sarepta. "We commence our EMBARK pivotal trial – currently the only truly global Phase 3 trial with a Duchenne gene therapy – with great conviction in the transformative potential of SRP-9001. But while our expression, tolerability, functional evidence and CMC achievements may place SRP-9001 alone among potential therapies, we never forget that we remain in a daily race against a life-ending degenerative disease. To that end, Sarepta, along with our partner Roche, will continue working with tenacity and urgency to bring this potentially transformative treatment to individuals with Duchenne around the world."

"When compared to a matched natural history cohort, individuals with Duchenne who received SRP-9001 are performing better on the NSAA or showing stabilization of NSAA scores where we would expect to see a decline. The functional results from Study 103, as early as 6 months following treatment, provide additional confidence in our ability to confirm a treatment effect with SRP-9001 as we advance our pivotal Phase 3 trial," said Louise Rodino-Klapac, Ph.D., executive vice president and chief scientific officer, Sarepta. "Given our experience with the AAVrh74 vector in more than 80 individuals with Duchenne and limb-girdle muscular dystrophy, we are very encouraged by the sustained and meaningful clinical results and consistency of the safety profile of SRP-9001."

The safety and tolerability profile of SRP-9001 is similar to past reports. Across all three studies, treatment-related adverse events (TRAEs) generally occurred within 90 days of treatment and subsequently resolved. No clinically relevant complement activation was observed in any of the studies. The most common treatment-related adverse event was vomiting, generally within the first week post-infusion. Increases in liver enzymes were transient and responsive to steroids. In Study 9001-103, safety data were consistent with data from previous studies of SRP-9001 (101 and 102). There was one immune-mediated myositis serious adverse event in Cohort 2 specific to the participant's mutation; participant received treatment including plasmapheresis and has since returned to pre-event function.

About the SRP-9001 Clinical Development Program
The SRP-9001 clinical development program currently consists of four studies:

- **EMBARK, Study SRP-9001-301:** a global, randomized, double-blind, placebo-controlled clinical trial of commercially representative SRP-9001 material in 120 participants with Duchenne muscular dystrophy between the ages of 4 to 7. The primary endpoint will assess the change in NSAA total score from baseline to week 52 compared to placebo.

  Key features of EMBARK include stratification of participants by age and baseline NSAA, with a minimum of 50 percent of patients ages 4 to 5 enrolled. Inclusion criteria include a stable daily dose of oral corticosteroids for at least 12 weeks before screening and rAAVrh74 antibody titers of less than 1:400. Participants with mutations between or including exons 1-17 or mutations fully contained within exon 45 (inclusive) are not eligible.

  Secondary endpoints include the number of skills gained or improved at week 52 as measured by NSAA, the quantity of micro-dystrophin protein expression at week 12 (Part 1) as measured by western blot, timed function tests and safety. In Part 1, results from the treatment and placebo groups are compared through 52 weeks following treatment. In Part 2, the study remains blinded to investigators and participants while all participants in the placebo group cross over to active treatment and all participants are followed for another 52 weeks while safety and efficacy continue to be evaluated.

- **ENDEAVOR, Study SRP-9001-103 (Study 103):** an open-label clinical trial of SRP-9001 that has enrolled 32 participants with Duchenne muscular dystrophy, with 20 participants ages 4 to 7 and expanded cohorts that include older ambulant and non-ambulant individuals. Study 103 uses commercially representative SRP-9001 material and the primary endpoint is the change from baseline in the quantity of micro-dystrophin protein expression measured by western blot at 12 weeks. Secondary outcome measures include change from baseline in micro-dystrophin expression fiber intensity as measured by immuno-fluorescence and micro-dystrophin expression measured by IF percent dystrophin positive fibers at 12 weeks. Exploratory endpoints include the change in vector genome copies per nucleus, NSAA and certain timed functional tests. Including the initial 12-week period, patients will be followed for a total of five years.

- **Study SRP-9001-102 (Study 102):** a double-blind, 1:1 randomized, placebo-controlled clinical trial of SRP-9001 in 41 participants with Duchenne muscular dystrophy between the ages of 4 to 7. Study 102 uses clinical process SRP-9001 material and has two primary endpoints: micro-dystrophin expression at 12 weeks and change in NSAA total score at 48 weeks compared to placebo. Secondary endpoints include certain timed functional tests; micro-dystrophin expression measured by immuno-fluorescence fiber intensity; and micro-dystrophin expression measured by immuno-fluorescence percent dystrophin positive fibers. In Part 1, results from the treatment and placebo groups are compared through 48 weeks following treatment. In Part 2, the study remains blinded while all participants in the placebo group cross over to active treatment and all participants are followed for another 48 weeks while safety and efficacy continue to be evaluated and for five years total after infusion.

- **SRP-9001-101 (Study 101):** a single-center, open-label clinical trial of SRP-9001 to evaluate the safety, tolerability and proof of concept of a single dose of clinical process SRP-9001 material. The trial enrolled 4 ambulatory participants with Duchenne muscular dystrophy between the ages of 4 to 7. The primary endpoint was safety, and secondary endpoint included the change in micro-dystrophin expression pre- and post-treatment, decreases in creatine kinase, NSAA total score and timed function test. Participants are being followed for five years after treatment, while safety and efficacy continue to be evaluated.

*The NSAA is a 17-item rating scale that is used to measure functional motor abilities in ambulant children with Duchenne. It is used to monitor the progression of the disease and treatment effects which makes it suitable as an endpoint in clinical trials for Duchenne.

About SRP-9001 (rAAVrh74.MHCK7.micro-dystrophin)

SRP-9001 is an investigational gene transfer therapy intended to deliver the micro-dystrophin-encoding gene to muscle tissue for the targeted production of the micro-dystrophin protein. Sarepta is responsible for global development and manufacturing for SRP-9001 and plans to commercialize SRP-9001 in the United States upon receiving FDA approval. In December 2019, Roche partnered with Sarepta to combine Roche's global reach, commercial presence and regulatory expertise with Sarepta's gene therapy candidate for Duchenne to accelerate access to SRP-9001 for patients outside the United States. Sarepta has exclusive rights to the micro-dystrophin gene therapy program initially developed at the Abigail Wexner Research Institute at Nationwide Children's Hospital.

About Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a rare, fatal neuromuscular genetic disease that occurs in approximately one in every 3,500-5,000 males worldwide. DMD is caused by a change or mutation in the gene that encodes instructions for dystrophin. Symptoms of DMD usually appear in infants and toddlers. Affected children may experience developmental delays such as difficulty in walking, climbing stairs or standing from a sitting position. As the disease progresses, muscle weakness in the lower limbs spreads to the arms and other areas. Most patients require full-time use of a wheelchair in their early teens, and then progressively lose the ability to independently perform activities of daily living such as using the restroom, bathing and feeding. 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 patients usually succumb to the disease in their twenties.

About Sarepta Therapeutics

Sarepta is on an urgent mission: engineer precision genetic medicine for rare diseases that devastate lives and cut futures short. We hold leadership positions in Duchenne muscular dystrophy (DMD) and limb-girdle muscular dystrophies (LGMDs), and we currently have more than 40 programs in various stages of development. Our vast pipeline is driven by our multi-platform Precision Genetic Medicine Engine in gene therapy, RNA and gene

editing. For more information, please visit www.sarepta.com or follow us on Twitter, LinkedIn, Instagram and Facebook.

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.

Forward-Looking Statements
This press release contains "forward-looking statements." Any statements that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "believe," "anticipate," "plan," "expect," "will," "may," "intend," "prepare," "look," "potential," "possible" and similar expressions are intended to identify forward-looking statements. These forward-looking statements include statements relating to the potential benefits of SRP-9001; the potential of our collaborations and partnerships; and expected plans and milestones, including initiating SRP-9001-301 in the U.S., Europe and Asia.

Known risk factors include, among others: success in pre-clinical trials and clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful; 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 regulatory authorities; 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; 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, 2020, 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, except as required by law.

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