Sarepta Therapeutics' Investigational Gene Therapy SRP-9001 for Duchenne Muscular Dystrophy Demonstrates Significant Functional Improvements Across Multiple Studies

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- ***Sarepta and its partner Roche present new results and analyses at the International Congress on Neuromuscular Diseases (ICNMD), which demonstrate that SRP-9001 shows consistent, statistically significant functional benefits in individuals with Duchenne versus a propensity-weighted external control that continue to positively diverge from natural history disease course***

- ***In the 20-patient Cohort 1 of SRP-9001-103 (ENDEAVOR), SRP-9001-treated participants improved 4 points from their pre-therapy baselines, and 3.8 points (unadjusted means) and 3.2 points (least squared means) at 52 weeks on the North Star Ambulatory Assessment (NSAA) compared to a propensity-weighted external control group (p=<0.0001)***
    - ***The results from ENDEAVOR, using commercially representative SRP-9001, provide further support to reinforce confidence in our ongoing Phase 3 Study SRP-9001-301, EMBARK***

- ***In the 4-patient Study SRP-9001-101, at 4 years, patients – currently on average over 9 years old and in the predicted steep decline phase of disease – did not decline but showed a 7-point increase above their pre-treatment baselines on NSAA, and 9.9 point (unadjusted means) and a 9.4 point (least squared means) improvement versus a propensity-weighted external control (p=0.0125)***

- ***In a 52-patient integrated analysis across Studies 101, 102, and 103 at target dose, at one year, SRP-9001 treated patients improved 3.1 points (unadjusted means) and 2.4 points (least squared means) on NSAA versus propensity-weighted external control (p=<0.0001)***

- ***Safety and tolerability profile for SRP-9001 remains consistent across treated patients***

CAMBRIDGE, Mass., July 06, 2022 (GLOBE NEWSWIRE) -- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today shared new functional data across multiple studies from the clinical development program for SRP-9001 (delandistrogene moxeparvovec) for the treatment of Duchenne muscular dystrophy. SRP-9001 is an investigational gene therapy for Duchenne being developed in partnership with Roche. Data are being presented this week at the 17th International Congress on Neuromuscular Diseases (ICNMD 2022) in Brussels.

Key findings include new, one-year functional results from Study SRP-9001-103 (ENDEAVOR), which employs commercially representative SRP-9001 material at the target commercial dose. Results from Cohort 1 (n=20, ages 4 to 7) demonstrated a 3.8-point improvement (unadjusted means) and 3.2-point improvement (least squared means) on the North Star Ambulatory Assessment* (NSAA) 52 weeks after treatment compared to a propensity-score weighted external control.** Additionally, across multiple new analyses, discussed below, SRP-9001 treated patients showed statistically significant and clinically meaningful benefit versus propensity-matched external controls and results positively diverge from the natural history of this degenerative disease over time.

"We are absolutely delighted by these most recent results. We now have positive results across multiple studies and multiple time points, including one-, two- and four-years after treatment, and are very pleased with the consistent safety profile across more than 80 treated patients," said Doug Ingram, president and chief executive officer, Sarepta. "We are particularly excited about the results of cohort 1 of Study 103, as these results come from our commercially representative process at our intended commercial dose. We robustly powered our 120-patient Phase 3 study, known as EMBARK, and the results from Study 103 provide even greater conviction on the powering and probability of success of EMBARK. Duchenne is a relentlessly degenerative disease and every day of delay is a day of muscle and function loss that cannot be recovered. Sarepta and our partner Roche are dedicated and determined to bring this potentially transformative gene therapy to patients around the globe as rapidly as possible."

"In Study 103, we continue to see statistically significant improvements in NSAA scores and timed function tests for SRP-9001-treated patients from baseline and when compared to a propensity-weighted external control group. With the progressive nature of this disease, what has been particularly gratifying is seeing these treatment effects increase over time compared to the external control, as well as the maintenance of ability in older patients who would otherwise be declining," said Louise Rodino-Klapac, Ph.D., executive vice president and chief scientific officer, Sarepta. "We're excited to share these data more broadly in the coming months, particularly with the Duchenne community. We are grateful to the patients, families, investigators and site teams, whose support has been critical to the advancement of this program."

Results and Safety

Results from Study SRP-9001-103, ENDEAVOR (commercially representative material):

- In Cohort 1 (n=20, ages 4 to 7), SRP-9001-treated patients demonstrated a 3.8-point improvement (unadjusted means)

and a 3.2-point improvement (least squared means) on the NSAA one-year after treatment when compared to a propensity-score weighted external control (p=0.0001).
    - At one year, using unadjusted means, NSAA total scores in the SRP-9001 treated patients improved 4 points from 22.1 to 26.1 and participants in the external control improved 0.2 points from 21.9 to 22.1.
    - At one year, using least squared means, NSAA total scores in the SRP-9001 treated patients improved 3.9 points and participants in the external control improved 0.8 points (difference 3.2 points allowing for appropriate rounding).

- Participants in the study also recorded statistically significant improvements in timed function tests one year after treatment compared to external control
    - At one year, using unadjusted means, time to rise in the SRP-9001 treated patients improved 0.9 seconds compared to external control
    - At one year, using least squared means, time to rise in the SRP-9001 treated patients improved 1.2 seconds compared to external control (p <0.0001)
    - At one year, using unadjusted means, SRP-9001 treated patients improved 1.0 seconds on the ten-meter walk test compared to external control
    - At one year, using least squared means, SRP-9001 treated patients improved 1.0 seconds on the ten-meter walk test compared to external control (p = 0.0018)

Results from Study SRP-9001-101:

- In long-term results from Study SRP-9001-101, after four years, SRP-9001-treated participants (n=4, ages 4-7 at time of treatment) had a positive mean 7.0-point difference on total NSAA scores compared to baseline. These patients are now on average over 9 years old, an age where one would expect to see rapid declines in function.
- When compared to a propensity-weighted external control, total NSAA scores for the SRP-9001 treated patients were 9.9 points (unadjusted means) and 9.4 points (least square means) greater (p=0.0125).

Results from Integrated Analysis of Studies 101, 102 and 103 versus propensity weighted external control:

- In an integrated analysis of one-year functional data from patients who received the target dose of SRP-9001 in Studies 101, 102 and 103 (n=52), SRP-9001-treated patients improved 3.1 points (unadjusted means) and 2.3 points (least squared means) in NSAA total scores from baseline
- When compared to the propensity-weighted external control group, NSAA change from baseline one-year after treatment for SRP-9001 treated patients was 2.4 points higher (p=0.001).

The safety and tolerability profile of SRP-9001 is similar to past reports. The most common treatment-related adverse event was vomiting. Increases in liver enzymes were transient and responsive to steroids. In Study 9001-103, there was one new serious adverse event of myocarditis in Cohort 2 (older ambulatory patients >8 years old). The patient had no signs or symptoms of systolic dysfunction and received IV methyl-prednisolone and additional chronic cardiac medications added post-event. Cardiac MRI at one month showed normal function and partial resolution of myocarditic changes, and ECHO at four months showed normal systolic function.

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

**The external control used contemporary datasets taken from three separate studies in Duchenne, two randomized controlled clinical trials and one natural history study, creating a prospectively defined consolidated comparison group of Duchenne patients, matched for variables, including age, steroid usage, baseline NSAA and timed function tests with the participants across the SRP-9001 clinical development program. The prospectively defined propensity score analysis allows for a robust and rigorous balancing of multiple variables.

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.

- **ENDEAVOR, Study SRP-9001-103 (Study 103):** an open-label clinical trial of SRP-9001 that has enrolled 38 participants with Duchenne muscular dystrophy, with 20 participants ages 4 to 7 and expanded cohorts that include older ambulant and non-ambulant individuals, and a younger cohort. 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 immunofluorescence (IF) 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 immunofluorescence 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.

About SRP-9001 (delandistrogene moxeparvovec)
SRP-9001 (delandistrogene moxeparvovec) is an investigational gene transfer therapy intended to deliver SRP-9001 to muscle tissue for the targeted production of essential components of dystrophin. 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.

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 newborn 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 potentially transformative benefits of SRP-9001; our ongoing Phase 3 Study SRP-9001-301 EMBARK; the potential market opportunities with respect to Duchenne; and our plan to share data more broadly in the coming months, particularly with the Duchenne community.

These forward-looking statements involve risks and uncertainties, many of which are beyond our control. Known risk factors include, among others: success in pre-clinical trials and early 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 use 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 other global 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, 2021, 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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