Sarepta Therapeutics' Investigational Gene Therapy SRP-9003 for the Treatment of Limb-Girdle Muscular Dystrophy Type 2E Shows Sustained Expression and Functional Improvements 2 Years After Administration

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-- Protein expression in muscle was sustained for two years following treatment in the low dose cohort, with mean beta-sarcoglycan expression of 54% at 24 months, compared to 36% at Day 60, as measured by western blot --
-- Mean NSAD score improvement of 5.7 points from baseline was sustained through 24 months in low-dose cohort, and mean NSAD score improvement of 4.0 points from baseline at one year in high-dose cohort --
-- Results in both cohorts continue to reinforce the safety and tolerability profile of SRP-9003 --

CAMBRIDGE, Mass., March 18, 2021 (GLOBE NEWSWIRE) -- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today shared new results from the ongoing study of SRP-9003 (rAAVrh74.MHCK7.hSGCB), the Company's investigational gene therapy for limb-girdle muscular dystrophy Type 2E (LGMD2E). In the first look at expression data from biopsies taken two years after a single administration of SRP-9003, results found sustained protein expression in muscle tissue. In functional outcomes assessments taken two years following treatment in Cohort 1 (low-dose cohort) and one year after treatment in Cohort 2 (high-dose cohort), patients continued to demonstrate stability in their NSAD (North Star Assessment for Dysferlinopathies) total score and improvements on timed function tests. Results are being presented today at the 2021 Muscular Dystrophy Association (MDA) Annual Clinical and Scientific Conference.

SRP-9003 is in development for the treatment of LGMD2E (also known as beta-sarcoglycanopathy and LGMDR4), a devastating monogenic neuromuscular disease caused by a lack of beta-sarcoglycan (beta-SG) proteins. SRP-9003 is a gene therapy construct that transduces skeletal and cardiac muscle, delivering a gene that codes for the full-length beta-SG protein, the absence of which is the sole cause of the progressive degeneration and a shortened lifespan characterized by the disease.

"This data is the first look at longer-term expression data with any gene therapy for muscular dystrophy. The meaningful and sustained levels of beta-sarcoglycan protein expression at two years and continued strength of the functional outcomes measured are tremendously positive and support continued advancement of this investigational treatment for patients," said Louise Rodino-Klapac, Ph.D., executive vice president and chief scientific officer, Sarepta Therapeutics. "In Cohort 2, we also saw strong expression of delta-sarcoglycan and gamma-sarcoglycan proteins in addition to beta-sarcoglycan, which suggests that SRP-9003 is working to restore the dystrophin associated protein complex, or DAPC, which provides biological support for the sustained functional benefits observed in both cohorts. LGMD2E is one of the most severe forms of LGMD and causes significant disability in children while frequently leading to early mortality and the data continue to suggest this treatment could bring much needed hope to these patients."

Efficient transduction in skeletal muscle and robust beta-sarcoglycan protein expression were seen in both dose cohorts following infusion with SRP-9003, and significant creatine kinase (CK) reductions were observed.

Cohort 1 (Dosed at 1.85×10^{13} vg/kg), 24 months following treatment:

- As measured by western blot, mean beta-SG of 54% at 24 months of normal control, compared to 36% measured at Day 60.
- Percent immunofluorescent (IF) positive fibers was 48% compared to normal control, compared to 51% at Day 60.
- Participants showed a mean intensity of 35% of transduced beta-SG, properly localized to the muscle sarcolemma, as measured by IF, compared to 47% at Day 60.
- The mean NSAD improvement from baseline of 5.7 points at 18 months was sustained through 24 months.
- All three participants demonstrated continued improvements from baseline across all functional measures, including time-to-rise, four-stair climb, 100-meter walk test and 10-meter walk test.

Cohort 2 (Dosed at 7.41×10^{13} vg/kg), 12 months following treatment:

- At Day 60, the expression of beta-SG (72% mean positive fibers and 73% mean intensity) resulted in increased expression of delta-sarcoglycan, with 65% mean positive fibers and 103% intensity, and gamma-sarcoglycan, 60% mean positive fibers and 97% intensity. These results suggest treatment with SRP-9003 demonstrates reconstitution of the DAPC, which could lead to improved membrane integrity and thus improved clinical motor outcomes measures.
- All three participants demonstrated improvements from baseline across all functional measures, including the NSAD, time-to-rise, four-stair climb, 100-meter walk test and 10-meter walk test.
- The mean NSAD improvement from baseline was 4.0 points at one year, compared to 3.7 at 6 months.

In an exploratory evaluation of all SRP-9003 treated patients compared to a natural history cohort; patients treated with SRP-9003 demonstrated significant improvements in functional outcomes after 24 months. The mean decline in total NSAD score for patients in the natural history cohort was 4.6 points while SRP-9003 treated patients demonstrated a mean improvement of 4.6 points for a clinically meaningful difference of 9.2 points.

Since the last update from this study in October 2020, there have been no new drug-related safety signals observed, and no decreases in platelet

counts outside of the normal range and no evidence of clinical complement activation observed in either dose cohort.

About SRP-9003 and the Study
SRP-9003 uses the AAVrh74 vector, which is designed to be systemically and robustly delivered to skeletal, diaphragm and cardiac muscle, making it an ideal candidate to treat peripheral neuromuscular diseases. AAVrh74 has lower immunogenicity rates than reported with other human AAV vectors. The MHCK7 promoter has been chosen for its ability to robustly express in the heart, which is critically important for patients with limb-girdle muscular dystrophy Type 2E (LGMD2E), also known as beta-sarcoglycanopathy and LGMDR4, many of whom die from pulmonary or cardiac complications.

This open label, first-in-human study is evaluating a single intravenous infusion of SRP-9003 among children with LGMD2E between the ages of 4 and 15 years with significant symptoms of disease. The SRP-9003 study has two cohorts, each studying a different dose-per-kilogram based on the weight of the patient. Three participants in the low-dose cohort (Cohort 1) were treated with a one-time infusion of SRP-9003 dosed at 1.85×10^{13} vg/kg and an additional three participants in the high-dose cohort (Cohort 2) received a one-time infusion dosed at 7.41×10^{13} vg/kg based on linear standard qPCR titer method. The six participants were between the ages of 4 and 13. Post-treatment biopsies were taken at 60 days.

Sarepta has exclusive rights to the LGMD2E gene therapy program initially developed at the Abigail Wexner Research Institute at Nationwide Children's Hospital.

About Limb-girdle Muscular Dystrophy
Limb-girdle muscular dystrophies are genetic diseases that cause progressive, debilitating weakness and wasting that begin in muscles around the hips and shoulders before progressing to muscles in the arms and legs.

Patients with limb-girdle muscular dystrophy Type 2E (LGMD2E) begin showing neuromuscular symptoms such as difficulty running, jumping and climbing stairs before age 10. The disease, which is an autosomal recessive subtype of LGMD, progresses to loss of ambulation in the teen years and often leads to early mortality. There is currently no treatment or cure for LGMD2E.

Sarepta has five LGMD gene therapy programs in development, including subtypes for LGMD2E, LGMD2D, LGMD2C, LGMD2B and LGMD2L, and holds an option for a sixth program for LGMD2A.

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, SRP-9003 being the ideal candidate to treat peripheral neuromuscular diseases; the potential benefits of SRP-9003, including its potential to restore the dystrophin associated protein complex (DAPC); the potential benefits of MHCK7 and the AAVrh74 vector, including its potential to be systemically and robustly delivered to skeletal, diaphragm and cardiac muscle; 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 LGMD 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, 2020 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.*

Source: Sarepta Therapeutics, Inc.

Sarepta Therapeutics, Inc.

Investors:
Ian Estepan, 617-274-4052
iestepan@sarepta.com

Media:
Tracy Sorrentino, 617-301-8566
tsorrentino@sarepta.com