Sarepta Therapeutics Announces Results from Part 2 of the EMBARK Study Demonstrating Sustained Benefits and Disease Stabilization in Ambulatory Individuals with Duchenne Muscular Dystrophy Following Treatment with ELEVIDYS

1/27/25

– ***Treatment with ELEVIDYS corresponded with increases on the North Star Ambulatory Assessment (NSAA) at one year in crossover patients, while the study remained blinded***

– ***MRI results at two years in patients treated in Part 1 show minimal muscle pathology progression, aligning closely with observed functional benefits***

– ***Crossover-treated patients show statistically significant benefits of ELEVIDYS treatment on NSAA, Time to Rise (TTR), and 10-meter walk/run (10MWR), when compared to a pre-specified, well-matched external control (EC)***

– ***Part 1-treated patients show sustained expression at week 64, and functional improvements on NSAA, TTR and 10MWR were sustained two years after treatment and show a widening divergence compared to EC***

– ***Safety remained consistent with the profile of ELEVIDYS already established across a broad Duchenne population***

– ***Investor webcast to be held today at 8:30 a.m. ET***

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 27, 2025-- Sarepta Therapeutics, Inc. (NASDAQ: SRPT), the leader in precision genetic medicine for rare diseases, today announced positive topline results from Part 2 of EMBARK (Study SRP-9001-301), a global, randomized, double-blind, placebo-controlled, Phase 3 clinical study of ELEVIDYS (delandistrogene moxeparvovec-rokl), the only approved gene therapy in patients with Duchenne muscular dystrophy.

Crossover-treated patients, those who received a placebo in Part 1 and crossed over at 52 weeks and were treated with ELEVIDYS in Part 2, improved 2.34 points from baseline compared to matched external controls on the North Star Ambulatory Assessment (NSAA) 52 weeks after treatment (P<0.0001), during which time the study remained blinded.

Despite being one year older (average age 7.18 years) than those treated in Part 1 (average age 5.98 years), crossover-treated patients showed clinically meaningful and statistically significant functional benefit for NSAA, Time to Rise (TTR), and 10-meter walk/run (10MWR) function tests compared with a pre-specified, propensity-weighted external control group* (EC).

Crossover-Treated Patients (n=59) vs. EC

Functional Outcomes	LSM	P-Value
NSAA	+2.34 points	P<0.0001
TTR	-2.70 seconds (improvement)	P<0.0001
10MWR	-1.07 seconds (improvement)	P=0.0001

Two-Year Results

In patients treated in Part 1, biopsies taken 64 weeks after dosing showed consistent and sustained expression of ELEVIDYS micro-dystrophin compared to week 12 biopsies, as measured by western blot, and provide biological support for observed functional outcomes.

At two years, patients treated in Part 1 of EMBARK showed clinically meaningful and statistically significant functional benefit in NSAA, TTR and 10MWR compared with EC. Furthermore, the least square means (LSM) differences seen between the patients treated in Part 1 and the EC group increase from year one to year two for all three functional outcomes. This indicates that the trajectory of disease in patients treated with ELEVIDYS is continuing to diverge from the natural history of DMD.

Part 1, Year 2 (n=63) ELEVIDYS-Treated vs. EC

Functional Outcomes	LSM	P-Value
NSAA	+2.88 points	P=0.0001
TTR	-2.06 seconds (improvement)	P=0.0033
10MWR	-1.36 seconds (improvement)	P=0.0028

Skeletal muscle MRI conducted on patients treated in Part 1 found minimal progression in underlying muscle pathology and remain highly consistent with the functional benefits shown.

“We’re very encouraged to see the results from Part 2 of EMBARK as they further elucidate the impact ELEVIDYS has on disease progression in a blinded, controlled study. Skeletal muscle MRI demonstrates the importance of preserving muscle, and the functional outcome results show disease stabilization sustained through two years after treatment,” said Louise Rodino-Klapac, Ph.D., executive vice president, Head of R&D, Chief Scientific Officer. “Over time, we continue to observe a statistically significant difference favoring ELEVIDYS compared to a well-matched external control on NSAA and timed tests. The consistency and totality of evidence supporting a long-term and clinically meaningful treatment benefit with ELEVIDYS

continues to grow. We look forward to sharing more details with the clinical community in upcoming scientific forums."

No new safety signals were observed, reinforcing the consistent and manageable safety profile of ELEVIDYS to date. Detailed results from Part 2 of the EMBARK study will be shared at future medical meetings.

"As a neuromuscular medicine specialist who has seen patients with Duchenne muscular dystrophy for over three decades, I've witnessed firsthand the positive impact of gene therapy on the trajectory of Duchenne," said Craig McDonald, M.D., professor and chair of the UC Davis Health Department of Physical Medicine and Rehabilitation, and an investigator in the EMBARK study. "These longer-term results are even more striking when compared to external control given the progressive nature of the disease, and we'd expect to see this divergence grow over time. The efficacy of ELEVIDYS gives me great hope as we continue to follow these patients and see others treated in the clinical setting."

As part of a collaboration agreement signed in 2019, Sarepta is working with Roche to transform the future for the Duchenne community, enabling those living with the disease to maintain and protect their muscle function. Sarepta is responsible for regulatory approval and commercialization of ELEVIDYS in the U.S., as well as manufacturing. Roche is responsible for regulatory approvals and bringing ELEVIDYS to patients across the rest of the world.

ELEVIDYS is approved for people living with Duchenne aged four years old and over regardless of their ambulatory status in the U.S., United Arab Emirates (UAE), Qatar, Kuwait, Bahrain and Oman. ELEVIDYS is also approved for the treatment of ambulatory patients aged four through seven years in Brazil and Israel.

*The pre-specified external control used data from five separate studies in Duchenne, comprising DMD controls from two randomized trials and three natural history cohorts who met predefined matching criteria. Comparison of treated and control patients was based on a pre-specified, propensity score weighting approach using age, steroid usage, baseline NSAA and timed function tests in order to balance key prognostic factors between the groups.

Sarepta Investor Call Details

At 8:30 a.m. ET on Jan. 27, 2025, Sarepta will host a conference call and webcast to discuss these results.

The event will be webcast live under the investor relations section of Sarepta's website at https://investorrelations.sarepta.com/events-presentations and following the event a replay will be archived there for one year. Interested parties participating by phone will need to register using this online form. After registering for dial-in details, all phone participants will receive an auto-generated e-mail containing a link to the dial-in number along with a personal PIN number to use to access the event by phone.

About EMBARK, Study 9001-301

Study SRP-9001-301, also known as EMBARK, is a multinational, phase 3, randomized, two-part crossover, placebo-controlled study of ELEVIDYS in individuals with Duchenne muscular dystrophy between the ages of 4 to 7 years. The primary endpoint is change from baseline in NSAA Total Score at Week 52 following treatment. Eligible participants received a single dose of ELEVIDYS during either Part 1 or Part 2 of the study.

In Part 1, participants (n=125) were randomized according to age (≥4 to <8 years) or NSAA Total Score at screening (>16 to <29) and received either 1.33 x1014 vg/kg of ELEVIDYS or placebo with a follow-up period for 52 weeks. In Part 2, participants cross over - meaning, those who were previously treated with placebo in Part 1 receive ELEVIDYS and participants who were previously treated with ELEVIDYS receive placebo, with a follow-up period for 52 weeks. All patients remained blinded through Part 1 and Part 2.

Secondary outcome measures in EMBARK include the quantity of shortened dystrophin produced by ELEVIDYS at week 12 as measured by western blot in a subset of participants, timed function tests, stride velocity and validated patient reported outcome measures for mobility and upper limb function. One-year results from the Part 1 placebo-controlled period of the EMBARK study were published in Nature Medicine in October 2024.

About ELEVIDYS (delandistrogene moxeparvovec-rokl)

ELEVIDYS (delandistrogene moxeparvovec-rokl) is a single-dose, adeno-associated virus (AAV)-based gene transfer therapy for intravenous infusion designed to address the underlying genetic cause of Duchenne muscular dystrophy – mutations or changes in the DMD gene that result in the lack of dystrophin protein – through the delivery of a transgene that codes for the targeted production of ELEVIDYS micro-dystrophin in skeletal muscle.

ELEVIDYS is indicated for the treatment of Duchenne muscular dystrophy (DMD) in individuals at least 4 years of age.

- For patients who are ambulatory and have a confirmed mutation in the DMD gene
- For patients who are non-ambulatory and have a confirmed mutation in the DMD gene.

The DMD indication in non-ambulatory patients is approved under accelerated approval based on expression of ELEVIDYS micro-dystrophin (noted hereafter as "micro-dystrophin") in skeletal muscle. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION: ELEVIDYS is contraindicated in patients with any deletion in exon 8 and/or exon 9 in the DMD gene.

WARNINGS AND PRECAUTIONS:

Infusion-related Reactions:

- Infusion-related reactions, including hypersensitivity reactions and anaphylaxis, have occurred during or up to several hours following ELEVIDYS administration. Closely monitor patients during administration and for at least 3 hours after the end of infusion. If symptoms of infusion-related reactions occur, slow, or stop the infusion and give appropriate treatment. Once

symptoms resolve, the infusion may be restarted at a lower rate.
- ELEVIDYS should be administered in a setting where treatment for infusion-related reactions is immediately available.
- Discontinue infusion for anaphylaxis.

Acute Serious Liver Injury:

- Acute serious liver injury has been observed with ELEVIDYS, and administration may result in elevations of liver enzymes (such as GGT, GLDH, ALT, AST) or total bilirubin, typically seen within 8 weeks.
- Patients with preexisting liver impairment, chronic hepatic condition, or acute liver disease (e.g., acute hepatic viral infection) may be at higher risk of acute serious liver injury. Postpone ELEVIDYS administration in patients with acute liver disease until resolved or controlled.
- Prior to ELEVIDYS administration, perform liver enzyme test and monitor liver function (clinical exam, GGT, and total bilirubin) weekly for the first 3 months following ELEVIDYS infusion. Continue monitoring if clinically indicated, until results are unremarkable (normal clinical exam, GGT, and total bilirubin levels return to near baseline levels).
- Systemic corticosteroid treatment is recommended for patients before and after ELEVIDYS infusion. Adjust corticosteroid regimen when indicated. If acute serious liver injury is suspected, consultation with a specialist is recommended.

Immune-mediated Myositis:

- In clinical trials, immune-mediated myositis has been observed approximately 1 month following ELEVIDYS infusion in patients with deletion mutations involving exon 8 and/or exon 9 in the DMD gene. Symptoms of severe muscle weakness, including dysphagia, dyspnea, and hypophonia, were observed.
- Limited data are available for ELEVIDYS treatment in patients with mutations in the DMD gene in exons 1 to 17 and/or exons 59 to 71. Patients with deletions in these regions may be at risk for a severe immune-mediated myositis reaction.
- Advise patients to contact a physician immediately if they experience any unexplained increased muscle pain, tenderness, or weakness, including dysphagia, dyspnea, or hypophonia, as these may be symptoms of myositis. Consider additional immunomodulatory treatment (immunosuppressants [e.g., calcineurin-inhibitor] in addition to corticosteroids) based on patient's clinical presentation and medical history if these symptoms occur.

Myocarditis:

- Acute serious myocarditis and troponin-I elevations have been observed following ELEVIDYS infusion in clinical trials.
- If a patient experiences myocarditis, those with pre-existing left ventricle ejection fraction (LVEF) impairment may be at higher risk of adverse outcomes. Monitor troponin-I before ELEVIDYS infusion and weekly for the first month following infusion and continue monitoring if clinically indicated. More frequent monitoring may be warranted in the presence of cardiac symptoms, such as chest pain or shortness of breath.
- Advise patients to contact a physician immediately if they experience cardiac symptoms.

Preexisting Immunity against AAVrh74:

- In AAV-vector based gene therapies, preexisting anti-AAV antibodies may impede transgene expression at desired therapeutic levels. Following treatment with ELEVIDYS, all patients developed anti-AAVrh74 antibodies.
- Perform baseline testing for presence of anti-AAVrh74 total binding antibodies prior to ELEVIDYS administration.
- ELEVIDYS administration is not recommended in patients with elevated anti-AAVrh74 total binding antibody titers greater than or equal to 1:400.

Adverse Reactions:

- The most common adverse reactions (incidence ≥5%) reported in clinical studies were vomiting, nausea, liver injury, pyrexia, and thrombocytopenia.

Report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to Sarepta Therapeutics at 1-888-SAREPTA (1-888-727-3782).

For further information, please see the full Prescribing Information.

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 LinkedIn, X, 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

In order to provide Sarepta's investors with an understanding of its current results and future prospects, this press release contains statements that are forward-looking. 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," "may," "intends," "prepares," "looks," "potential," "possible" and similar expressions are intended to identify forward-looking statements. These forward-looking statements include statements relating to ELEVIDYS; the potential benefits of our agreements with strategic partners; and expected milestones and plans, including sharing more details with the clinical community in upcoming scientific forums.

These forward-looking statements involve risks and uncertainties, many of which are beyond Sarepta's control. Actual results could materially differ from those stated or implied by these forward-looking statements as a result of such risks and uncertainties. Known risk factors include the following: success in clinical trials does not ensure that later clinical trials will be successful, and the results of future research may not be consistent with past positive results; we may not be able to execute on our business plans, including meeting our expected or planned regulatory milestones and timelines, research and clinical development plans for various 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, 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 those risks identified under the heading "Risk Factors" in our 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.

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