Sarepta Therapeutics Announces Topline Results from EMBARK, a Global Pivotal Study of ELEVIDYS Gene Therapy for Duchenne Muscular Dystrophy

10/30/23

– ***Results support submission of an efficacy supplement to the BLA; US FDA has indicated openness to reviewing the data for label expansion based on the totality of evidence from EMBARK***

– ***In EMBARK, participants treated with ELEVIDYS (delandistrogene moxeparvovec-rokl) showed an increase on the North Star Ambulatory Assessment, a measure of motor function, compared to placebo-treated patients at 52 weeks, although the primary endpoint was not met***

– ***Robust, statistically significant results on all key pre-specified secondary endpoints, including time to rise (p=0.0025), and 10-meter walk test (p=0.0048), demonstrated evidence of a clinically meaningful treatment benefit that was similar in magnitude and statistical significance across all age groups***

– ***No new safety signals were observed***

– ***Sarepta to host investor call on October 30 at 4:30 p.m. Eastern time***

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 30, 2023-- Sarepta Therapeutics, Inc. (NASDAQ: SRPT), the leader in precision genetic medicine for rare diseases, today announced topline results from EMBARK (Study SRP-9001-301), a global, randomized, double-blind, placebo-controlled, Phase 3 clinical study of ELEVIDYS (delandistrogene moxeparvovec-rokl) in patients with Duchenne muscular dystrophy between the ages of 4 through 7 years.

“The results of EMBARK, our double-blind, placebo-controlled trial, support the conclusion that ELEVIDYS modifies the trajectory of Duchenne and benefits patients across age groups living with this ferociously degenerative disease. The results favored ELEVIDYS across all endpoints in the study, including achieving statistical significance on all pre-specified key secondary endpoints and in each age subgroup of the key secondary endpoints. Indeed, passing 5 seconds on time to rise is the strongest predictor of early loss of ambulation and in EMBARK, ELEVIDYS reduced those odds over 52 weeks by greater than 90 percent,” said Doug Ingram, president and chief executive officer, Sarepta. “Based on the EMBARK results, we intend to move swiftly to request an update to expand the labeled indication to treat all patients. Importantly, we have shared the EMBARK topline results with FDA leadership and they have confirmed that, based on the totality of the evidence, they are open to such label expansion if supported by review of the data, and that they intend to proceed rapidly with consideration of the submission.”

In the study, ELEVIDYS-treated patients improved 2.6 points on their North Star Ambulatory Assessment (NSAA) total score 52 weeks after treatment compared to 1.9 points in placebo-treated patients. The difference of 0.65-points between treated and placebo groups did not reach statistical significance (n=125; p=0.24).

All key pre-specified functional secondary endpoints demonstrated robust evidence for a clinically meaningful treatment benefit that was consistent across age groups in ELEVIDYS-treated patients compared to placebo at 52 weeks. These include:

Time to rise (TTR)	**Change vs Placebo LSM* Diff in Seconds**
Overall (n=124)	-0.64 (p=0.0025)
Ages 4-5 (n=59)	-0.50 (p=0.0177)
Ages 6-7 (n=65)	-0.78 (p=0.0291)

10-meter walk test	**Change vs Placebo LSM Diff in Seconds**
Overall (n=124)	-0.42 (p=0.0048)
Ages 4-5 (n=59)	-0.33 (p=0.0319)
Ages 6-7 (n=65)	-0.52 (p=0.0363)

**least squared means*

All other timed functional endpoints – including stride velocity 95th centile (SV95C) and time to ascend 4 steps – demonstrated consistent treatment benefit in favor of ELEVIDYS. Full results from EMBARK will be shared at future medical meetings and publication will be pursued in a medical journal.

“The strong prognostic power of time to rise, and the particular importance of the 5 second milestone in predicting functional decline and future loss of ambulation, is clearly demonstrated in natural history.[1] In EMBARK, the reduction in patients progressing past this milestone when treated with ELEVIDYS is highly clinically relevant,” 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. “The consistency of the positive effect across all timed function tests and age groups provides evidence of a meaningful treatment effect. In addition, it is important to note that this is the first clinical trial in the history of DMD trials to show a statistically significant and meaningful improvement on the novel measure of 95th centile stride velocity derived from an objective community wearable activity monitor.”

There were no new safety signals in the EMBARK study, reinforcing the favorable and manageable safety profile observed with ELEVIDYS to date. The most common treatment-related adverse events were gastrointestinal events (vomiting, nausea, and decreased appetite) and pyrexia. Seven participants (11.1%) experienced a treatment-related serious adverse event (SAE) and there were no clinically meaningful changes observed in SAEs

associated with known risks of ELEVIDYS.

Conference call details

On October 30, 2023, at 4:30 p.m. Eastern time, 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.

As part of a collaboration agreement signed in 2019, Roche is working with Sarepta Therapeutics to transform the future for the Duchenne community, enabling those living with the disease to maintain and protect their muscle function, keeping them stronger for longer. 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. Together, the companies are implementing a comprehensive joint clinical development plan to maximize the chances of broad approval and access so that ELEVIDYS can reach as many individuals with Duchenne as rapidly as possible.

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 1.33×10^{14} 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 remain blinded.

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.

About ELEVIDYS (delandistrogene moxeparvovec-rokl)

ELEVIDYS (delandistrogene moxeparvovec-rokl) is a single-dose gene transfer therapy for intravenous infusion designed to address the underlying cause of Duchenne muscular dystrophy through the targeted production of ELEVIDYS micro-dystrophin in skeletal muscle. ELEVIDYS is indicated for the treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the *DMD* gene and is approved under accelerated approval based on expression of ELEVIDYS micro-dystrophin in skeletal muscle observed in patients treated with ELEVIDYS. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials. ELEVIDYS has met the full statutory standards for safety and effectiveness and as such is not considered investigational or experimental.

In addition to EMBARK, which serves as the postmarketing confirmatory study, ELEVIDYS has been evaluated in three ongoing clinical studies: SRP-9001-101, SRP-9001-102 and SRP-9001-103. Accelerated approval was primarily based on data from SRP-9001-102 and SRP-9001-103.

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:

Acute Serious Liver Injury:

- Acute serious liver injury has been observed with ELEVIDYS. Administration of ELEVIDYS may result in elevations of liver enzymes (e.g., 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, a 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 between exons 1 to 17 and 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.
- 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.

Pre-existing 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 subjects developed anti-AAVrh74 antibodies.
- Perform baseline testing for the 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 function test increased, pyrexia, and thrombocytopenia.

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 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, without limitation, statements relating to our future operations, business plans, priorities, research and development programs; our understanding that U.S. FDA has indicated openness to reviewing the data for label expansion based on the totality of evidence from EMBARK, if supported by review of the data, and that they intend to proceed rapidly with consideration of the submission; the potential benefits of ELEVIDYS, including the potential to modify the trajectory of Duchenne and benefit patients across age groups living with Duchenne; and expected plans and milestones, including moving swiftly to request an update to expand the labeled indication to treat all patients for ELEVIDYS, and sharing full results from EMBARK at future medical meetings and a publication pursued in a medical journal.

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: the FDA may not approve a supplement to expand the approved label for ELEVIDYS; we may not be able to comply with all FDA requests in a timely manner or at all; the possible impact of regulations and regulatory decisions by the FDA and other regulatory agencies on our business; our data may not be sufficient for obtaining regulatory approval; we are subject to uncertainty related to reimbursement policies; success in preclinical and clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful, and the results of future research may not be consistent with past positive results or with advisory committee recommendations, or may fail to meet regulatory approval requirements for the safety and efficacy of product candidates; continued approval may be contingent upon verification of a clinical benefit in confirmatory trials; the commencement and completion of our clinical trials and announcement of results may be delayed or prevented for a number of reasons, including, among others, denial by the regulatory agencies of permission to proceed with our clinical trials, or placement of a clinical trial on hold, challenges in identifying, recruiting, enrolling and retaining patients to participate in clinical trials and inadequate quantity or quality of supplies of a product candidate or other materials necessary to conduct clinical trials; 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, including meeting our expected or planned regulatory milestones and timelines, research and clinical development plans, and bringing our product candidates to market, for various reasons, many 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 those risks identified under the heading "Risk Factors" in our most recent Annual Report on Form 10-K for the year ended December 31, 2022, and 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.

Reference: 1) Zambon, AA, et al; The UK Northstar Clinical Network. Peak functional ability and age at loss of ambulation in Duchenne muscular dystrophy. *Dev Med Child Neurol*. 2022; 64: 979–988.

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

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

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