Sarepta Provides Safety Update for ELEVIDYS and Initiates Steps to Strengthen Safety in Non-Ambulatory Individuals with Duchenne

6/15/25

- ***The Company is developing an enhanced immunosuppressive regimen in consultation with a panel of multi-disciplinary clinical experts and engaging with regulators***

- ***Shipments of ELEVIDYS for infusions in non-ambulatory patients in commercial setting are suspended until enhanced regimen is approved and in place***

- ***ENVISION study is paused while seeking a protocol amendment to incorporate additional immunosuppression***

- ***Sarepta to host investor call on June 16, 2025, at 8:00 am Eastern time***

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 15, 2025-- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today provided a safety update regarding ELEVIDYS (delandistrogene moxeparvovec-rokl), the only approved gene therapy for patients with Duchenne muscular dystrophy, and steps the Company is taking to strengthen the safety profile in non-ambulatory patients. These steps follow a second reported case of acute liver failure (ALF) resulting in death. The cases of ALF to date have both occurred in non-ambulatory individuals with Duchenne. Sarepta extends its deepest sympathies to the affected families and care teams.

Key Safety Initiatives

Evaluating and Enhancing Immunosuppressive Regimen: As part of a comprehensive review of safety data, Sarepta is taking proactive steps to mitigate the risk of acute liver failure in non-ambulatory patients. Sarepta is working to immediately convene an independent group of leading experts in Duchenne and liver health to consider an enhanced immunosuppression regimen for ELEVIDYS. This panel will evaluate data and assess our proposed regimen, which includes sirolimus and is supported by preclinical data demonstrating the effectiveness of additional immunosuppression in moderating liver enzyme elevations, a key factor in mitigating potential safety events. Sarepta will share the panel's recommendations with the U.S. Food & Drug Administration (FDA), and implementation of any new regimen will be subject to FDA guidance and allowance.

Suspending Shipments of ELEVIDYS for Non-Ambulatory Patients: Sarepta is temporarily suspending shipments of ELEVIDYS for non-ambulatory patients while an enhanced immunosuppressive regimen is evaluated, discussed with regulatory bodies, and put in place.

For ambulatory patients, no treatment changes are being proposed and the current practice of administering corticosteroids before and after ELEVIDYS infusion, along with post-treatment monitoring, remains the same.

ENVISION Study Paused: Sarepta has voluntarily paused dosing in the ENVISION clinical study (also known as Study SRP-9001-303). FDA concurs with this action. The pause will allow for the evaluation of a protocol amendment to incorporate an enhanced immunosuppressive regimen for the non-ambulatory patient cohort and incorporate any additional feedback from the FDA. Regulatory alignment is needed before screening and dosing in ENVISION may resume.

ENVISION is a global, randomized, double-blind, placebo-controlled trial evaluating ELEVIDYS in older ambulatory and non-ambulatory individuals living with Duchenne muscular dystrophy. In the U.S., it serves as the confirmatory trial required under the FDA's accelerated approval pathway for non-ambulatory patients.

“Our paramount priority is the safety and well-being of the patients we serve. We are taking immediate, decisive steps to better understand and mitigate the risk of acute liver failure, including enhancing the immunosuppressive regimen, for those with Duchenne who are non-ambulatory,” said Louise Rodino-Klapac, Ph.D., chief scientific officer and head of research & development, Sarepta. “We are deeply saddened by the loss of a second patient and extend our heartfelt condolences to the patient's family and his care team during this incredibly difficult time. Duchenne muscular dystrophy is a devastating disease that profoundly affects lives and often cuts them far too short. With more than 900 individuals treated to-date, we know how much hope families place in new treatment options like ELEVIDYS – and we are committed to honoring that hope by acting swiftly, guided by scientific rigor and the insights of leading experts, to strengthen safety for all future patients.”

Commitment to Long-Term Safety and Understanding

Sarepta remains committed to a thorough approach and the highest standards of patient safety and scientific rigor. The event has been reported to FDA and global health authorities and will inform ongoing discussions around a potential label update to reflect the risk of severe ALF and additional immune management strategies for non-ambulatory patients. While elevated liver enzymes are a known class effect of all AAV-based gene therapies, the exact mechanism behind AAV-related liver toxicity remains unclear. Current evidence suggests it is likely driven by an adaptive immune response. The Company will provide additional updates as appropriate.

Investor Conference Call Details

Sarepta will be hosting a conference call and webcast to discuss this update and provide an update on the Company’s business on Monday, June 16, 2025, at 8:00 am Eastern time. 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 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 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 (Duchenne) and limb-girdle muscular dystrophies (LGMDs) and are building a robust portfolio of programs across muscle, central nervous system, and cardiac diseases. 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

This statement 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, research and development programs, clinical trials, ELEVIDYS, the potential benefits of an enhanced immunosuppression regimen in dosing in non-ambulatory patients, and expected plans and milestones, including providing additional updates as appropriate and engaging with regulators on an enhanced immunosuppressive regimen for dosing in non-ambulatory patients.

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: 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 are positive, these data may not be sufficient to support approval by the FDA or other global regulatory authorities; success in 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; our products or product candidates may be perceived as insufficiently effective, unsafe or may result in unforeseen adverse events; our products or product candidates may cause undesirable side effects that result in significant negative consequences following any marketing approval; 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; 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.

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 herein. 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20250614701775/en/

Investor Contact:
Ian Estepan
617-274-4052
iestepan@sarepta.com

Media Contacts:
Tracy Sorrentino
617-301-8566

tsorrentino@sarepta.com

Kara Hoeger
617-710-3898
KHoeger@sarepta.com

Source: Sarepta Therapeutics, Inc.