Sarepta Provides Regulatory Update on AMONDYS 45® and VYONDYS 53®

3/19/26

– ***Following feedback from FDA, Company intends to submit supplemental new drug applications to FDA by the end of April 2026 requesting conversion to traditional approval***

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 19, 2026-- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today provided an update on its ongoing regulatory interactions with the U.S. Food and Drug Administration (FDA) regarding AMONDYS 45® (casimersen) and VYONDYS 53® (golodirsen) for the treatment of Duchenne muscular dystrophy (DMD).

Sarepta requested a meeting with FDA to discuss submitting supplemental new drug applications (sNDA) seeking conversion of the accelerated approvals of AMONDYS 45 and VYONDYS 53 to traditional approvals. This request was supported by data from the ESSENCE confirmatory study; substantial, published real-world evidence supporting treatment; and the favorable safety profiles of both therapies. Sarepta has received feedback from the Agency confirming that we can submit our data from ESSENCE and real-world evidence as part of the sNDAs. The adequacy of the data to support conversion to traditional approval will be a matter of review. The Company intends to submit the sNDAs by the end of April.

“In rare diseases like Duchenne, where progression varies widely and meaningful functional changes unfold over years—not months—incorporating real-world data alongside clinical findings can help us better understand long-term outcomes. This is especially true for therapies targeting ultra-rare, genetically defined subgroups, where confirmatory studies are inherently complex,” said Louise Rodino-Klapac, Ph.D., president of research & development and technical operations, Sarepta. “We appreciate the FDA’s openness to our submitting the supplemental applications for AMONDYS 45 and VYONDYS 53 and willingness to consider all available data – from the ESSENCE confirmatory study and the real-world evidence generated over the past several years.”

AMONDYS 45 and VYONDYS 53 are exon-skipping therapies approved under the FDA’s accelerated approval pathway for patients with DMD who have mutations amenable to exon 45 and exon 53 skipping, respectively. The ESSENCE study is a global, Phase 3 randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of AMONDYS 45 and VYONDYS 53 compared to placebo in 225 patients, ages 6-13 years old, with Duchenne amenable to exon 45 or 53 skipping.

Topline results from ESSENCE presented at 2026 Muscular Dystrophy Association Clinical & Scientific Congress found that numerical trends favored treatment versus placebo; however, the observed difference of 0.06 steps/second in least square means (LSM), did not reach statistical significance (P=0.309) on the primary endpoint, the 4-step ascend velocity at 96 weeks.

The ESSENCE study was conducted over a time period that included the COVID-19 pandemic, which impacted the study. An updated analysis that excludes data from 23 participants (~10% of the intent-to-treat population) whose baseline 4-step ascend velocity occurred during the COVID-19 impact period, shows LSM difference of 4-step ascend velocity at week 96 was 0.12 steps/second (P=0.050).

There were no new safety signals in the ESSENCE study, reinforcing the favorable and stable safety profile observed with exon-skipping therapies over years. Adverse events were mostly mild (88%) or moderate (10.9%) and comparable between treatment and placebo groups.

For more than a decade, Sarepta’s PMO (phosphorodiamidate morpholino oligomer) therapies have been used to treat over 1,800 amenable patients worldwide, from infants as young as 7 months to adults well into their 30s. The results from ESSENCE add to the available evidence for VYONDYS 53 and AMONDYS 45, including real-world studies demonstrating that treatment with VYONDYS 53 is associated with a 7.5 year delay in the need for nighttime ventilation[1] and treatment with AMONDYS 45 is associated with a statistically significant slowing of lung function decline and a potentially meaningful benefit in the predicted time to use of a cough assist device[2]. Across our PMO portfolio, real-world evidence indicates a multi-year benefit on survival[3,4], delays in time to loss of ambulation of 3 and 4 years[5,6], a substantial reduction in risk of reaching a left ventricular ejection fraction (LVEF) of less than 55%[7], and a significant reduction in emergency room and other hospital visits[8].

About VYONDYS 53

VYONDYS 53 (golodirsen) uses Sarepta’s proprietary phosphorodiamidate morpholino oligomer (PMO) chemistry and exon-skipping technology to bind to exon 53 of dystrophin pre-mRNA, resulting in exclusion, or “skipping,” of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein.

VYONDYS 53 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with VYONDYS 53. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

VYONDYS 53 has met the full statutory standards for safety and effectiveness and as such is not considered investigational or experimental.

Important Safety Information for VYONDYS 53

CONTRAINDICATIONS: VYONDYS 53 is contraindicated in patients with a serious hypersensitivity reaction to golodirsen or to any of the inactive ingredients in VYONDYS 53. Anaphylaxis has occurred in patients receiving VYONDYS 53.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions: Hypersensitivity reactions, including anaphylaxis, rash, pyrexia, pruritus, urticaria, dermatitis, and skin exfoliation have occurred in VYONDYS 53-treated patients, some requiring treatment. If a hypersensitivity reaction occurs, institute appropriate medical treatment and consider slowing the infusion, interrupting, or discontinuing the VYONDYS 53 therapy and monitor until the condition resolves. VYONDYS 53 is contraindicated in patients with a history of a serious hypersensitivity reaction to golodirsen or to any of the inactive ingredients in VYONDYS 53.

Kidney Toxicity: Kidney toxicity was observed in animals who received golodirsen. Although kidney toxicity was not observed in the clinical studies with VYONDYS 53, the clinical experience with VYONDYS 53 is limited, and kidney toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. Kidney function should be monitored in patients taking VYONDYS 53. Because of the effect of reduced skeletal muscle mass on creatinine measurements, creatinine may not be a reliable measure of kidney function in DMD patients. Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting VYONDYS 53. Consider also measuring glomerular filtration rate using an exogenous filtration marker before starting VYONDYS 53. During treatment, monitor urine dipstick every month, and serum cystatin C and urine protein-to-creatinine ratio every three months. Only urine expected to be free of excreted VYONDYS 53 should be used for monitoring of urine protein. Urine obtained on the day of VYONDYS 53 infusion prior to the infusion, or urine obtained at least 48 hours after the most recent infusion, may be used. Alternatively, use a laboratory test that does not use the reagent pyrogallol red, as this reagent has the potential to cross react with any VYONDYS 53 that is excreted in the urine and thus lead to a false positive result for urine protein.

If a persistent increase in serum cystatin C or proteinuria is detected, refer to a pediatric nephrologist for further evaluation.

ADVERSE REACTIONS: Adverse reactions observed in at least 20% of treated patients and greater than placebo were (VYONDYS 53, placebo): headache (41%, 10%), pyrexia (41%, 14%), fall (29%, 19%), abdominal pain (27%, 10%), nasopharyngitis (27%, 14%), cough (27%, 19%), vomiting (27%, 19%), and nausea (20%, 10%).

Other adverse reactions that occurred at a frequency greater than 5% of VYONDYS 53-treated patients and at a greater frequency than placebo were: administration site pain, back pain, pain, diarrhea, dizziness, ligament sprain, contusion, influenza, oropharyngeal pain, rhinitis, skin abrasion, ear infection, seasonal allergy, tachycardia, catheter site related reaction, constipation, and fracture.

Other adverse events may occur.

To report SUSPECTED ADVERSE REACTIONS, contact Sarepta Therapeutics, Inc. at 1-888-SAREPTA (1-888-727-3782) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For further information, please see the full US Prescribing Information for VYONDYS 53 (golodirsen).

About AMONDYS 45

AMONDYS 45 (casimersen) uses Sarepta's proprietary phosphorodiamidate morpholino oligomer (PMO) chemistry and exon-skipping technology to bind to exon 45 of dystrophin pre-mRNA, resulting in exclusion, or "skipping," of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 45 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein.

AMONDYS 45 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 45 skipping. This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with AMONDYS 45. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

AMONDYS 45 has met the full statutory standards for safety and effectiveness and as such is not considered investigational or experimental.

Important Safety Information for AMONDYS 45

CONTRAINDICATION: AMONDYS 45 is contraindicated in patients with a known serious hypersensitivity to casimersen or any of the inactive ingredients in AMONDYS 45. Instances of hypersensitivity including angioedema and anaphylaxis have occurred.

WARNINGS AND PRECAUTIONS

Hypersensitivity: Hypersensitivity reactions, including angioedema and anaphylaxis, have occurred in patients who were treated with AMONDYS 45. If a hypersensitivity reaction occurs, institute appropriate medical treatment, and consider slowing the infusion, interrupting, or discontinuing the AMONDYS 45 infusion and monitor until the condition resolves. AMONDYS 45 is contraindicated in patients with known serious hypersensitivity to casimersen or to any of the inactive ingredients in AMONDYS 45.

Kidney Toxicity: Kidney toxicity was observed in animals who received casimersen. Although kidney toxicity was not observed in the clinical studies with AMONDYS 45, kidney toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. Kidney function should be monitored in patients taking AMONDYS 45. Because of the effect of reduced skeletal muscle mass on creatinine measurements, creatinine may not be a reliable measure of kidney function in DMD patients. Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting AMONDYS 45. Consider also measuring glomerular filtration rate using an exogenous filtration marker before starting AMONDYS 45. During treatment, monitor urine dipstick every month, and serum cystatin C and urine protein-to-creatinine ratio (UPCR) every three months. Only urine expected to be free of excreted AMONDYS 45 should be used for monitoring of urine protein. Urine obtained on the day of AMONDYS 45 infusion prior to the infusion, or urine obtained at least 48 hours after the most recent infusion, may be used. Alternatively, use a laboratory test that does not use the reagent pyrogallol red, as this reagent has the potential to cross react with any AMONDYS 45 that is excreted in the urine and thus lead to a false positive result for urine protein.

If a persistent increase in serum cystatin C or proteinuria is detected, refer to a pediatric nephrologist for further evaluation.

Adverse Reactions: Adverse reactions occurring in at least 20% of patients treated with AMONDYS 45 and at least 5% more frequently than in the placebo group were (AMONDYS 45, placebo): upper respiratory infections (65%, 55%), cough (33%, 26%), pyrexia (33%, 23%), headache (32%, 19%), arthralgia (21%, 10%), and oropharyngeal pain (21%, 7%).

Other adverse reactions that occurred in at least 10% of patients treated with AMONDYS 45 and at least 5% more frequently than in the placebo group

were: ear pain, nausea, ear infection, post-traumatic pain, and dizziness and light-headedness.

Other adverse events may occur.

To report SUSPECTED ADVERSE REACTIONS, contact Sarepta Therapeutics, Inc. at 1-888-SAREPTA (1-888-727-3782) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For further information, please see the full US Prescribing Information for AMONDYS 45 (casimersen).

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 a leadership position in Duchenne muscular dystrophy (Duchenne) 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.

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 our future operations, business plans, market opportunities, priorities and research and development programs, technologies and products, including AMONDYS and VYONDYS; real-world evidence; our ESSENCE trial; and expected plans and milestones, including our intention to submit a sNDA by end of April.

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: our ability to obtain and maintain regulatory approvals; we may not be able to comply with all FDA post-approval commitments and requirements with respect to our products in a timely manner or at all, including through studies that confirm clinical efficacy, effectiveness and safety of our products, and acceptance of the same by the FDA; we may not be able to reach alignment with the FDA regarding traditional approval for casimersen and golodirsen, including due to any limitations on the FDA's reliance of real-world evidence; results in clinical trials, even if successful, may fail to meet regulatory approval requirements for the safety and efficacy of product candidates, and could lead to potential regulatory actions from the FDA, including directives to remove these products from the market or alter labels; 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, 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; the impact of the federal government shutdown on the FDA; 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, 2025 filed with the Securities and Exchange Commission (SEC) as well as other SEC filings made by the Company which you are encouraged to review.

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.

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[1] Iff J, et al. Delayed Pulmonary Progression in Golodirsen-Treated Patients With Duchenne Muscular Dystrophy vs Mutation-Matched External Controls. Presented at MDA 2024.

[2] Kuntz N, et al. Pulmonary Function in Advanced-Stage Patients With Duchenne Muscular Dystrophy Treated With Casimersen. Presented at WMS 2025.

[3] Iff J, , et al. Survival among patients receiving eteplirsen for up to 8 years for the treatment of Duchenne muscular dystrophy and contextualization with natural history controls. *Muscle & Nerve*. 2024; 70(1): 60-70. doi:10.1002/mus.28075.

[4] Data on file.

[5] Mathews K, et al. Comparative Analysis of Loss of Ambulation in Eteplirsen-Treated Patients With DMD in the EVOLVE Study and Propensity Score–Weighted External Controls. Presented at MDA 2025.

[6] Muntoni F, et al. Comparing Ambulatory Outcomes of Golodirsen-Treated Patients vs Mutation-Matched External Controls. Presented at CNS 2025.

[7] Iff J, et al. Association Between Exon-Skipping Therapy With Eteplirsen and Cardiac Outcomes in Duchenne Muscular Dystrophy. Presented at MDA 2025.

[8] Iff J, et al. Journal Comp Eff Res. 2023 Sep;12(9):e230086. doi: 10.57264/cer-2023-0086.

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