Sarepta Announces FDA Acceptance of sNDAs for AMONDYS 45® and VYONDYS 53®

6/30/26

– ***Accepted for review with target action date of February 28, 2027***

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 30, 2026-- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today announced that the U.S. Food and Drug Administration (FDA) has accepted for filing the supplemental New Drug Applications (sNDAs) for AMONDYS 45® (casimersen) and VYONDYS 53® (golodirsen) for the treatment of Duchenne muscular dystrophy (DMD). The FDA has assigned a Prescription Drug User Fee Act (PDUFA) target action data of February 28, 2027.

The sNDA submissions seek conversion of the accelerated approvals of AMONDYS 45 and VYONDYS 53 to traditional approvals. The applications are supported by data from the ESSENCE confirmatory study, as well as substantial published real-world evidence and the favorable and consistent safety profiles of both exon-skipping therapies.

"The FDA's acceptance of these applications for review is an important step for the Duchenne community. The submissions draw on the ESSENCE study and years of published real-world evidence, which together offer a fuller understanding of how these therapies benefit patients and change the progression of disease," said Louise Rodino-Klapac, Ph.D., president of research & development and technical operations, Sarepta. "Within Duchenne, each amenable mutation defines an ultra-rare population—a small subset of an already rare disease. Across our exon skipping therapies, more than 1,800 people worldwide have been treated, and we continue to observe preservation of muscle function and slowed disease progression. In populations this small and in a disease where damage unfolds over years, real-world experience is essential to understanding how these therapies impact the disease course. We look forward to working with the FDA throughout the review."

"We appreciate the FDA's continued willingness to apply regulatory adaptability in addressing the unique challenges of rare disease drug development. The acceptance of these supplemental applications for review reflects both the progress the Duchenne community has made over the past several years and the needs that remain, while maintaining a commitment to evaluating therapies with rigor," said Pat Furlong, president and founder, Parent Project Muscular Dystrophy. "We are grateful for the FDA's engagement with the Duchenne community and the Agency's dedication to advancing therapeutic options through pathways adaptable to rare disease."

About Sarepta's Exon-Skipping Portfolio

EXONDYS 51 (eteplirsen), AMONDYS 45 (casimersen) and VYONDYS 53 (golodirsen) are exon-skipping therapies approved under the FDA's accelerated approval pathway for patients with DMD who have mutations amenable to exon 51, exon 45 and exon 53 skipping, respectively. For more than a decade, Sarepta's exon-skipping 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.

In the Phase 3 ESSENCE study evaluating casimersen and golodirsen versus placebo, the primary endpoint was not met; however, numerical trends favored treatment. Additional post-hoc analyses were performed to evaluate heterogeneity challenges related to DMD progression and the impact of conducting ESSENCE during COVID-19. At week 96, treatment was associated with increased dystrophin expression and a consistent reduction in 4-step ascend decline across multiple analyses. The therapies were well tolerated over 144 weeks with no new safety signals observed, consistent with established clinical and real-world experience.

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 EXONDYS 51

EXONDYS 51 uses Sarepta's proprietary phosphorodiamidate morpholino oligomer (PMO) chemistry and exon-skipping technology to bind to exon 51 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 51 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein.

EXONDYS 51 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 51 skipping. This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with EXONDYS 51. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

EXONDYS 51 has met the full statutory standards for safety and effectiveness and as such is not considered investigational or experimental.

Important Safety Information About EXONDYS 51

Hypersensitivity reactions, including bronchospasm, chest pain, cough, tachycardia, and urticaria have occurred in patients who were treated with EXONDYS 51. If a hypersensitivity reaction occurs, institute appropriate medical treatment and consider slowing the infusion or interrupting the EXONDYS 51 therapy.

Adverse reactions in DMD patients (N=8) treated with EXONDYS 51 30 mg or 50 mg/kg/week by intravenous (IV) infusion with an incidence of at least 25% more than placebo (N=4) (Study 1, 24 weeks) were (EXONDYS 51, placebo): balance disorder (38%, 0%), vomiting (38%, 0%) and contact dermatitis (25%, 0%). The most common adverse reactions were balance disorder and vomiting. Because of the small numbers of patients, these represent crude frequencies that may not reflect the frequencies observed in practice. The 50 mg/kg once weekly dosing regimen of EXONDYS 51 is not recommended.

The most common adverse reactions from observational clinical studies (N=163) seen in greater than 10% of patients were headache, cough, rash, and vomiting.

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 U.S. Prescribing Information for EXONDYS 51 (eteplirsen).

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 U.S. 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 U.S. 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. Forward-looking statements may be accompanied by words such as "believes," "anticipates," "plans," "expects," "will," "may," "intends," "prepares," "looks," "potential," "possible" and similar expressions. 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; the sNDAs for AMONDYS and VYONDYS; real-world evidence and clinical trial results; and expected plans and milestones including the PDUFA dates for the sNDAs.

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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