Spruce Biosciences Announces Long-Term Tralesinidase Alfa Enzyme Replacement Therapy Data in Sanfilippo Syndrome Type B (MPS IIIB) Presented at the 18th International MPS Symposium

June 8, 2026

Data Highlight TA-ERT's Potential as the First Disease-Modifying Treatment Option for MPS IIIB, a Fatal Condition With No Approved Therapies

Treatment With Weekly TA-ERT Demonstrated Rapid and Durable Normalization of CSF Heparan Sulfate Non-Reducing End (CSF HS-NRE), a Surrogate Endpoint Reasonably Likely to Predict Clinical Benefit

TA-ERT Stabilized and Preserved Cognitive and Non-Cognitive Outcomes, Including Communication and Motor Skills, Over a Six-Year Period Relative to Natural History Patients

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 8, 2026-- Spruce Biosciences, Inc. (Nasdaq: SPRB), a late-stage biopharmaceutical company focused on developing and commercializing novel therapies for neurological disorders with significant unmet medical need, today announced that data demonstrating the long-term benefit of tralesinidase alfa enzyme replacement therapy (TA-ERT) in patients with Sanfilippo Syndrome Type B (MPS IIIB) were presented at the 18th International MPS & Related Lysosomal Diseases Symposium, which took place June 4-7, 2026 in Florence, Italy. The data show that long-term administration of TA-ERT resulted in rapid and durable reduction of heparan sulfate and preserved cognitive and non-cognitive outcomes relative to natural history patients.

The presentation, which includes data previously presented at the 22nd Annual WORLD*Symposium* ™, was delivered by Nicole Muschol, M.D., of the International Center for Lysosomal Disorders (ICLD) at the University Medical Center Hamburg-Eppendorf in Germany and Principal Investigator for the TA-ERT clinical development program.

"In a progressive neurodegenerative disease like MPS IIIB, stability itself is a clinically meaningful outcome," said Dr. Muschol. "Over six years of treatment, cerebral spinal fluid heparan sulfate fell rapidly and remained low, while cognition, communication, and motor function were preserved relative to the decline seen in untreated patients. These long-term findings support the potential of tralesinidase alfa enzyme replacement therapy as the first disease-modifying treatment option for a fatal condition that currently has no approved therapies, and they matter greatly to the affected children and families."

In an analysis of 22 patients who enrolled in interventional studies of TA-ERT with follow-up of up to six years, TA-ERT treatment:

- Rapidly and durably normalized levels of cerebral spinal fluid heparan sulfate non-reducing end (CSF HS-NRE), a surrogate endpoint reasonably likely to predict clinical benefit in patients with MPS IIIB;
- Stabilized cognitive function, as assessed by the Bayley-III Cognitive Raw Score (BSID-C), the cognitive subscale of the validated Bayley Scales of Infant and Toddler Development – Third Edition (Bayley-III), relative to declines seen in untreated natural history patients;
- Stabilized receptive and expressive communication, as well as fine and gross motor skills, compared with a decline in these outcomes in untreated natural history patients, as assessed by the Vineland Adaptive Behavior Scales – Second Edition (VABS-II);
- Stabilized cortical gray matter volume, which declined in untreated natural history patients, and normalized liver and spleen volume; and
- Was generally consistent with the safety profile of intracerebroventricular (ICV) administration; over the six-year study, approximately 6,000 doses were administered to 22 patients.

For more information, the presentation can be found on the Spruce Biosciences website at https://investors.sprucebio.com/news-and-events/presentations.

About Sanfilippo Syndrome Type B (MPS IIIB)

Sanfilippo Syndrome Type B (MPS IIIB) is an ultra-rare, serious, and fatal genetic disease characterized by deficiency in N-Acetyl-Alpha-Glycosaminidase (NAGLU), an enzyme required for the catabolism of heparan sulfate (HS) in lysosomes. It is estimated that MPS IIIB affects fewer than one in 200,000 people in the United States, but the true incidence and prevalence are difficult to ascertain because MPS IIIB is a disease currently not included in newborn screening. The accumulation of toxic levels of cerebral spinal fluid heparan sulfate in the brain is the underlying pathophysiology of MPS IIIB. Although signs and symptoms of MPS IIIB can vary amongst affected individuals, progressive neurodegeneration typically follows a predictable path to brain atrophy, cognitive and developmental impairment, hyperactivity with aggressive and destructive behavior, delayed speech, hearing loss, and motor skill deficits. Somatic manifestations include coarse facial features, hepatosplenomegaly, and gastrointestinal symptoms. The final stage of MPS IIIB is typically marked by severe dementia, loss of motor function, and seizure activity, with patients largely bed-ridden and requiring constant care, requiring feeding tubes for hydration and nutrition, and ultimately leading to death. The estimated life expectancy of individuals with MPS IIIB ranges from 15 to 19 years of age. Currently, there are no FDA-approved therapies for MPS IIIB, and management of the disease consists of limited palliative care to improve quality of life.

About Tralesinidase Alfa Enzyme Replacement Therapy (TA-ERT)

Tralesinidase Alfa Enzyme Replacement Therapy (TA-ERT) is a fusion protein comprised of recombinant human alpha-N-acetylglucosaminidase (rhNAGLU). TA-ERT is intended as an enzyme replacement therapy for the treatment of patients with Sanfilippo Syndrome Type B (MPS IIIB) who lack rhNAGLU enzyme activity. TA-ERT is expected to restore rhNAGLU enzyme activity in the central nervous system following intracerebroventricular injection. rhNAGLU typically lacks the mannose-6 phosphate residues that are essential for efficient cellular uptake via the M6P receptor pathway. As a result, the naked enzyme is poorly absorbed by cells, including neurons. To address this challenge, TA-ERT is fused to an insulin-like growth factor 2 peptide, which binds to the cation-independent mannose-6-phosphate on cell surfaces. This fusion enables the enzyme to be internalized and delivered to the lysosome, thereby enhancing its therapeutic potential for treating MPS IIIB. By restoring NAGLU enzymatic activity and promoting clearance of lysosomal heparan sulfate and heparan sulfate non-reducing end in the brain, TA-ERT therapy is expected to preserve neuronal cell health and potentially halt or slow the neurological decline and improve clinical outcomes in affected patients. TA-ERT has been evaluated in three clinical studies in participants with MPS IIIB: the interventional study 201 and extension studies 202 and 401. TA-ERT has been administered to 22 individuals diagnosed with MPS IIIB, and has demonstrated an adequate safety profile based on integrated six years of safety data.

About Spruce Biosciences

Spruce Biosciences is a late-stage biopharmaceutical company focused on developing and commercializing novel therapies for neurological disorders with significant unmet medical need. Spruce's lead product candidate, tralesinidase alfa enzyme replacement therapy (TA-ERT), is in late-stage development for the treatment of mucopolysaccharidoses type IIIB (MPS IIIB), or Sanfilippo Syndrome Type B, a devastating pediatric neurodegenerative disorder for which there are no FDA-approved therapies. TA-ERT has received Breakthrough Therapy Designation, Rare Pediatric Disease Designation, Fast Track Designation and Orphan Drug Designation from the FDA, as well as Orphan Drug Designation in the European Union. To learn more, visit www.sprucebio.com and follow us on X, LinkedIn, Facebook and YouTube.

Forward Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding, among other things, the ability to seek accelerated approval of TA-ERT for MPS IIIB based on existing clinical data; the timing and likelihood of regulatory filings and approvals for TA-ERT, including advancing this program through a biologics license application submission and potential U.S. FDA approval; the potentially transformative clinical impact for TA-ERT; and TA-ERT's potential to be the first and best-in-class disease-modifying therapy to treat MPS IIIB. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as "anticipate," "will," "potential," "intend," "expect," and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Spruce's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks and uncertainties associated with Spruce's business in general, the impact of geopolitical and macroeconomic events, and the other risks described in Spruce's filings with the U.S. Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date. Spruce undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

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