Spruce Biosciences Receives U.S. FDA Breakthrough Therapy Designation for Tralesinidase Alfa Enzyme Replacement Therapy (TA-ERT) in Sanfilippo Syndrome Type B (MPS IIIB)

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Breakthrough Therapy Designation Supported by Integrated Long-Term Clinical Data Demonstrating Normalization in Cerebral Spinal Fluid Heparan Sulfate Non-Reducing End (CSF HS-NRE)

U.S. FDA Confirmed that CSF HS-NRE is a Surrogate Biomarker Reasonably Likely to Predict Clinical Benefit and Could Serve as Basis for Accelerated Approval

Biologics License Application Submission of TA-ERT for MPS IIIB Remains on Track for the First Quarter of 2026

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Oct. 6, 2025-- 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 the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation (BTD) to tralesinidase alfa enzyme replacement therapy (TA-ERT) for the treatment of Sanfilippo Syndrome Type B (MPS IIIB).

“We are pleased to receive U.S. FDA Breakthrough Therapy Designation as we prepare to submit the Biologics License Application of TA-ERT for the treatment of MPS IIIB in the first quarter of 2026. This designation highlights TA-ERT’s potentially transformative clinical impact as the first disease-modifying therapy to treat MPS IIIB in children impacted by this devastating condition,” said Javier Szwarcberg, M.D., M.P.H., Chief Executive Officer of Spruce Biosciences. “The integrated group-level clinical data demonstrates a rapid, profound, and durable effect of TA-ERT in normalizing CSF HS-NRE, the pathogenic factor leading to neurodegeneration, and stabilizing cortical grey matter volume and cognitive function in children with MPS IIIB.”

BTD is designed to expedite the development and regulatory review of promising therapies for serious or life-threatening conditions where preliminary clinical evidence suggests the potential for substantial improvement over existing treatments. The designation facilitates more intensive FDA guidance, cross-disciplinary collaboration, and eligibility for rolling submission and priority review.

About Sanfilippo Syndrome Type B (MPS IIIB)

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 1:200,000 people in the United States (U.S.), 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 MPS IIIB (Sanfilippo Syndrome Type B) 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. Twenty-two individuals with MPS IIIB have been administered TA-ERT therapy. TA-ERT has demonstrated an adequate safety profile based on integrated five 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. 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, and TA-ERT’s potential to preserve neuronal cell health and

potentially halt or slow neurological decline and improve clinical outcomes in affected patients. 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 “potential,” “intend,” “on track,” “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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