REGENXBIO Announces Regulatory Update on RGX-121 BLA for MPS II

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- *FDA issues Complete Response Letter for RGX-121 (clemidsogene lanparvovec) for treatment of Mucopolysaccharidosis II (MPS II)*
- *REGENXBIO plans to work with FDA on a path forward with the goal of resubmitting the BLA*

ROCKVILLE, Md., Feb. 9, 2026 /PRNewswire/ -- REGENXBIO Inc. (Nasdaq: RGNX) today announced that the U.S. Food and Drug Administration (FDA) has issued a Complete Response Letter (CRL) regarding its Biologics License Application (BLA) for RGX-121 (clemidsogene lanparvovec) for the treatment of Mucopolysaccharidosis II (MPS II), an ultra-rare neurodegenerative disease also known as Hunter syndrome.

In May 2025, the FDA accepted the RGX-121 BLA under the accelerated approval pathway. In the February 7, 2026 CRL, the FDA stated that it had agreed to the study protocol in principle and outlined several reasons for not approving the gene therapy, including uncertainty regarding the study eligibility criteria to adequately define a population with neuronopathic disease (vs. attenuated disease), the comparability of the natural history external control to the study population, and the appropriateness of CSF HS D2S6 as a surrogate endpoint reasonably likely to predict clinical benefit. The CRL lists several potential paths forward, including a new study, treating additional patients and conducting longer-term follow up, and using an untreated control arm, all of which would be challenging in an ultra-rare disease population, like MPS II.

"This decision is devastating for the families of boys living with this progressive, life-threatening disease," said Curran Simpson, President and CEO of REGENXBIO. "We are concerned about FDA's feedback regarding the overall development path and evaluation of the data in the context of the urgent need for this irreversible ultra-rare disease. We remain confident in the quality and volume of evidence demonstrating the long-term potential of RGX-121 to positively change the trajectory of Hunter syndrome. This program has been in development for over 10 years. We are incredibly grateful to all the patients, their families, investigators, and site staff who have supported this program and our continued efforts to bring a much-needed new treatment option to the Hunter syndrome community. We will continue those efforts."

Throughout active discussions during the BLA process, REGENXBIO believed it had addressed the points raised in the CRL through the submission of additional data and responses to numerous information requests. Independent, leading global MPS and biomarker experts conducted analyses and reviews with the FDA, as well. Ultimately, the FDA did not agree the data set provided substantial evidence of effectiveness to support approval of RGX-121 for the treatment of MPS II.

REGENXBIO plans to request a Type A meeting to discuss the CRL, as well as the planned BLA resubmission to provide additional evidence from global MPS II experts to further clarify the neuronopathic patient population and additional longer-term clinical data to support evidence of effectiveness. REGENXBIO intends to find a path forward as quickly as possible with the goal of resubmitting the BLA.

"MPS II is a very complex disease, but its impact is well established, resulting in irreversible brain damage for the majority of patients; without appropriate treatments stopping this neurocognitive decline, the neuronopathic MPS II child will die prematurely, usually in their mid-teens," said Joseph Muenzer, M.D., Ph.D., Director, Muenzer MPS Research and Treatment Center, Bryson Distinguished Professor in the Division of Genetics and Metabolism, Department of Pediatrics Genetics, University of North Carolina at Chapel Hill. "I remain encouraged by the clinical data behind RGX-121. New innovations like gene therapy could make a significant impact for these patients, and time is precious for these families."

"I've seen the severe impact of MPS II on patients and their families firsthand and am extremely disheartened by today's news," said Terri Klein, President and CEO, National MPS Society. "Families know the devastating trajectory of this disease all too well and have waited 20 years for new treatment options. They cannot wait any longer. Drug development for ultra-rare disease must be streamlined to allow new medicines to reach patients. We urge the FDA to find a swift path forward so that boys living with MPS II and their families have the chance for a better life."

About RGX-121 (clemidsogene lanparvovec)
RGX-121 is a potential one-time gene therapy for the treatment of boys with MPS II, designed to deliver the iduronate-2-sulfatase (*IDS*) gene to the CNS. Delivery of the *IDS* gene within cells in the CNS could provide a permanent source of secreted iduronate-2-sulfatase (I2S) protein beyond the blood-brain barrier, allowing for long-term cross correction of cells throughout the CNS. RGX-121 expressed protein is structurally identical to normal I2S.

The BLA for RGX-121 for MPS II was supported by positive biomarker, functional and safety data from the CAMPSIITE I/II/III trial, including out to 12 months. RGX-121 has been well tolerated in all patients dosed across all phases of the CAMPSIITE trial.

RGX-121 has received Orphan Drug Product, Rare Pediatric Disease, Fast Track and Regenerative Medicine Advanced Therapy (RMAT) designations from the FDA and advanced therapy medicinal products (ATMP) classification from the European Medicines Agency.

About Mucopolysaccharidosis Type II (MPS II)
MPS II, or Hunter Syndrome, is a rare, X-linked recessive disease caused by a deficiency in the lysosomal enzyme I2S leading to an accumulation of glycosaminoglycans (GAGs), including heparan sulfate (HS) in tissues which ultimately results in cell, tissue, and organ dysfunction, including in the central nervous system (CNS). In severe forms of the disease, early developmental milestones may be met, but developmental delay is readily apparent by 18 to 24 months. Specific treatment to address the neurological manifestations of MPS II remains a significant unmet medical need. Key biomarkers of I2S enzymatic activity in MPS II patients include its substrate CSF HS D2S6, which has been shown to correlate with neurocognitive manifestations of the disorder.

ABOUT REGENXBIO Inc.
REGENXBIO is a biotechnology company on a mission to improve lives through the curative potential of gene therapy. Since its founding in

2009, REGENXBIO has pioneered the field of AAV gene therapy. REGENXBIO is advancing a late-stage pipeline of one-time treatments for rare and retinal diseases, including RGX-202 for the treatment of Duchenne; clemidsogene lanparvovec (RGX-121) for the treatment of MPS II and RGX-111 for the treatment of MPS I, both in partnership with Nippon Shinyaku; and surabgene lomparvovec (ABBV-RGX-314) for the treatment of wet AMD and diabetic retinopathy, in collaboration with AbbVie. Thousands of patients have been treated with REGENXBIO's AAV platform, including those receiving Novartis' ZOLGENSMA®. REGENXBIO's investigational gene therapies have the potential to change the way healthcare is delivered for millions of people. For more information, please visit **www.REGENXBIO.com**.

FORWARD-LOOKING STATEMENTS
This press release includes "forward-looking statements," within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements express a belief, expectation or intention and are generally accompanied by words that convey projected future events or outcomes such as "believe," "may," "will," "estimate," "continue," "anticipate," "assume," "design," "intend," "expect," "could," "plan," "potential," "predict," "seek," "should," "would" or by variations of such words or by similar expressions. The forward-looking statements include statements relating to, among other things, REGENXBIO's future operations, clinical trials, costs and cash flow. REGENXBIO has based these forward-looking statements on its current expectations and assumptions and analyses made by REGENXBIO in light of its experience and its perception of historical trends, current conditions and expected future developments, as well as other factors REGENXBIO believes are appropriate under the circumstances. However, whether actual results and developments will conform with REGENXBIO's expectations and predictions is subject to a number of risks and uncertainties, including the timing of enrollment, commencement and completion and the success of clinical trials conducted by REGENXBIO, its licensees and its partners, the timing of commencement and completion and the success of preclinical studies conducted by REGENXBIO and its development partners, the timing or likelihood of payments from AbbVie or Nippon Shinyaku, the monetization of any priority review voucher, the timely development and launch of new products, the ability to obtain and maintain regulatory approval of product candidates, the ability to obtain and maintain intellectual property protection for product candidates and technology, trends and challenges in the business and markets in which REGENXBIO operates, the size and growth of potential markets for product candidates and the ability to serve those markets, the rate and degree of acceptance of product candidates, and other factors, many of which are beyond the control of REGENXBIO. Refer to the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of REGENXBIO's Annual Report on Form 10-K for the year ended December 31, 2024, and comparable "risk factors" sections of REGENXBIO's Quarterly Reports on Form 10-Q and other filings, which have been filed with the SEC and are available on the SEC's website at **WWW.SEC.GOV**. All of the forward-looking statements made in this press release are expressly qualified by the cautionary statements contained or referred to herein. The actual results or developments anticipated may not be realized or, even if substantially realized, they may not have the expected consequences to or effects on REGENXBIO or its businesses or operations. Such statements are not guarantees of future performance and actual results or developments may differ materially from those projected in the forward-looking statements. Readers are cautioned not to rely too heavily on the forward-looking statements contained in this press release. These forward-looking statements speak only as of the date of this press release. Except as required by law, REGENXBIO does not undertake any obligation, and specifically declines any obligation, to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

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CONTACTS:
Dana Cormack
Corporate Communications
Dcormack@regenxbio.com

George E. MacDougall
Investor Relations
IR@regenxbio.com

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