REGENXBIO Presents Additional Positive Interim Data from Phase I/II Trial of RGX-121 for the Treatment of MPS II (Hunter Syndrome) at American Society of Gene and Cell Therapy's 24th Annual Meeting

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- *RGX-121, a one-time gene therapy for MPS II, continues to be well-tolerated with no drug-related serious adverse events*
- *Biomarkers and measures of neurodevelopmental function from patients in Cohorts 1 and 2 continue to indicate CNS activity following RGX-121 administration*
- *Evidence of systemic enzyme expression and biomarker activity continues to be observed*
- *REGENXBIO recently initiated dosing of patients in Cohort 3*

REGENXBIO Inc. (Nasdaq: RGNX) today announced a safety update and additional positive interim data from the ongoing Phase I/II trial of RGX-121 for the treatment of patients up to 5 years old diagnosed with Mucopolysaccharidosis Type II (MPS II), also known as Hunter Syndrome. The latest data from this trial will be presented today at the American Society of Gene and Cell Therapy (ASGCT) 24th Annual Meeting by Dr. Roberto Giugliani, Professor, Department of Genetics, UFRGS, Medical Genetics Service, HCPA, Porto Alegre, Brazil.

"I am pleased to report additional data from the Phase I/II trial of RGX-121 in patients with MPS II. The biomarker data from these patients continues to demonstrate that the I2S enzyme is active in the CNS and importantly, continued cognitive development has been observed in the majority of patients who have been followed for more than 6 months. In addition, emerging evidence of systemic enzyme expression and activity has been shown in urine and plasma, including in patients who are naive to enzyme replacement therapy, the current standard of care," said Dr. Giugliani. "The potential to provide therapeutic benefit from a one-time gene therapy would be a meaningful advancement for the treatment of MPS II patients."

"It is encouraging to see continued efficacy signals up to two years after administration of RGX-121 in our Phase I/II trial. The safety profile we have seen to date, combined with evidence of CNS and systemic effects, are encouraging as we seek to bring a one-time gene therapy treatment to the MPS II community," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. "We have begun dosing patients in Cohort 3, and we look forward to providing further program updates later this year."

RGX-121 is an investigational one-time gene therapy designed to deliver the gene that encodes the iduronate-2-sulfatase (I2S) enzyme using the AAV9 vector. RGX-121 is administered directly to the central nervous system (CNS). Patients in Cohorts 1 and 2 received doses of RGX-121 at $1.3x10^{10}$ genome copies per gram (GC/g) of brain mass and $6.5x10^{10}$ GC/g of brain mass, respectively. REGENXBIO began dosing patients in Cohort 3 at an increased dose of $2.0x10^{11}$ GC/g of brain mass. As of April 25, 2021, RGX-121 is reported to be well-tolerated with no drug-related serious adverse events (SAEs) in nine patients dosed with RGX-121 in Cohorts 1-3.

Data Summary and Safety Update from Cohort 1 and 2

Time of post-administration follow-up for patients in Cohorts 1 and 2 ranges from 24 weeks to two years. Five patients have completed the 48-week immunosuppression regimen, per study protocol. Six of the patients were receiving weekly, intravenous enzyme replacement therapy (ERT) at the time of enrollment; two of these patients have since discontinued ERT.

CSF Biomarker Data from Cohort 1 and 2

Biomarker data from patients in Cohorts 1 and 2 indicate encouraging signals of I2S enzyme activity in the CNS following one-time administration of RGX-121. Heparan sulfate (HS) levels are a key biomarker of I2S enzyme activity and the patients in Cohorts 1 and 2 demonstrated decreased HS in the cerebrospinal fluid (CSF) up to 2 years following RGX-121 administration. Combined median reductions from baseline were 30.3% at Week 8 and 35.0% at the last timepoint available for each patient. Similarly, these patients demonstrated decreased levels of D2S6, a component of HS, up to 2 years following RGX-121 administration, with median reductions from baseline of 44.1% at Week 8 and 40.4% at the last timepoint available for each patient. In addition, I2S enzyme concentration in the CSF, which was undetectable in all patients prior to dosing, was measurable in all five patients from Cohort 2 after RGX-121 administration.

Neurocognitive Development Data from Cohort 1 and 2

Patients in Cohorts 1 and 2 also demonstrated continued neurocognitive development up to two years after RGX-121 administration. Five patients have assessments of neurodevelopment function at timepoints beyond 6 months, and of those patients, four have continued to demonstrate neurocognitive development, according to the Bayley Scales[1]. One patient entered the study with significant delay in neurocognitive development at baseline but has demonstrated relative stabilization following RGX-121 administration and has continued to acquire expressive and receptive language skills based on the Bayley Scales.

Systemic Biomarker Data and Clinical Efficacy

Patients in Cohorts 1 and 2 demonstrated evidence of I2S enzyme activity in urine following administration of RGX-121. Notably, two patients in

Cohort 2 who were naive to ERT demonstrated rapid reductions in urine total glycosaminoglycans (GAG) levels of over 50% at the latest timepoint available following RGX-121 administration. Two patients in Cohort 1 discontinued ERT over one year after administration of RGX-121, and the total urine GAG levels following ERT withdrawal remained relatively consistent with total urine GAG levels prior to ERT withdrawal. Total urine GAG levels decreased among four patients who continue to receive ERT following administration of RGX-121. Patients in both cohorts demonstrated increases in I2S protein concentration levels in plasma over time following administration of RGX-121.

The study findings are available at https://www.asgct.org.

About RGX-121

RGX-121 is a product candidate for the treatment of Mucopolysaccharidosis Type II (MPS II), also known as Hunter Syndrome. RGX-121 is designed to use the AAV9 vector to deliver the human iduronate-2-sulfatase gene (*IDS*) which encodes the iduronate-2-sulfatase (I2S) enzyme to the central nervous system (CNS). Delivery of the *IDS* gene within cells in the CNS could provide a permanent source of secreted I2S beyond the blood-brain barrier, allowing for long-term cross correction of cells throughout the CNS. RGX-121 has received orphan drug product, rare pediatric disease and Fast Track designations from the U.S. Food and Drug Administration.

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 iduronate-2-sulfatase (I2S) leading to an accumulation of glycosaminoglycans (GAG), including heparan sulfate (HS) in tissues which ultimately results in cell, tissue, and organ dysfunction. 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 and prevent or stabilize cognitive decline remains a significant unmet medical need. Key biomarkers of I2S enzymatic activity in MPS II patients include its substrate heparan sulfate (HS), which has been shown to correlate with neurocognitive manifestations of the disorder.

About REGENXBIO Inc.

REGENXBIO is a leading clinical-stage biotechnology company seeking to improve lives through the curative potential of gene therapy. REGENXBIO's NAV Technology Platform, a proprietary adeno-associated virus (AAV) gene delivery platform, consists of exclusive rights to more than 100 novel AAV vectors, including AAV7, AAV8, AAV9 and AAVrh10. REGENXBIO and its third-party NAV Technology Platform Licensees are applying the NAV Technology Platform in the development of a broad pipeline of candidates in multiple therapeutic areas.

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 and clinical trials. 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 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, the impact of the COVID-19 pandemic or similar public health crises on REGENXBIO's business, 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, 2020 and comparable "risk factors" sections of REGENXBIO's Quarterly Reports on Form 10-Q and other filings, which have been filed with the U.S. Securities and Exchange Commission (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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[1] Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III)

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