REGENXBIO Presents Additional Positive Interim Data from Phase I/II Trial of RGX-121 for the Treatment of MPS II (Hunter Syndrome) at 17th Annual WORLDSymposium™ 2021

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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 Cohort 1 and 2 indicate CNS activity following RGX-121 administration
  - Consistent reductions in CSF levels of biomarkers up to 2 years after RGX-121 administration
  - Continued cognitive development and skill acquisition observed
- Evidence of systemic enzyme expression and biomarker activity
  - Increased plasma enzyme levels
  - Rapid urine biomarker reductions observed in ERT-naïve patients; reduced liver and spleen volumes in one ERT-naïve patient
- REGENXBIO plans to initiate dosing of patients in Cohort 3 in the first quarter of 2021

ROCKVILLE, Md., Feb. 8, 2021 /PRNewswire/ -- REGENXBIO Inc. (Nasdaq: RGNX) today announced that additional positive interim data from a total of eight patients in Cohorts 1 and 2 of 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, will be presented at the 17th Annual WORLD*Symposium* ™ .

"We are pleased to report additional positive data from Cohorts 1 and 2 of our ongoing Phase I/II trial of RGX-121. Data from the eight patients dosed to date continue to show an encouraging safety profile of RGX-121, and highlight the potential of RGX-121 to restore biological enzyme activity and improve outcomes for MPS II patients," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. "We look forward to enrolling patients in Cohort 3 at a higher dose level of RGX-121, which we expect to begin in the first quarter of 2021."

"The consistent biomarker data and neurocognitive development updates from patients in the RGX-121 trial are compelling, especially the data from patients who were not treated with enzyme replacement therapy prior to enrolling in the trial," said Dr. Roberto Giugliani, Professor, Department of Genetics, UFRGS, Medical Genetics Service, HCPA, Porto Alegre, Brazil. "These patients have demonstrated decreased levels of GAGs in urine, increased I2S enzyme in plasma, and one patient has shown reduced liver and spleen dimensions several months after receiving RGX-121, suggesting that RGX-121 delivered to the CNS has the potential to deliver benefit to patients outside of the CNS. I am encouraged by these results and look forward to further evaluations and advancement of this program."

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 expects to begin enrolling patients in Cohort 3 in the first quarter of 2021 at an increased dose of $2.0x10^{11}$ GC/g brain mass.

The study findings that will be presented at the WORLD*Symposium* are available under the Presentations & Publications page in the Media section of the company's website located at www.regenxbio.com.

Data Summary and Safety Update

As of January 4, 2021, RGX-121 is reported to be well-tolerated with no drug-related serious adverse events (SAEs) in eight patients dosed with RGX-121. Time of post-administration follow-up ranges from four weeks to two years. All four patients that reached 48-weeks of follow-up completed the 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

Biomarker data from patients in both cohorts indicate encouraging signals of I2S enzyme activity in the CNS following one-time administration of RGX-121. Heparan sulfate (HS) and D2S6, a component of HS, are glycosaminoglycans (GAGs) that are key biomarkers of I2S enzyme activity and are being measured in the cerebrospinal fluid (CSF) at baseline and after administration of RGX-121. Elevated levels of HS and D2S6 correlate closely with the neuronopathic phenotype of MPS II. HS levels in the first six patients in Cohorts 1 and 2 demonstrated consistent reductions in the CSF up to 2 years following RGX-121 administration, with median reductions from baseline of 30.3% at Week 8 and 35.8% at the last timepoint available for each patient. Similarly, these patients demonstrated consistent reductions of D2S6 up to 2 years following RGX-121 administration, with median reductions from baseline of 44.2% at Week 8 and 39.2% 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 patients from Cohort 2 after RGX-121 administration.

Neurocognitive Development Data

Patients in Cohorts 1 and 2 also demonstrated continued neurocognitive development up to two years after RGX-121 administration. Five patients in Cohorts 1 and 2 have reached at least 6 months of follow-up since RGX-121 administration, and of those five patients, three continued to demonstrate neurocognitive development within a normal range, according to the Bayley Scales[1]. Two patients entered the study with significant delay in neurocognitive development at baseline. After RGX-121 administration, one of these patients demonstrated ongoing neurocognitive development, and both patients 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 plasma and urine following administration of RGX-121. Five of six patients demonstrated increases in I2S enzyme concentration levels in plasma over time. Six of eight patients dosed with RGX-121 were receiving ERT at the time of enrollment in the study. All six of these patients have shown decreased total GAG levels in urine up to two years following RGX-121 administration. Notably, two patients in Cohort 2 who were naïve to ERT demonstrated rapid reductions in urine total GAG levels following RGX-121 administration; one of these patients with 24 weeks of follow-up showed significant reductions in liver and spleen volumes.

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, 2019, 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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