Additional Positive Interim Data from Phase I/II Trial of REGENXBIO'S RGX-111 for the Treatment of Severe MPS I Presented at WORLDSymposium™

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- *RGX-111 is an investigational AAV Therapeutic for the treatment of severe MPS I that is part of REGENXBIO's clinical-stage pipeline of neurodegenerative disease programs*
  - *RGX-111, a potential one-time gene therapy for MPS I, continues to be well-tolerated across two dose levels, with no drug-related serious adverse events*
  - *New biomarker and neurodevelopmental data continue to indicate encouraging CNS profile in patients dosed with RGX-111*
- *Company is on track to manufacture commercial-scale cGMP material to support the continued development of RGX-111*

ROCKVILLE, Md., Feb. 24, 2023 /PRNewswire/ -- REGENXBIO Inc. (Nasdaq: RGNX) today announced positive interim data from the Phase I/II trial of RGX-111 for the treatment of severe Mucopolysaccharidosis Type I (MPS I). Data from the Phase I/II trial and single-patient Investigational New Drug (IND) application of RGX-111 were presented by Ray Wang, M.D., Campbell Foundation Director of the Multidisciplinary Lysosomal Program, Division of Metabolic Disorders, CHOC Children's Hospital, Department of Pediatrics, University of California, Irvine, at the 19th Annual WORLD*Symposium* ™ .

"RGX-111 is our second-most advanced clinical candidate in our neurodegenerative disease pipeline and is part of our '5x'25' strategy to have five gene therapies either on the market or in late-stage development by 2025. We are encouraged to see that this potential one-time gene therapy using our NAV AAV9 vector continues to demonstrate compelling evidence of CNS biomarker activity," said Kenneth T. Mills, President and Chief Executive Officer of REGENXBIO. "In connecting with MPS I families, we understand the need for new treatment options that can impact daily living, and we're pleased to see that most patients in this trial demonstrated continued skill acquisition across multiple neurodevelopmental assessments."

"There is a great need for new treatment options that provide lasting expression of the IDUA enzyme and the reduction of glycosaminoglycans in the central nervous system," said Dr. Wang. "I am encouraged by the emerging clinical profile of RGX-111 based on this data, including the important neurodevelopment gains in cognition, language, fine motor skills and personal and social skills for daily living."

RGX-111 is an investigational one-time gene therapy designed to deliver the gene that encodes the IDUA enzyme using the AAV9 vector. RGX-111 is administered directly to the central nervous system (CNS). The primary endpoint of the trial is to evaluate the safety of RGX-111. Secondary and exploratory endpoints include biomarkers of IDUA enzyme activity in the cerebrospinal fluid (CSF), serum and urine, neurodevelopmental assessments, and caregiver reported outcomes. Patients were treated across two dose cohorts: $1.0x10^{10}$ genome copies per gram (GC/g) of brain mass (n=2) and $5.0x10^{10}$ GC/g of brain mass (n=6). In the single-patient IND for RGX-111, a severe MPS I patient was dosed with $1x10^{10}$ GC/g of brain mass.

REGENXBIO plans to continue having early and frequent communication with regulatory agencies about pathways to expedite the development of its neurodegenerative disease pipeline. In the first half of 2023, REGENXBIO expects to use its Manufacturing Innovation Center to produce RGX-111 commercial-scale cGMP material from its proprietary, high-yielding suspension-based manufacturing process, named NAVXPress™.

Data Summary and Safety Data
As of January 17, 2023, RGX-111 was reported to be well tolerated in the eight patients enrolled in the Phase I/II clinical trial with no drug-related serious adverse events (SAEs). Time of post-administration follow-up ranged from seven to 103 weeks. Two patients in Cohort 1 and three patients in Cohort 2 have completed the 48-week immunosuppression regimen, per the study protocol.

RGX-111 continued to be well-tolerated in the single-patient IND with no drug-related SAEs as of December 12, 2021. Time of post-administration follow-up was 87 weeks. This patient has completed the 48-week immunosuppression regimen, per the study protocol, and continues to receive weekly ERT.

CSF Biomarker Data
Data from patients in the Phase I/II trial and the single-patient IND indicate positive IDUA biomarker activity in the CNS following one-time administration of RGX-111. Heparan sulfate (HS) is a glycosaminoglycan (GAG) that is a key biomarker of IDUA enzyme activity. In the Phase I/II trial, a decrease in CSF HS was observed through the last timepoint available in the majority of patients following administration of RGX-111. Measurable CSF IDUA enzyme activity was detected after RGX-111 administration in four of the five Phase I/II trial patients and in the single patient IND participant.

Neurodevelopmental Data
Patients in the Phase I/II trial and the single-patient IND demonstrated encouraging continued neurodevelopmental skill acquisition, as measured by age and developmentally appropriate validated instruments for neurodevelopmental testing, including the Bayley Scales of Infant Development (BSID-III) for chronological or developmental ages 0-42 months, Wechsler Abbreviated Scale of Intelligence (WASI-II) for chronological and developmental age greater than six years, and the Vineland Adaptive Behavior Scale (VABS-III; across all age groups).

All five patients assessed with BSID-III demonstrated continued developmental skill acquisition on all subsets (cognition, expressive language and fine motor). At the last assessment, four of the five patients had function ≥ -2 standard deviations of the normative mean on the cognition, expressive language and fine motor subtests. Cognitive function in a Phase I/II trial patient and the single IND patient was higher than the age equivalent scores in the available natural history data.

One patient in Cohort 1 who entered the trial at 13 years old demonstrated neurodevelopmental improvements as measured by the WASI-II and showed improvement in the majority of subdomains of the VABS-III at approximately 18 months after RGX-111 administration.

Systemic Biomarker Data
Evidence of systemic biomarker activity was observed in patients in both cohorts of the Phase I/II trial and the single-patient IND. Patients who had elevated baseline levels of I0S6 in plasma, a key biomarker of IDUA enzyme activity in MPS I patients, demonstrated decreases in I0S6 levels following administration of RGX-111. In addition, the majority patients dosed with RGX-111 maintained low levels of total urine GAGs at the last timepoint available.

The study findings 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.

About RGX-111
RGX-111 is designed to use the AAV9 vector to deliver the α-l-iduronidase (IDUA) gene to the central nervous system (CNS). Delivery of the IDUA gene within the cells in the central nervous system (CNS) could provide a permanent source of secreted IDUA beyond the blood-brain barrier, allowing for long-term cross-correction of cells throughout the CNS. By providing rapid IDUA delivery to the brain, RGX-111 could potentially help prevent the progression of cognitive deficits that otherwise occurs in MPS I patients. RGX-111 has received orphan drug product, rare pediatric disease and Fast Track designations from the U.S. Food and Drug Administration.

About Mucopolysaccharidosis Type I (MPS I)
MPS I is a rare autosomal recessive genetic disease caused by a deficiency in the lysosomal enzyme alpha-L-iduronidase (IDUA), 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). This can include excessive accumulation of fluid in the brain, spinal cord compression, and cognitive impairment. MPS I is estimated to occur in 1 in 100,000 births. Current disease modifying therapies for MPS I include hematopoietic stem cell transplant (HSCT) and enzyme replacement therapy with a recombinant form of human IDUA administered intravenously. However, intravenous enzyme therapy does not treat the CNS manifestations of MPS I, and HSCT can be associated with clinically significant morbidity and mortality. Key biomarkers of IDUA enzymatic activity in MPS I 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, including late-stage and commercial programs, in multiple therapeutic areas. REGENXBIO is committed to a "5x'25" strategy to progress five AAV Therapeutics from our internal pipeline and licensed programs into pivotal-stage or commercial products by 2025.

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, 2021, 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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