REGENXBIO Presents Positive Initial Data from Phase I/II Trial of RGX-111 for the Treatment of Severe MPS I at 18th Annual WORLD*Symposium*™ 2022

- *RGX-111, a potential one-time gene therapy for MPS I, is well-tolerated across two dose levels, with no drug-related serious adverse events*
- *Biomarker and neurodevelopmental assessments indicate encouraging CNS profile in patients dosed with RGX-111*
- *Evidence of systemic biomarker activity observed*
- *Phase I/II trial data are consistent with positive results from an RGX-111 single-patient IND*
- *Completed dosing of three patients in Cohort 2; Cohort 2 has been expanded to enroll up to 6 additional patients*

ROCKVILLE, Md., February 9th, 2022 (PRNewswire) -- REGENXBIO Inc. (Nasdaq: RGNX) today announced positive interim data are being presented at the 18th Annual WORLD*Symposium*™ from five patients in the ongoing Phase I/II trial and one patient from a single-patient Investigational New Drug (IND) application of RGX-111 for the treatment of severe Mucopolysaccharidosis Type I (MPS I).

“This marks our first data presentation from the Phase I/II trial evaluating RGX-111 as a potential one-time gene therapy delivered directly to the central nervous system (CNS) for the treatment of severe MPS I. We are encouraged to see that RGX-111 has been well-tolerated with emerging evidence of CNS biomarker activity and improvements in neurodevelopmental function, which suggest biological activity in the CNS following one-time administration of RGX-111. We also saw emerging evidence of biomarker activity outside of the CNS,” said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. “We plan to enroll additional patients in the Phase I/II trial and look forward to providing additional updates.”

“MPS I is a rare inherited disorder caused by a mutation in the gene that encodes human α-l-iduronidase (IDUA), an enzyme needed by cells to break down long chains of sugar molecules known as mucopolysaccharides. Current treatment options for MPS I have limitations and can be associated with significant morbidity and mortality,” said 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, CA. “Initial data indicate encouraging CNS and systemic biomarker activity following RGX-111 administration.”

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 CNS. The primary endpoint of the trial is to evaluate the safety of RGX-111. Secondary and exploratory endpoints include biomarkers of α-l-iduronidase (IDUA) enzyme activity in the cerebrospinal fluid (CSF), serum and urine, neurodevelopmental assessments, and caregiver reported outcomes. Patients were treated across two dose cohorts: 1.0×10^{10} genome copies per gram (GC/g) of brain mass (n=2) and 5.0×10^{10} GC/g of brain mass (n=3). In the single-patient IND for RGX-111, a severe MPS I patient was dosed with 1×10^{10} GC/g of brain mass.

REGENXBIO plans to immediately expand enrollment of patients in Cohort 2 of the Phase I/II trial based on support from MPS I treating-physicians and the Independent Data Monitoring Committee, to enroll up to six additional patients.

Data Summary and Safety Update
As of December 20, 2021, RGX-111 is reported to be well-tolerated in the five patients enrolled in the Phase I/II clinical trial with no drug-related serious adverse events (SAEs). Time of post-administration follow-up ranges from three weeks to 56 weeks. One patient in Cohort 1 has completed the 48-week immunosuppression regimen per the study protocol. Two patients were not receiving enzyme replacement therapy (ERT) at the time of enrollment, and they continue to not receive ERT.

RGX-111 continues to be well-tolerated in the single-patient IND with no drug-related SAEs as of December 20, 2021. Time of post-administration follow-up is 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 HS in the CSF from baseline was observed through the last timepoint available in all four patients following administration of RGX-111. Measurable IDUA enzyme activity in the CSF was detected after RGX-111 administration in three of the four patients, all of whom had undetectable levels of IDUA activity at baseline.

The patient dosed with RGX-111 under the single-patient IND demonstrated a decrease from baseline in HS in the CSF at 59 weeks after dosing, the last timepoint available. IDUA enzyme activity in the CSF, which was at undetectable at baseline, was detected following RGX-111 administration.

Neurodevelopmental Data
Patients in the Phase I/II trial and the single-patient IND demonstrated encouraging continued neurodevelopment, as measured by age and using 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).
Three patients in the Phase I/II trial had neurodevelopmental assessments with at least one post-baseline assessment after administration of RGX-111. Early assessments from the two patients under the age of six years old demonstrated continued skill acquisition within two standard deviations of the normative mean at last assessment on the BSID-III cognition, expressive language and fine motor subtests. One patient in Cohort 1 who entered the trial at the age of 13 years old demonstrated neurodevelopmental improvements as measured by the WASI-II and six of the nine scales of the VABS-III at one year after RGX-111 administration.

The single-patient IND patient demonstrated continued skill acquisition within two standard deviations of the normative mean on the BSID-III cognition, expressive language and fine motor subtests, as well as higher age equivalent scores than available natural history data at last assessment, 20 months after administration of RGX-111.

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, patients dosed with RGX-111 maintained low levels of total urine GAGs at the last timepoint available, regardless of ERT treatment.

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 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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