Additional Positive Interim Data from Phase I/II/III CAMPSIITE™ Trial of REGENXBIO's RGX-121 for the Treatment of MPS II (Hunter Syndrome) Presented at 19th Annual WORLDSymposiumTM

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- *RGX-121, a potential one-time gene therapy for the treatment of MPS II, continues to be well-tolerated with no drug-related SAEs across three dose levels*
- *Additional data from patients in Cohort 3 using pivotal program dose level continue to demonstrate largest reductions in CSF GAGs, continuing to approach normal levels at 48 weeks*
- *New, longer-term clinical measures demonstrated continued improvement in neurodevelopmental and daily activity skill acquisition up to three years after RGX-121 administration*
- *Positive interim data continues to support plan to file Biologics License Application in 2024 using the accelerated approval pathway*

ROCKVILLE, Md., Feb. 22, 2023 /PRNewswire/ -- REGENXBIO Inc. (Nasdaq: RGNX) today announced additional positive interim data from the Phase I/II/III CAMPSIITE™ 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 results were presented at the 19th Annual WORLD*Symposium* ™ .

"These new results demonstrate sustained reductions in CSF GAGs and an encouraging, long-term clinical profile of RGX-121 up to three years," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. "GAGs measured in CSF, specifically heparan sulfate, reflect disease manifestations in the CNS and are a direct cause of disease pathophysiology. Our data provide additional evidence to support the finding that meaningful changes in CSF heparan sulfate is an appropriate and reliable surrogate endpoint reasonably likely to predict the clinical benefit of CNS-targeted therapies for MPS II. We are excited to have taken RGX-121 into a pivotal program and plan to file a Biologics License Application in 2024 using the accelerated approval pathway."

"Treatment options to address the neurological manifestations of MPS II remain a significant unmet medical need for patients," said Can Ficicioglu, M.D., Ph.D., Professor of Pediatrics at the Perelman School of Medicine, University of Pennsylvania. "The data presented today are encouraging and continue to show the potential of a one- time gene therapy to provide meaningful, durable clinical benefits to the MPS II community. I look forward to continuing to follow RGX-121 as it progresses through the pivotal 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. Data presented were from the Phase I/II portion of the CAMPSIITE trial in which the primary endpoint is to evaluate the safety of RGX-121. Secondary and exploratory endpoints include cerebral spinal fluid (CSF) glycosaminoglycans (GAGs), neurodevelopmental assessments, caregiver reported outcomes and systemic biomarkers. RGX-121 is administered directly to the central nervous system (CNS). As of January 3, 2023, 15 patients had been treated across three dose levels, $1.3x10^{10}$ genome copies per gram (GC/g) of brain mass (n=3), $6.5x10^{10}$ GC/g of brain mass (n=7), and $2.9x10^{11}$ GC/g of brain mass (n=5).

Data Summary and Safety Update

As of January 3, 2023, RGX-121 was reported to be well tolerated across all cohorts with no drug-related serious adverse events (SAEs) in 15 patients dosed. Time of post-administration follow-up ranges from eight weeks to more than three years. Thirteen patients have completed the 48-week immunosuppression regimen per study protocol. Twelve patients were receiving weekly, intravenous enzyme replacement therapy (ERT) at the time of enrollment, per standard of care; five of these patients remain discontinued from ERT at last time point available, per investigator discretion, as allowed in the protocol.

CSF GAGs Data

Biomarker data from patients in all three cohorts indicate encouraging, dose-dependent reductions of CSF GAGs following one-time administration of RGX-121. Heparan sulfate (HS) and D2S6, a component of HS closely correlated with severe MPS II, are GAGs that are key biomarkers of I2S enzyme activity and are being measured in the CSF at baseline and after administration of RGX-121. CSF GAGs have the potential to be considered a surrogate endpoint that is reasonably likely to predict clinical benefit in MPS II disease under the accelerated approval pathway, as buildup of GAGs in the CSF of MPS II patients correlates with clinical manifestations including neurodevelopmental deficits.

The majority of patients in all cohorts demonstrated reductions of CSF HS from baseline at the last time point available with dose-dependent reductions seen at Weeks 8, 24, and 48 post RGX-121 administration. At Week 48, median reduction of CSF HS from baseline was 33.5% in Cohort 1, 48.9% in Cohort 2 and 64.7% in Cohort 3.

Similarly, dose-dependent reductions of CSF HS D2S6 from baseline were observed at last time point available in the majority of patients, with Cohort

3 patients approaching normal levels at 48 weeks. All three cohorts demonstrated a reduction in HS D2S6 with dose-dependent reductions seen at Weeks 8, 24, and 48. Median reductions from baseline of 31.9% in Cohort 1, 71.9% in Cohort 2 and 83.3% in Cohort 3 were seen at Week 48.

In addition, I2S protein concentration in the CSF, which was undetectable in all patients prior to dosing, was measurable in 10 of 11 Cohort 2 and 3 patients after RGX-121 administration.

Neurodevelopmental and Systemic Data
Improvements in neurodevelopmental function and caregiver reported outcomes demonstrated CNS activity on two developmental scales up to three years after RGX-121 administration. As measured by the Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III), the majority of participants with baseline function ≥-2 standard deviations (SD) from the normative mean had developmental function that remained within that range on at least two domains. The majority of participants with baseline function below -2SD from the normative mean stabilized or had an increase of ≥ 3 months in age equivalent scores on cognitive, expressive language or fine motor subtests. As measured by the Vineland Adaptive Behavior Scales Second Edition (VABS-II), the majority of participants demonstrated stabilization or ongoing skill acquisition on age-appropriate subtests of communication, daily living and socialization.

Additionally, evidence of systemic enzyme expression and biomarker activity was observed in all cohorts following RGX-121 administration. The majority of patients demonstrated increases in I2S protein concentration levels in plasma following administration of RGX-121. Total urine GAG measures demonstrated evidence of a systemic effect of RGX-121, independent of ERT treatment.

The study findings presented at the 2023 WORLD*Symposium* will be available under the Presentations & Publications page in the Media section of REGENXBIO's website located at www.regenxbio.com. Dr. Ficicioglu will share this data in a platform presentation at the WORLD*Symposium* Sunday, February 26, 2023, at 9 a.m. ET.

About the CAMPSIITE™ Trial
CAMPSIITE is a Phase I/II/III multicenter, open-label trial enrolling boys with MPS II, aged four months up to five years of age. As part of a pivotal program expansion, CAMPSIITE is expected to enroll up to 10 MPS II patients to support the BLA filing using the accelerated approval pathway, with the potential to enroll additional patients. These patients will receive a dose of $2.9x10^{11}$ GC/g of brain mass of RGX-121, which is the same dose being evaluated in Cohort 3 of the Phase I/II trial. The pivotal program is using commercial-scale cGMP material from REGENXBIO's proprietary, high-yielding suspension-based manufacturing process, named NAVXpress™. In addition to measuring GAGs in the CSF, the trial will continue to collect neurodevelopmental data and caregiver-reported outcomes.

CAMPSIITE is a global trial, which is expected to include sites in the United States, Brazil and Canada. REGENXBIO has begun dosing patients in the pivotal program.

About RGX-121
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 (GAGs), including heparan sulfate (HS) in tissues which ultimately results in cell, tissue, and organ dysfunction, including in the central nervous system (CNS). MPS II is estimated to occur in 1 in 100,000 to 170,000 births. 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 heparan sulfate (HS) D2S6, 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.

Contacts:
Dana Cormack
Corporate Communications
dcormack@regenxbio.com

Investors:
Chris Brinzey
ICR Westwicke
339-970-2843
chris.brinzey@westwicke.com

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