



REGENXBIO Presents Additional Positive Interim Data from the Phase I/II/III CAMPSIITE™ Trial of RGX-121 for the Treatment of MPS II (Hunter Syndrome) at the Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium

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- *New data in Cohort 3 using pivotal program dose level demonstrates largest median reduction in CSF GAGs, continuing to approach normal levels at 48 weeks*
- *RGX-121, a one-time gene therapy for MPS II, continues to be well-tolerated with no drug-related SAEs across three dose levels*
- *Positive interim data supports recently announced plan to file Biologics License Application in 2024 using the accelerated approval pathway*

ROCKVILLE, Md., Aug. 31, 2022 /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 Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium.

"We are pleased to share new, positive interim data from our Phase I/II/III CAMPSIITE trial that continues to demonstrate encouraging reductions of CSF GAGs and supports the selection of dose level 3 for our pivotal program," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. "This interim data of Cohorts 1-3 demonstrate dose-dependent reductions in CSF GAGs, key biomarkers of I2S enzyme activity, in additional patients and at longer timepoints than previously presented. RGX-121 has also demonstrated positive impact on neurodevelopmental function. We believe the data supports our plan to advance RGX-121 as quickly as possible using the accelerated approval pathway with the aim of providing a much-needed new treatment option for the MPS II community."

"RGX-121 continues to demonstrate compelling data showing its potential to impact the neurodevelopmental decline of MPS II patients, which remains an unmet need for most affected individuals," said Roberto Giugliani, M.D., Ph.D., Professor, Department of Genetics, UFRGS, Medical Genetics Service, HCPA, Porto Alegre, Brazil. "A successful gene therapy with the potential to provide advantages over current standard of care is something that could provide a meaningful treatment option to the MPS II patient community. I look forward to continuing to follow this trial as the recently announced pivotal program progresses."

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 at SSIEM was from the Phase I/II portion of the CAMPSIITE trial where 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 August 1, 2022, patients had been treated across three dose levels, 1.3×10^{10} genome copies per gram (GC/g) of brain mass (n=3), 6.5×10^{10} GC/g of brain mass (n=7), and 2.9×10^{11} GC/g of brain mass (n=4).

Data Summary and Safety Update

As of August 1, 2022, RGX-121 is reported to be well-tolerated across all cohorts with no drug-related serious adverse events (SAEs) in 14 patients dosed with RGX-121. Time of post-administration follow-up ranges from eight weeks to two years. Eleven 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; three of these patients have discontinued ERT, 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. GAGs in the CSF have the potential to be considered a surrogate biomarker 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 three cohorts demonstrated reductions of HS in the CSF following RGX-121 administration 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, 52.9% in Cohort 2 and 62.5% in Cohort 3.

Similarly, dose-dependent reductions of CSF HS D2S6 were observed at last time point available following RGX-121 administration in the majority of patients, with Cohort 3 patients approaching normal levels at 48 weeks. All three cohorts demonstrated reduction in HS D2S6 with dose-dependent reductions seen at Weeks 8, 24, and 48. Median reduction from baseline of 31.9% in Cohort 1, 69.4% in Cohort 2 and 83.1% in Cohort 3 was seen at Week 48.

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

Neurodevelopmental and Systemic Data

As previously reported at the 2022 *WORLDSymposium™*, improvements in neurodevelopmental function and caregiver reported outcomes in Cohorts 1 and 2 demonstrated CNS activity up to 2 years after RGX-121 administration. Additionally, evidence of systemic enzyme expression and biomarker

activity was observed in patients across all three 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 SSIEM Annual Symposium will be available under the Presentations & Publications page in the Media section of REGENXBIO's website located at www.regenxbio.com.

About the CAMPSIITE™ Trial

CAMPSIITE is a multicenter, open-label trial enrolling boys with MPS II, aged 4 months up to five years of age. 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 2.9×10^{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), 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 "5x25" 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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