



REGENXBIO Presents Additional Positive Interim Data from Phase I/II Trial of RGX-121 for the Treatment of MPS II (Hunter Syndrome) at 18th Annual WORLDSymposium™ 2022

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- RGX-121, a one-time gene therapy for MPS II, continues to be well-tolerated with no drug-related SAEs across three dose levels
- Dose-dependent reductions in CSF biomarkers observed; Cohort 3 patients approach normal levels of D2S6 biomarker
- Measures of neurodevelopmental function from patients in Cohorts 1 and 2 demonstrate continued developmental skill acquisition up to two years after RGX-121 administration
- Evidence of systemic enzyme expression and biomarker activity continues to be observed
- Cohort 3 expansion using commercial-scale cGMP material is planned to start in 1H 2022

REGENXBIO Inc. (Nasdaq: RGNX) today announced additional positive interim data from Cohorts 1-3 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, are being presented at the 18th Annual *WORLDSymposium™*.

"We are pleased to share additional data from patients in Cohorts 1-3 of our RGX-121 Phase I/II trial," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. "The interim data demonstrate dose-dependent reductions in CSF biomarkers across cohorts, and we are encouraged by the neurodevelopmental trajectories in patients from Cohorts 1 and 2, now up to two years after administration of RGX-121. We look forward to providing additional updates in this trial."

"MPS II patients are in need of new treatment options that could address the neurological manifestations of the disease and help address the neurodevelopmental decline observed with currently available therapies," said Roberto Giugliani, M.D., Ph.D., Professor, Department of Genetics, UFRGS, Medical Genetics Service, HCPA, Porto Alegre, Brazil. "The data presented today continues to support the early positive signals seen in the emerging clinical profile of RGX-121 for the treatment of MPS II. I am encouraged by the biomarker activity and impact on neurodevelopmental improvements observed in this trial, and I look forward to additional updates."

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. The primary endpoint of the trial is to evaluate the safety of RGX-121. Secondary and exploratory endpoints include biomarkers of a iduronate-2-sulfatase (I2S) enzyme activity in the CSF, serum and urine, neurodevelopmental assessments, and caregiver reported outcomes.

RGX-121 is administered directly to the central nervous system (CNS). Patients were 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=3). REGENXBIO has expanded Cohort 3 to include patients who will be dosed using commercial-scale cGMP material, and plans to begin dosing these patients in the first half of 2022.

Data Summary and Safety Update

As of December 20, 2021, RGX-121 is reported to be well-tolerated across all cohorts with no drug-related serious adverse events (SAEs) in 13 patients dosed with RGX-121. Time of post-administration follow-up ranges from eight weeks to two years. Eight patients have completed the 48-week immunosuppression regimen per study protocol. Eight 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 Biomarker Data

Biomarker data from patients in all three 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 closely correlated with severe MPS II, 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. 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 and 24 post RGX-121 administration. At 8 weeks post RGX-121 administration, the median reduction in CSF HS from baseline was 29.5% in Cohort 1, 42.3% in Cohort 2, and 67.3% in Cohort 3. Cohorts 1 and 2 continued to demonstrate reductions in CSF HS at Week 24, with median reduction from baseline of 20.6% and 36.4%, respectively; one patient in Cohort 3 who had data at 24 weeks post-administration demonstrated a CSF HS reduction from baseline of 63.9%.

Similarly, dose-dependent reductions of CSF D2S6 were observed at last time point available following RGX-121 administration, with Cohort 3 patients approaching normal levels. The majority of patients in all three cohorts demonstrated reductions from baseline of D2S6 at the last time point available. The median reduction from baseline of D2S6 at Week 8 was 40.5% in Cohort 1, 50.9% in Cohort 2, and 80.5% in Cohort 3. Cohorts 1 and 2 continued to demonstrate reduction in D2S6 at Week 24, with median reduction from baseline of 33.0% and 61.8%, respectively; one patient in Cohort 3 who had data at 24 weeks post-administration demonstrated an 85.5% reduction from baseline of D2S6 at Week 24.

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

Neurodevelopmental Data

Improvements in neurodevelopmental function and Caregiver Reported Outcomes in Cohorts 1 and 2 demonstrated CNS activity up to two years after RGX-121 administration.

Eight patients had more than six months of follow up in neurodevelopmental assessments after RGX-121 administration, and data are reported for the BSID-III cognitive, expressive language and fine motor subtests. In the four patients who were above -2 standard deviations (SD) of the normative mean on the BSID-III cognitive subtest at baseline, three patients acquired skills and remained within two SD of the normative mean on the cognitive, expressive language, and fine motor subtests at the last time point available following RGX-121 administration; the fourth patient acquired expressive language skills. Of the four patients with baseline cognitive function below -2 SD from the normative mean, two patients demonstrated minimal skill acquisition in cognition, and one additional patient demonstrated minimal gains in expressive language following RGX-121 administration.

Patients also demonstrated improvements in Caregiver Reported Outcomes, including positive trends in toileting skills, reduction in maladaptive behaviors, and improved sleep breathing following RGX-121 administration.

Systemic Biomarker Data and Clinical Efficacy

Evidence of systemic enzyme expression and biomarker activity was observed in patients across all three cohorts. The majority of patients demonstrated increases in I2S protein concentration levels in plasma following administration of RGX-121.

Additionally, total urine GAG measures demonstrated evidence of a systemic effect of RGX-121, independent of ERT treatment. In all patients who continued to receive ERT, total urine GAG levels decreased at last time point available. One of two patients who was ERT-naïve demonstrated a notable decline in urine GAGs through the last time point available following RGX-121 administration. In the three patients who discontinued ERT approximately one year after administration of RGX-121, the total urine GAG levels following ERT withdrawal remained relatively consistent with total urine GAG levels prior to ERT withdrawal.

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

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 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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