REGENXBIO Announces Positive Interim Data and Update for Phase I/II Trial of RGX-121 for the Treatment of MPS II

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- Consistent reductions in CSF levels of heparan sulfate up to 2 years after administration, as well as continued developmental skill acquisition

- Initial data from Cohort 2 indicates evidence of systemic enzyme expression and biomarker activity

- Additional data from Cohorts 1 and 2 to be presented at WORLDSymposium in February 2021

- REGENXBIO expects to initiate dosing of patients in Cohort 3 at an increased dose in the first quarter of 2021

ROCKVILLE, Md., Dec. 9, 2020 /PRNewswire/ -- REGENXBIO Inc. (Nasdaq: RGNX), a leading clinical-stage biotechnology company seeking to improve lives through the curative potential of gene therapy based on its proprietary NAV® Technology Platform, today announced interim data from Cohorts 1 and 2 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). In addition, REGENXBIO announced plans to evaluate a higher dose of RGX-121 in a third cohort of patients at an increased dose of $2.0x10^{11}$ GC/g brain mass. REGENXBIO expects to begin enrolling patients in Cohort 3 in the first quarter of 2021.

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. RGX-121 is delivered directly to the central nervous system (CNS) via intracisternal administration.

"We are very pleased to see the encouraging safety profile of RGX-121, as well as additional evidence of long-term biomarker activity and neurocognitive development in patients with MPS II up to two years after RGX-121 administration. The consistent reduction in heparan sulfate in the CSF suggests that the gene therapy may potentially restore intracellular activity of the I2S enzyme, and improve neurocognitive development and outcomes for patients," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. "We are also encouraged by the I2S enzyme systemic expression observed at the second dose level. We look forward to presenting additional details from these first two cohorts at the WORLD*Symposium* in early 2021."

Dr. Pakola continued, "based on the data from Cohorts 1 and 2, we plan to initiate enrollment in a third cohort at a higher dose to further enhance our understanding of the potential treatment effects of RGX-121, including potential systemic benefit for patients. We are committed to advancing this novel gene therapy as quickly as possible to address the significant unmet medical need for patients with MPS II."

"Patients with MPS II often meet early development milestones, but delays in many areas of development become apparent at about 18 months of age. I am encouraged by the preliminary evidence of durable biomarker response in the CNS of patients dosed with RGX-121, as well as the rates of neurocognitive development seen in these patients. I'm eager to see additional data from the CNS and potential systemic effects of this gene therapy," said Paul Harmatz, MD, professor, Department of Pediatrics, UCSF Benioff Children's Hospital Oakland.

Data Summary and Safety Update

As of November 13, 2020, RGX-121 is reported to be well-tolerated with no drug-related serious adverse events (SAEs) in eight patients dosed with RGX-121 to date, including two additional patients who were dosed in the expanded Cohort 2 that was announced in September 2020.

The interim data announced today includes assessments for the first six patients in Cohorts 1 and 2. Three patients in Cohort 1 ($1.3x10^{10}$ genome copies per gram (GC/g) of brain mass) were dosed at the ages of 5 months (Patient 1), 35 months (Patient 2), and 7 months (Patient 3). Time of post-administration follow-up ranges from 13 months to two years. Three patients in Cohort 2 ($6.5x10^{10}$ GC/g of brain mass) were dosed at the ages of 59 months (Patient 4), 40 months (Patient 5), and 25 months (Patient 6). Time of post-administration follow-up ranges from four to nine months.

CSF Biomarker Data from Cohorts 1 and 2

Heparan sulfate (HS) is a key biomarker of I2S enzyme activity and is being measured in the cerebral spinal fluid (CSF) following administration of RGX-121. Consistent, long-term reductions in HS in the CSF were observed in patients in Cohort 1 up to 2 years following administration of RGX-121. Patient 1 demonstrated a 45.5% reduction from baseline to 2 years. Patients 2 and 3 demonstrated a reduction of 12.5% and 33.5%, respectively, from baseline to about one year.

Patients in Cohort 2 similarly demonstrated consistent reductions in HS in the CSF up to six months after administration of RGX-121. Patients 4 and 5 demonstrated reductions of HS in the CSF from baseline at six months of 16.8% and 52.6%, respectively. Patient 6 demonstrated a 38.0% reduction of HS levels in the CSF from baseline at four months.

Summary of Neurocognitive Development Data from Cohort 1

Patients in Cohort 1 have continued to acquire developmental skills up to two years after administration of RGX-121, based on the neurodevelopment parameters of cognitive, behavioral and adaptive function as measured by the Bayley[1] and Vineland[2] Scales. Neurocognitive and adaptive behavior scores for Patient 1 at two years and Patient 3 at fourteen months suggest continued developmental skill acquisition. Patient 2 was diagnosed with

developmental delay prior to dosing with RGX-121, but cognitive and adaptive behavior assessments at fourteen months show an increase in age equivalent scores, indicating continued skill acquisition.

Summary of Systemic Biomarker Data from Cohort 2

Interim data from two patients in Cohort 2 indicates changes in plasma and urine biomarkers that provide evidence of systemic I2S enzyme expression. Patient 6 who has never been treated with ERT had increased levels of I2S enzyme in plasma compared to baseline beginning two weeks after administration of RGX-121. The increased levels of I2S enzyme have been sustained out to four months, the latest timepoint available. Urinary glycosaminoglycans (GAG) levels were reduced to within normal range in this patient at four months. Patient 5 continues to receive weekly treatment with ERT, and at six months, had increased levels of I2S enzyme in plasma compared to baseline and a reduction of urinary GAG levels to within normal range.

New data from patients in Cohorts 1 and 2, including additional neurocognitive development data, will be presented at the 17th Annual WORLD*Symposium* ™, taking place February 8-12, 2021.

About RGX-121

RGX-121 is a product candidate for the treatment of Mucopolysaccharidosis Type II (MPS II), also known as Hunter syndrome. RGX-121 is designed to use the AAV9 vector to deliver the human iduronate-2-sulfatase (IDS) gene 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 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 (GAG), including heparan sulfate (HS) in tissues which ultimately results in cell, tissue, and organ dysfunction. 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 and prevent or stabilize cognitive decline 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," "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, 2019, 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. 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:

Tricia Truehart
Investor Relations and Corporate Communications
347-926-7709
ttruehart@regenxbio.com

Investors:
Eleanor Barisser, 212-600-1902
eleanor@argotpartners.com

Media:
David Rosen, 212-600-1902
david.rosen@argotpartners.com

[1] Bayley Scales of Infant and Toddler B, 3rd Edition (BSID-III)
[2] Vineland Adaptive Behavior Scale, 2nd Edition (VABS-II)

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