REGENXBIO Announces Interim Data from Phase I/II Trial of RGX-121 for the Treatment of Mucopolysaccharidosis Type II (MPS II)

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-- Well-tolerated in patients with MPS II following one-time intracisternal administration

-- Consistent and sustained reduction in CSF levels of heparan sulfate, a key biomarker of I2S enzyme activity in MPS II, up to 48 weeks after administration of RGX-121

-- Early signs of neurocognitive stability in patient with previously diagnosed developmental delay; continued normal cognitive development in a younger patient

-- First patient has been dosed in Cohort 2 and additional clinical sites now active in United States and Brazil

ROCKVILLE, Md., Dec. 18, 2019 /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 the first cohort of the ongoing Phase I/II trial of RGX-121 for the treatment of Mucopolysaccharidosis Type II (MPS II), also known as Hunter syndrome. RGX-121 is an investigational one-time gene therapy designed to deliver the gene that encodes the iduronate-2-sulfatase (I2S) enzyme direct to the central nervous system (CNS) using the AAV9 vector.

"Patients with MPS II continue to have significant difficulties despite the availability of systemic enzyme replacement therapy which doesn't address manifestations of the disease in the central nervous system such as impaired cognitive development. We are pleased with the emerging safety profile in the first patients dosed with RGX-121 via single intracisternal administration. We are also encouraged by the positive results from this cohort, including a meaningful and sustained reduction in heparan sulfate suggesting that the gene therapy can potentially restore intracellular activity of the I2S enzyme, as well as the early signs of neurocognitive stability that have been observed," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. "Based on the data from these patients, we have advanced the study into a second cohort of patients at an increased dose level, and look forward to expanding the RGX-121 clinical program in order to bring this novel therapy to patients as quickly as possible."

In Cohort 1 of the Phase I/II study, three patients were dosed intracisternally at the ages of 5 months (Patient 1), 35 months (Patient 2), and 7 months (Patient 3) with $1.3x10^{10}$ genome copies per gram (GC/g) of brain mass. Safety follow-up post-administration of RGX-121 ranges from 12 weeks to 68 weeks. As of December 16, 2019, RGX-121 is reported to be well-tolerated, with no drug-related serious adverse events (SAEs) reported. Two SAEs were reported and are not considered to be related to the gene therapy or the administration of RGX-121. Per protocol, patients received a 48 week immunosuppression regimen to minimize the potential for immune-mediated reactions and importantly, Patient 1 has completed the immunosuppression regimen.

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. In MPS II patients, high amounts of HS accumulate in the CNS, closely correlating with neurocognitive decline. In the CSF of all three patients enrolled in Cohort 1, HS levels demonstrated a mean reduction of 33.3% from baseline to Week 8. Patient 1 demonstrated consistent decreases in HS levels in the CSF over time, with a 27.4% reduction from baseline at Week 8 and a 43.6% reduction from baseline at Week 48, the latest timepoint available. Patient 2 also demonstrated a decrease of HS levels in the CSF, with a 30.9% reduction from baseline to Week 8, the latest timepoint available. Patient 3 demonstrated a decrease in HS levels in the CSF with a reduction of 41.6% from baseline to Week 8, the latest timepoint available.

In addition, for the two patients who have progressed beyond Week 24, preliminary data indicates stability of neurocognitive development. Patient 1 has continued to exhibit normal cognitive development as expected at Week 48, the time of last assessment. Patient 2 was diagnosed with a neurocognitive decline prior to dosing with RGX-121 and remains developmentally delayed, but preliminary assessments suggest stable neurocognitive development since dosing.

"It is encouraging to see a reduction in heparan sulfate in the CSF as it is a strong marker of the decline in neurocognitive development experienced by patients with MPS II, and closely correlates with the severity of the disease. The potential to provide therapeutic benefit directly to the CNS would be a meaningful advancement for the treatment of MPS II patients," commented Barbara Burton, M.D., Professor of Pediatrics at the Northwestern University Feinberg School of Medicine and pediatric geneticist at Ann & Robert H. Lurie Children's Hospital of Chicago.

Additional data will be presented at an upcoming medical conference in early 2020.

Following review of the safety and efficacy data from all three patients in Cohort 1, the Independent Data Monitoring Committee for the Phase I/II study of RGX-121 approved the continuation and dose escalation into Cohort 2. Subsequently, RGX-121 was administered to the first patient in Cohort 2 at a dose of $6.5x10^{10}$ GC/g of brain mass. Clinical sites are active and recruiting patients, including University of Pittsburgh School of Medicine, Children's Hospital of Philadelphia and UCSF Benioff Children's Hospital Oakland in the United States, and Hospital de Clínicas de Porto Alegre in Brazil.

"We are pleased that this program is continuing to advance as a potential CNS-specific treatment option for MPS II patients," said Terri Klein, President and Chief Executive Officer of the National MPS Society. "We appreciate REGENXBIO's dedication to the MPS community and look forward to additional development updates."

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 the Phase I/II Clinical Trial of RGX-121

RGX-121 is being evaluated in a Phase I/II, multi-center, open-label, multiple-cohort, dose-escalation study in patients with Mucopolysaccharidosis Type II (MPS II) in the United States and Brazil. The Phase I/II trial is designed to evaluate the safety of RGX-121 in up to 6 patients less than five years of age who have or are at high risk of developing neurocognitive effects. In addition, the study will evaluate the effect of RGX-121 on biomarkers of iduronate-2-sulfatase (I2S) enzyme activity as well as neurocognitive deficits and other clinical measures.

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, 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 Phase I/II trial of RGX-121 for the treatment of MPS II. 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, 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, 2018, 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:
Heather Savelle, 212-600-1902
heather@argotpartners.com

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

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