REGENXBIO Reports Update on Advancement of Programs for CLN2 Disease

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- *RGX-181 and RGX-381 are potential one-time AAV Therapeutics for the treatment of the CNS and ocular manifestations of CLN2 disease, the most common form of Batten disease*
- *Patient dosed under a single-patient investigator-initiated study of RGX-181*
- *Company announces approval of CTA for RGX-381 from the UK Health Authority and plans to initiate a Phase I/II clinical trial in the first half of 2023*

ROCKVILLE, Md., Dec. 21, 2022 /PRNewswire/ -- REGENXBIO Inc. (Nasdaq: RGNX) today announced a comprehensive program update to outline its progress and development plans for RGX-181 and RGX-381, both being developed as potential one-time gene therapies for the treatment of different manifestations in late-infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease, the most common form of Batten disease.

REGENXBIO announced today that physician investigators at the Hospital de Clinicas in Porto Alegre, Brazil have dosed the first child with CLN2 disease with RGX-181 in a single-patient, investigator-initiated study. As of December 20, 2022, RGX-181 is reported to be well-tolerated in this patient with no drug-related SAEs. Hospital de Clinicas is also part of ongoing clinical trials of RGX-111 for the treatment of MPS I and RGX-121 for the treatment of MPS II.

RGX-181 is an investigational one-time AAV Therapeutic designed to use the NAV AAV9 vector to deliver the *TPP1* gene directly to the central nervous system (CNS), which could induce sustained levels of TPP1 to treat the neurodegenerative manifestations of CLN2 disease such as progressive loss of language, intellectual abilities, and motor skills.

"We are pleased to have the opportunity to participate in the first-in-human study of RGX-181 for patients with CLN2," said Roberto Giugliani MD, PhD, Hospital de Clinicas. "Patients with this devastating disease need new treatment options with the potential for longer lasting effects on the CNS, and we hope that this gene therapy benefits this patient community," added Carolina Fischinger, MD, PhD, primary investigator of the single-patient study.

REGENXBIO also announced today that a clinical trial application (CTA) has been accepted by the UK Health Authority to support a first-in-human, open-label, dose-escalation Phase I/II clinical trial to evaluate the safety and tolerability, as well as the effect on retinal anatomic and functional outcomes, of the subretinal delivery of RGX-381 for the treatment of ocular manifestations of CLN2 disease. The trial will be conducted at Great Ormond Street Hospital in London and the Company expects to initiate the Phase I/II clinical trial in the first half of 2023.

RGX-381 is an investigational one-time AAV Therapeutic targeting the ocular manifestations of CLN2 disease. RGX-381 is designed to use the NAV AAV9 vector to deliver the *TPP1* gene directly to the retina, which could provide a durable source of TPP1 activity in the retina, thereby potentially preventing visual decline.

"REGENXBIO continues to make excellent progress advancing our AAV Therapeutics pipeline, and we are pleased to share the advancement of two more programs that may support our '5x'25' strategy to have five AAV Therapeutics either on the market or in late-stage development by 2025," said Steve Pakola, M.D., Chief Medical Officer of REGENXBIO. "With strong preclinical data highlighting the ability of both RGX-181 and RGX-381 to support widespread distribution and expression of the TPP1 enzyme that is lacking in patients with CLN2 disease, we believe that these programs have the potential to provide much-needed new treatment options for children with this devastating disease."

RGX-181 and RGX-381 have received Orphan Drug and Rare Pediatric Disease Designations from the U.S. Food and Drug Administration, as well as ATMP classification from the European Medicines Agency.

About RGX-181

RGX-181 is being developed as a novel, one-time treatment for CLN2 disease utilizing the NAV AAV9 vector to deliver the gene encoding for TPP1, the enzyme deficient in children with CLN2 disease. Following administration of a single intracisternal injection, RGX-181 treatment is designed to provide a durable source of TPP1 potentially leading to long-term correction of cells throughout the CNS. In an animal model for CLN2 disease, treatment with RGX-181 has been shown to restore TPP1 activity to levels greater than those in non-affected animals, and to improve neurobehavioral function and survival. The extent of CNS correction observed suggests that RGX-181 has the potential to be an important and suitable one-time therapeutic option for patients with CLN2 disease.

About RGX-381

RGX-381 is being developed as a novel, one-time treatment targeting the ocular manifestations of CLN2 disease utilizing the NAV AAV9 vector to deliver the *TPP1* gene directly to the retina. We believe that one-time subretinal administration of RGX-381 could provide a durable source of TPP1 activity in the retina, thereby potentially preventing visual decline. Vision loss in children with CLN2 disease progresses to blindness, despite treatment with enzyme replacement therapy. There is currently no available treatment for the ocular manifestations of CLN2 disease.

About CLN2 Disease

Late-infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease, a form of Batten disease, is a rare, pediatric-onset, autosomal recessive,

neurodegenerative lysosomal storage disorder caused by mutations in the *TPP1* gene. Deficiency in TPP1 enzymatic activity results in lysosomal accumulation of storage material and degeneration of nerve cells, particularly in the brain and retina. CLN2 disease is characterized by seizures, rapid deterioration of language and motor functions, cognitive decline, rapid loss of vision and blindness, and premature death by mid-childhood. Onset of symptoms is generally between two to four years of age with initial features of recurrent seizures (epilepsy), language delay, and difficulty coordinating movements (ataxia). There is currently no cure for CLN2 disease. Current treatment options include CNS enzyme replacement therapy, wherein recombinant TPP1 is administered into the lateral ventricles via a permanently implanted device on a biweekly basis, and palliative care. There are currently no approved treatments to treat ocular manifestations of CLN2 disease.

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.

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