REGENXBIO Announces FDA Clearance of IND for Clinical Trial of RGX-202, a Novel Gene Therapy Candidate for Duchenne Muscular Dystrophy

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- *Potential one-time gene therapy for the treatment of Duchenne includes a novel, optimized microdystrophin transgene and REGENXBIO's proprietary NAV® AAV8 vector*
- *Innovative trial design, including comprehensive immunosuppressive regimen, to evaluate safety and optimal dose*
- *cGMP process material made at commercial-scale to be used throughout clinical development of RGX-202*
- *REGENXBIO expects to initiate trial in the first half of 2022*

REGENXBIO Inc. (Nasdaq: RGNX) today announced the clearance of its Investigational New Drug (IND) application by the United States Food and Drug Administration (FDA) to evaluate RGX-202, a potential one-time gene therapy for the treatment of Duchenne muscular dystrophy (Duchenne) in a first-in-human clinical trial. RGX-202 is designed to deliver a transgene for a novel microdystrophin that includes the functional elements of the C-Terminal (CT) domain found in naturally occurring dystrophin. RGX-202 uses REGENXBIO's proprietary NAV® AAV8 vector. REGENXBIO plans to initiate the trial in the first half of 2022.

"We are excited to advance RGX-202, our investigational gene therapy for patients with Duchenne, into the clinic. Additional therapeutic options are still needed for the treatment of Duchenne, and our trial design follows compelling evidence from preclinical studies which demonstrated that one-time treatment with RGX-202 can express meaningful levels of a novel, functional microdystrophin protein in muscle, and showed significant improvements in muscle force and function in animal models," said Olivier Danos, Ph.D., Chief Scientific Officer of REGENXBIO. "This innovative AAV gene therapy candidate for Duchenne was developed in-house at REGENXBIO through a highly collaborative process between our expert research and manufacturing teams and we believe that RGX-202 can potentially address unmet needs for patients with Duchenne."

AFFINITY DUCHENNE™ Trial Design
The Phase I/II trial, named AFFINITY DUCHENNE, is a multicenter, open-label dose escalation and dose expansion clinical study to evaluate the safety, tolerability and clinical efficacy of a one-time intravenous (IV) dose of RGX-202 in patients with Duchenne. In the dose escalation phase of the trial, six ambulatory, pediatric patients (ages 4 to 11 years old) with Duchenne are expected to enroll in two cohorts with doses of $1x10^{14}$ genome copies (GC)/kg body weight (n=3) and $2x10^{14}$ GC/kg body weight (n=3). After an independent safety data review for each cohort, a dose expansion phase of the trial may allow for up to six additional patients to be enrolled at each dose level (for a total of up to nine patients in each dose cohort).

The trial design also consists of thorough safety measures informed by the Duchenne community and engagement with key opinion leaders, including a comprehensive, short-term, prophylactic immunosuppression regimen to proactively mitigate potential complement-mediated immunologic responses, and inclusion criteria based on dystrophin gene mutation status, including *DMD* gene mutations between exons 18 and 58. Trial endpoints include safety, immunogenicity assessments, pharmacodynamic and pharmacokinetic measures of RGX-202, including microdystrophin protein levels in muscle, and strength and functional assessments, including the North Star Ambulatory Assessment (NSAA) and timed function tests. Initial trial sites are expected to open in the U.S., with additional sites in Canada and Europe expected to follow.

"I am proud of our scientific and medical teams' work with the Duchenne community resulting in a thoughtful and innovative clinical trial design, which we believe addresses a number of important factors, including safety considerations," said Kenneth T. Mills, President and Chief Executive Officer of REGENXBIO. "This trial will use material derived from our proprietary commercial-scale process which is expected to enable consistent clinical supply and support efficient transition to later stage development. We are working quickly to start dosing patients in this trial and look forward to continuing our important work with stakeholders across the Duchenne community."

In support of the IND application, RGX-202 cGMP-grade material has been produced at commercial-scale capacity (1,000L) using REGENXBIO's proprietary suspension cell culture manufacturing process. REGENXBIO's internal cGMP facility is designed to enable production in 2,000L bioreactors and is on track to be fully operational in the first half of 2022. REGENXBIO plans to manufacture RGX-202 at the new facility.

About RGX-202
RGX-202 is designed to deliver a transgene for a novel microdystrophin that includes the functional elements of the C-Terminal (CT) domain found in naturally occurring dystrophin. Presence of the CT domain has been shown in preclinical studies to recruit several key proteins to the muscle cell membrane, leading to improved muscle resistance to contraction-induced muscle damage in dystrophic mice. Additional design features, including codon optimization and reduction of CpG content, may potentially improve gene expression, increase translational efficiency and reduce immunogenicity. RGX-202 is designed to support the delivery and targeted expression of genes throughout skeletal and heart muscle using the NAV AAV8 vector, a vector used in numerous clinical trials, and a well-characterized muscle-specific promoter (Spc5-12).

About Duchenne Muscular Dystrophy
Duchenne muscular dystrophy (Duchenne) is a rare genetic disorder, caused by mutations in the gene responsible for making dystrophin, a protein of central importance for muscle cell structure and function. Duchenne primarily affects males with approximately 1 in 3,500 to 1 in 5,000 males affected

worldwide. The absence of functional dystrophin protein in individuals with Duchenne results in cell damage during muscle contraction, leading to cell death, inflammation, and fibrosis in muscle tissues. Initial symptoms of Duchenne include muscle weakness that is often noticeable at an early age, with diagnosis typically occurring by 5 years of age. Over time, individuals with Duchenne experience progressive muscle weakness and eventually lose the ability to walk. Respiratory and heart muscles are also affected, leading to difficulty breathing and the need for ventilator assistance, along with the development of cardiomyopathy. There is presently no cure for Duchenne.

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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