REGENXBIO Announces Expansion of AFFINITY DUCHENNE® Trial to Include a New Cohort of Younger Patients

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- *Company to begin enrollment of patients aged 1-3 years*
  - *Expects data from younger cohort to be part of pivotal plans and BLA filing for broad label*
- *End-of-Phase II meeting with FDA scheduled for late July to finalize pivotal program design*
  - *Based on recent commercial landscape, confirmed accelerated approval pathway remains available given ongoing unmet need and RGX-202 differentiated design*
- *Remains on track to initiate pivotal trial in late Q3 to early Q4 2024*
  - *The next potential therapy to become available for Duchenne patients*

ROCKVILLE, Md., June 24, 2024 /PRNewswire/ -- REGENXBIO Inc. (Nasdaq: RGNX) today announced it initiated enrollment in a new cohort of patients ages 1-3 in its Phase I/II AFFINITY DUCHENNE® trial to evaluate the safety and efficacy of RGX-202 in boys with Duchenne muscular dystrophy (Duchenne).

RGX-202 is an investigational one-time AAV Therapeutic targeted to deliver a novel microdystrophin, representing the next wave of innovative design in Duchenne gene therapy. RGX-202 is the only gene therapy approved or in development for Duchenne that incorporates the C-Terminal domain, making the RGX-202 transgene the closest to the naturally occurring dystrophin gene.

With this announcement, REGENXBIO is enrolling ambulatory boys with Duchenne aged 1 to 11 in the AFFINITY DUCHENNE trial. The new cohort is expected to enroll up to five patients aged 1-3 to receive RGX-202 at the pivotal dose level ($2x10^{14}$ genome copies (GC)/kg body weight).

Additionally, REGENXBIO has confirmed an end-of-Phase II (EOP2) meeting is scheduled with the FDA at the end of July. This meeting is expected to finalize the AFFINITY DUCHENNE pivotal trial design, with the goal of continuing to expedite the development of RGX-202. The Company anticipates that all patients enrolled at dose level 2 (n=12) will be included in its pivotal trial data set. The Company plans to use RGX-202 microdystrophin expression as a surrogate endpoint to support a Biologics License Application (BLA) submission using the accelerated approval pathway with the potential to receive a broad label. REGENXBIO has recently confirmed with the FDA that the pathway can be used given the ongoing high unmet need for differentiated treatment options in the Duchenne community. RGX-202 is the most advanced gene therapy enrolling in active clinical trials and is anticipated to be the next gene therapy in a BLA filing for Duchenne.

"We believe RGX-202 has unique, differentiating features that support its potential to be a best-in-class product and we are pleased to expand its clinical development to reach a wider range of boys with Duchenne in need of treatment options," said Curran Simpson, Chief Operating Officer of REGENXBIO and President and CEO-elect. "Supported by the strong safety profile and positive microdystrophin data demonstrated in the AFFINITY DUCHENNE trial, today's news marks significant steps in rapidly accelerating RGX-202 towards pivotal stage and future commercialization."

"The Duchenne community remains in need of differentiated treatment options, and I'm pleased to see the expansion of the AFFINITY DUCHENNE trial to evaluate RGX-202 in younger patients," said Vamshi K. Rao, M.D., Lurie Children's Hospital, Associate Professor of Pediatrics, Northwestern University Feinberg School of Medicine and trial investigator. "With the wider adoption of newborn screening, there is now an increased opportunity to treat patients earlier, with the hope of impacting disease and preserving muscle."

Clinical Program Updates
The Company continues to rapidly enroll the remaining patients in the ages 4-11 cohort (dose level 2 expansion cohort) and expects to imminently complete the enrollment of up to seven patients at dose level 2 early third quarter of 2024.

REGENXBIO expects to share initial strength and functional assessment data for both dose levels of the AFFINITY DUCHENNE trial in the second half of 2024. Initiation of the pivotal trial is on track for late third quarter to early fourth quarter of 2024.

RGX-202 in the AFFINITY DUCHENNE trial is manufactured using REGENXBIO's proprietary, high-yielding NAVXpress™ platform process. This suspension-based manufacturing process has demonstrated robust scalability with consistent yield and product purity and is ready for product commercialization.

As of May 3, 2024, RGX-202 has been well tolerated with no drug-related serious adverse events in five patients, aged 4.4 to 12.1. All five patients who completed three-month trial assessments indicate encouraging increases in expression of RGX-202 microdystrophin and reduction from baseline in serum CK levels, supporting evidence of clinical improvement.

AFFINITY DUCHENNE Trial Design
The Phase I/II AFFINITY DUCHENNE trial 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 aged 1-11.

The trial design was 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 in exons 18 and above. 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.

About RGX-202
RGX-202 has differentiated and important biology most similar to naturally occurring dystrophin that protects from the muscle degradation associated with Duchenne. RGX-202 is designed with advanced science 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 is a severe, progressive, degenerative muscle disease, affecting 1 in 3,500 to 5,000 boys born each year worldwide. Duchenne is caused by mutations in the Duchenne gene which encodes for dystrophin, a protein involved in muscle cell structure and signaling pathways. Without dystrophin, muscles throughout the body degenerate and become weak, eventually leading to loss of movement and independence, required support for breathing, cardiomyopathy and premature death.

ABOUT REGENXBIO Inc.
REGENXBIO is a leading clinical-stage biotechnology company seeking to improve lives through the curative potential of gene therapy. Since its founding in 2009, REGENXBIO has pioneered the development of AAV Therapeutics, an innovative class of gene therapy medicines. REGENXBIO is advancing a pipeline of AAV Therapeutics for retinal and rare diseases, including ABBV-RGX-314 for the treatment of wet AMD and diabetic retinopathy, being developed in collaboration with AbbVie, RGX-202 for the treatment of Duchenne and RGX-121 for the treatment of MPS II. Thousands of patients have been treated with REGENXBIO's AAV Therapeutic platform, including Novartis' ZOLGENSMA for children with spinal muscular atrophy. Designed to be one-time treatments, AAV Therapeutics have the potential to change the way healthcare is delivered for millions of people. For more information, please visit www.regenxbio.com.

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, clinical trials, regulatory plans, costs and cash flow. 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, 2023, 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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