REGENXBIO Announces Completion of Enrollment in Cohort 2 and Additional Positive Interim Data in AFFINITY DUCHENNE® Trial

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- *Completed enrollment in cohort 2 of the Phase I/II AFFINITY DUCHENNE® trial of RGX-202, a potential one-time AAV Therapeutic for the treatment of Duchenne that includes an optimized transgene for a novel microdystrophin*
- *New three-month assessment in third patient at dose level 1 demonstrates largest increase in microdystrophin expression*
    - *Patient aged 6.6 years old had expression level at 83.4% of control*
- *On track to initiate pivotal trial in second half of 2024*
- *Company plans to discuss these new results as part of a full rare disease program update on its conference call today, Wednesday, February 7, 4:30 p.m. ET*

ROCKVILLE, Md., Feb. 7, 2024 /PRNewswire/ -- REGENXBIO Inc. (Nasdaq: RGNX) today announced that enrollment has completed at dose level 2 and reported additional interim safety and efficacy in the Phase I/II AFFINITY DUCHENNE® trial of RGX-202 in patients with Duchenne muscular dystrophy (Duchenne) ages 4 to11 years old.

"We are thrilled to see that RGX-202 is demonstrating strong microdystrophin expression across a wide range of patients," said Kenneth T. Mills, President and CEO, REGENXBIO. "RGX-202 microdystrophin is differentiated with important biology most similar to naturally occurring dystrophin that protects from the muscle degradation associated with Duchenne. All boys with Duchenne are in need of new treatment options that can meaningfully impact disease, and we are working with great urgency to accelerate RGX-202 as an option for them."

Safety Update
As of February 6, 2024, RGX-202 has been well tolerated with no drug-related serious adverse events in five patients, aged 4.4 to 12.1 at dose level 1 ($1x10^{14}$ genome copies (GC)/kg body weight) and dose level 2 ($2x10^{14}$ GC/kg body weight). Time of post-administration follow up ranges from approximately three weeks to over nine months. All patients who reached three-month follow-up have completed the immunosuppression regimen per study protocol.

Biomarker Data
In new data from the third patient, aged 6.6 years, who received RGX-202 at dose level 1, RGX-202 microdystrophin expression was measured to be 83.4% compared to control at three months. A reduction from baseline in serum creatinine kinase (CK) levels of 93% was observed at ten weeks.

All three patients, at dose level 1, 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.

RGX-202 microdystrophin levels were measured using an automated and precise western blot method (Jess), and comparable results were confirmed with a proprietary liquid chromatography-mass spectrometry (LC-MS) method. Elevated CK levels are associated with muscle injury and are uniformly elevated in patients with Duchenne. The mean (SD) RGX-202 microdsytrophin expression levels (change from baseline) at three months following RGX-202 administration were 44.4% (n=3, SD:36.5%). The patient data is presented below.

Patient	Age at Dosing (years)	Weight at Dosing (kg)	Western blot (Jess method), RGX-202 Microdystrophin (% Normal Control)	CK Levels, week 10 (% reduction from baseline)
1	4.4	17.8	38.8	-43
2	10.5	28.3	11.1	-44
3	6.6	26.8	83.4	-93

Clinical Program Updates
REGENXIO expects to make a pivotal dose determination in mid-2024. The Company also expects to share initial strength and functional assessment data for both dose levels and the initiation of a pivotal trial in the second half of 2024. The Company plans to use RGX-202 microdystrophin expression as a surrogate endpoint to support a Biologics License Application (BLA) filing using the accelerated approval pathway.

"On our call this afternoon, we look forward to discussing these new clinical results and also reaffirming our guidance for the submission of a BLA this year for RGX-121 for the treatment of MPS II. The exciting topline pivotal data supporting this submission will be released later this morning in conjunction with a presentation at the 20th Annual WORLD*Symposium* ™," said Mills.

Conference Call Details
REGENXBIO will host a conference call Wednesday, February 7 at 4:30 p.m. ET. Listeners can register for the webcast via this link. Analysts wishing

to participate in the question and answer session should use this link. A copy of the slides being presented will be available via the Company's investor website. Those who plan on participating are advised to join 15 minutes prior to the start time. A replay of the webcast will also be available via the Company's investor website approximately two hours after the call's conclusion.

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. In the dose evaluation phase of the trial, four ambulatory, pediatric patients (ages 4 to 11 years old) are expected to enroll in two cohorts with doses of $1x10^{14}$ GC/kg body weight (n=2) and $2x10^{14}$ GC/kg body weight (n=2). After an independent safety data review for each cohort, a dose expansion phase of the trial may allow for additional patients to be enrolled.

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 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 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. 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 and AAV9. 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, clinical trials, 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, 2022, 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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