REGENXBIO INITIATES PIVOTAL PHASE OF AFFINITY DUCHENNE® TRIAL OF RGX-202 GENE THERAPY AND REPORTS POSITIVE FUNCTIONAL DATA

November 18, 2024 08:05 AM EST

- *Alignment achieved with FDA on AFFINITY DUCHENNE® pivotal program and access to accelerated approval; BLA expected in 2026*
- *Pivotal trial of RGX-202 is enrolling ambulatory patients aged 1 and above with first patient dosed*
- *Phase I/II data show RGX-202 recipients exceeding external natural history and established benchmarks for clinical outcomes*
  - *Functional improvements seen in all patients treated with dose level 1 and dose level 2 at 12 and 9 months respectively*
  - *New biomarker data confirms consistent robust expression of differentiated RGX-202 microdystrophin in the muscle*
  - *Favorable safety profile observed at both dose levels; no serious adverse events or AEs of special interest*
- *Webcast to be held at 8:00 a.m. today*

ROCKVILLE, Md., Nov. 18, 2024 /PRNewswire/ -- REGENXBIO Inc. (Nasdaq: RGNX) today announced that AFFINITY DUCHENNE®, the multi-center, open-label trial of RGX-202, a potential best-in-class gene therapy for Duchenne muscular dystrophy (Duchenne), has advanced to pivotal stage and dosed its first patient. The company also announced new, positive efficacy and safety data from the Phase I/II portion of the study, including the first functional data.

"The initiation of our pivotal trial and newly released positive functional data are exciting milestones on our path to rapidly deliver RGX-202, the only next generation gene therapy in pivotal phase, to the Duchenne community," said Curran M. Simpson President and Chief Executive Officer of REGENXBIO. "The totality of our data demonstrates that RGX-202 provides evidence of improving outcomes for boys with Duchenne and altering the trajectory of this devastating disease, with consistent, robust expression of our novel microdystrophin translating into significant clinical benefit. Based on the strength of the Phase I/II data and our positive discussions and alignment with the FDA, we are quickly advancing RGX-202 toward a BLA filing in 2026 using the accelerated approval pathway. We continue to evaluate opportunities to expand the RGX-202 program to benefit Duchenne patients worldwide."

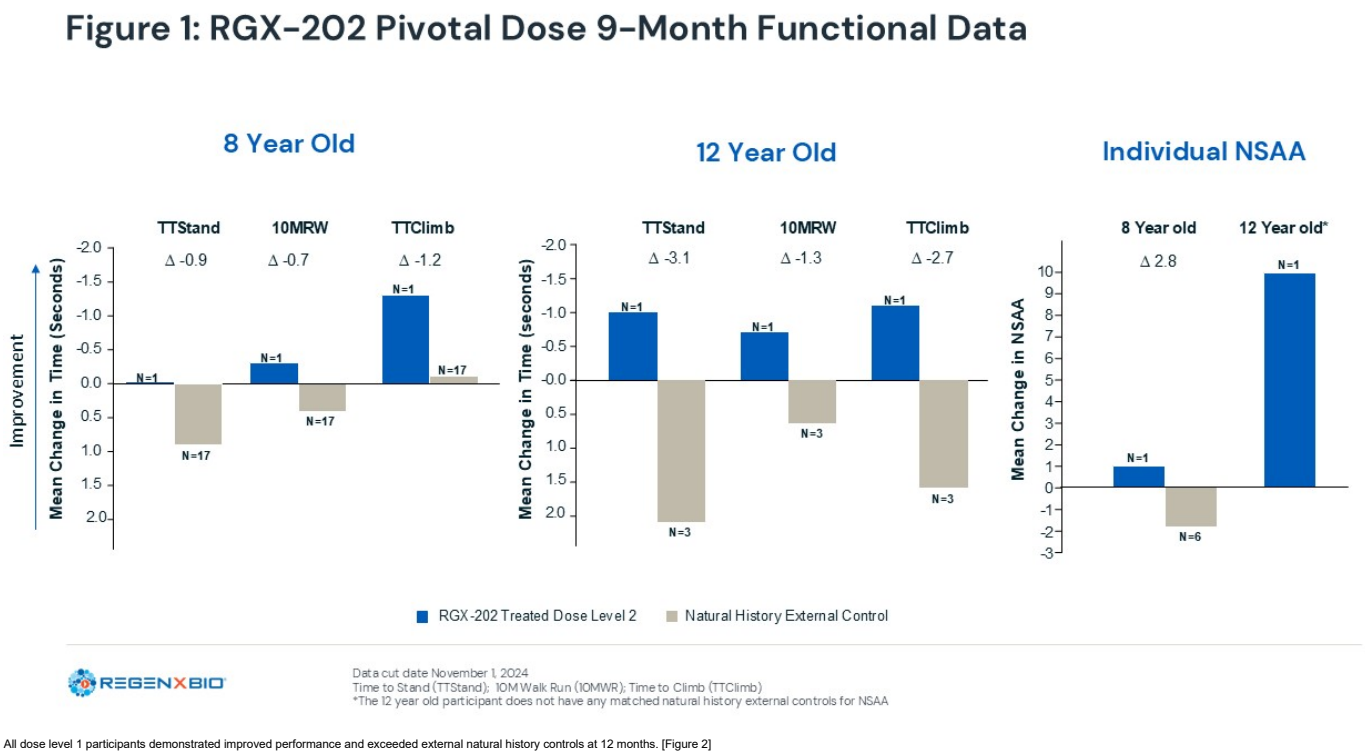
"There remains a critical need for new therapeutic options for patients with Duchenne muscular dystrophy", said Aravindhan Veerapandiyan M.D., Arkansas Children's Hospital. "I am very pleased to see the advancement of the RGX-202 program to the pivotal stage, which offers promise for a broader patient population and am highly encouraged by the functional data presented today demonstrating RGX-202's potential to alter the course of the disease. The safety, functional, and biomarker data shared today reinforce the positive feedback from families, highlighting improvements in patients' daily activities and underscoring the potential benefits of this treatment."

AFFINITY DUCHENNE Data Updates

Functional Data
Today, REGENXBIO announced positive functional results from the first five participants in the Phase I/II portion of the ongoing AFFINITY DUCHENNE trial. Results include 12-month data from three dose level 1 patients aged 4-10 and nine-month data from two dose level 2 (pivotal dose) patients aged 8 and 12.

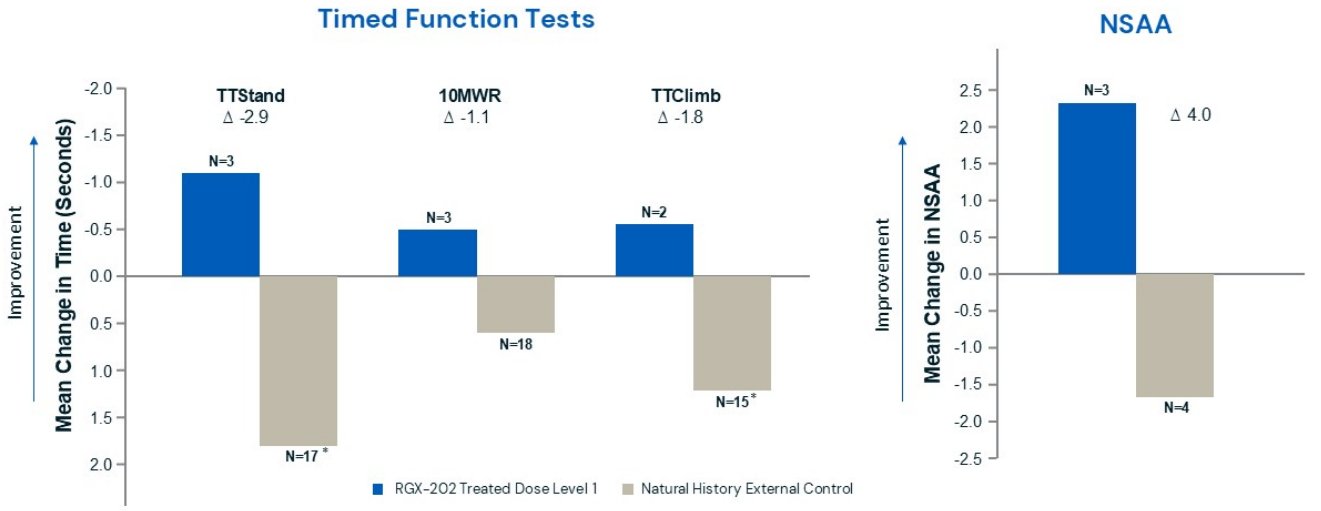
In all five participants, across both dose levels, RGX-202 demonstrates evidence of positively impacting disease trajectory, with patients demonstrating stable or improved function on the North Star Ambulatory Assessment (NSAA) and timed function tests. Results were measured against external natural history controls matched for age and baseline function.

Pivotal Dose Functional Data
Pivotal dose participants demonstrated improved performance on NSAA and timed function tests at nine months, exceeding external natural history controls. The NSAA mean score at this dose improved by 5.5 points. [Figure 1]



All dose level 1 participants demonstrated improved performance and exceeded external natural history controls at 12 months. [Figure 2]

Figure 2: RGX-202 Dose Level One 12-Month Functional Data



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Data cut date November 1, 2024
Time to Stand (TTStand); 10M Walk Run (10MWR); Time to Climb (TTClimb)
*One NH EC patient did not have a TTStand and one RGX-202 patient did not have TTClimb so associated NH EC also removed

Additionally, dose level 1 participants' timed task velocity changes exceeded minimal clinically important difference (MCID) benchmarks at 12 months, a measure referenced by the FDA in the approval of the available gene therapy.

Biomarker Data
REGENXBIO also announced new biomarker data that continues to support consistent, high expression and transduction of RGX-202 microdystrophin. RGX-202 was appropriately localized to the sarcolemma, demonstrating the differentiated construct with the CT-Domain is appropriately targeting the muscle.

RGX-202 microdystrophin expression results in ambulatory patients aged 8+ are the highest reported microdystrophin levels across approved or investigational gene therapies.

Mean at 12 Weeks (min,max)	**Dose Level 1 $1x10^{14}$ GC/kg**		**Dose Level 2 $2x10^{14}$ GC/kg**	
Age range (number with data)	**4-7** (2)	**8-11** (1)	**4-7** (1)	**8-11** (5)
RGX-202 Microdystrophin % normal control (Western Blot)	**60.6** (37.8, 83.4)	**10.4** (n/a)	**77.2** (n/a)	**39.7** (20.8, 75.7)
VCN copies/nucleus (qPCR)	**9.8** (7.4,12.1)	**5.4** (n/a)	**55.4** (n/a)	**17.8** (12.0,30.7)
Positive Fibers % (Immunofluorescence)	**79.3** (n/a)	**34.6** (n/a)	**71.1** (n/a)	**45.7** (21.3,70.6)

Safety and Tolerability Data
As of November 1, 2024, RGX-202 was well tolerated with no serious adverse events (SAEs) and no AEs of special interest (AESIs). Common drug-related AEs included nausea, vomiting and fatigue. All resolved and are typically anticipated with gene therapy administration.

RGX-202 Treatment Emergent Adverse Events		**Dose Level 1 Dose Evaluation ($1x10^{14}$ GC/kg)**	**Dose Level 2 Dose Evaluation / Expansion ($2x10^{14}$ GC/kg)**	**Dose Level 2 Younger Boys ($2x10^{14}$ GC/kg)**	**Total n=11**
Age Range (number dosed)		**4-11** (n=3)	**4-11** (n=7)	**1-3** (n=1)	**All Ages**
SAE		0	0	0	0
AESI	Central or peripheral neurotoxicity	0	0	0	0
	Drug-induced liver injury	0	0	0	0
	Thrombocytopenia	0	0	0	0
Myocarditis		0	0	0	0
Myositis		0	0	0	0

Pivotal Study
The Phase I/II AFFINITY DUCHENNE trial has been expanded into a multicenter, open-label pivotal Phase I/II/III trial of RGX-202. The pivotal trial is expected to support a Biologics License Application (BLA) submission using the accelerated approval pathway in 2026.

Based on a positive End of Phase 2 meeting with the FDA, the pivotal trial will evaluate the efficacy of RGX-202 at dose level 2 (2×10^{14} GC/kg) in approximately 30 ambulatory patients aged 1 and older. Patients under 4 years old have no access to gene therapy, and REGENXBIO is the only gene therapy sponsor recruiting patients in this age group in the U.S.

To support accelerated approval, the primary endpoint is the proportion of participants whose RGX-202 microdystrophin expression is ≥10% at Week 12, and secondary endpoints include change from baseline on timed function tests including TTStand, 10MWR and TTClimb in participants ages 4 and older. Participants aged 1 to < 4 years will be evaluated using the Peabody Developmental Motor Scale-Third Edition (PDMS-3) and SV95C. Patients will be assessed on the NSAA as an exploratory endpoint.

Webcast Details
REGENXBIO will host a webcast featuring Dr. Veerapandiyan, and Michael Kelly, PhD, Chief Scientific Officer of CureDuchenne, to discuss today's developments at 8:00 a.m. EST.

The live webcast can be accessed here and in the Investors section of REGENXBIO's website at www.regenxbio.com. An archived replay of the webcast will be available for approximately 30 days following the presentation.

About RGX-202
RGX-202 is a potential best-in-class investigational gene therapy designed for improved function and outcomes in Duchenne. RGX-202 is the only gene therapy approved or in late-stage development for Duchenne with a differentiated microdystrophin construct that encodes key regions of naturally occurring dystrophin, including the C-Terminal (CT) domain. In preclinical studies, the CT domain has been shown to protect the muscle from contraction-induced stress and improve its ability to repair itself.

Additional design features, including codon optimization and reduction of CpG content, may potentially improve gene expression, increase protein translation 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 and a well-characterized muscle-specific promoter (Spc5-12). RGX-202 is manufactured using REGENXBIO's proprietary, high-yielding NAVXpress™ suspension-based platform process.

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 rare and retinal diseases, including RGX-202 for the treatment of Duchenne, RGX-121 for the treatment of MPS II, and ABBV-RGX-314 for the treatment of wet AMD and diabetic retinopathy, being developed in collaboration with AbbVie. 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, and regulatory plans. 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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