RGX-202, an Investigational Gene Therapy for the Treatment of Duchenne Muscular Dystrophy: Interim Clinical Data

Stephen Pakola, M.D.
Chief Medical Officer
REGENXBIO

WMS2025 VIENNA
The 30th Annual Congress of the World Muscle Society
7th-11th October 2025, Vienna

Disclosure

- I have the following conflict/s of interest to declare:
  - Employee of REGENXBIO and owns stock/other equity

AFFINITY DUCHENNE® Phase I/II Trial Design

Dose escalation and expansion

Key Eligibility Criteria

- ✓ **Boys aged 1 to <12yo** at screening
- ✓ **Genetically confirmed DMD** (mutations in exons 18 and above)
- ✓ **No pre-existing antibodies** to the gene therapy (AAV8 capsid)

1 to <4yo

- 10-meter walk without assistance
- Stable dose on or off corticosteroids x 12 weeks
- Weight >10kg

4+ yo

- 100-meter walk without assistance
- Stable dose of corticosteroids x 12 weeks

Proactive Immune Modulation Regimen

- Designed for consistent, improved safety outcomes
- Tapered eculizumab (C5 inhibitor), sirolimus, prednisone based on weight, concluded by 3 months post-dosing
- Potential to reduce reactive safety intervention

Phase I/II Trial Endpoints

- **Primary Endpoint:** Safety
- **Biomarker Endpoint:** Microdystrophin expression
- **Secondary Endpoints:** Muscle function (including TTStand, 10 MRW, TTClimb, NSAA for 4+ yo; PDMS-3 for 1 to <4yo)

TTStand: Time to Stand; 10MWR: 10M Walk Run; TTClimb: Time to Climb
NSAA: North Star Ambulatory Assessment
PDMS-3: Peabody Developmental Motor Scale, Third Edition

RGX-202: AFFINITY DUCHENNE New Phase I/II Interim Functional Data, June 2025

Phase I/II Interim Safety

RGX-202 Treatment-Emergent Adverse Events		Dose Level 1 ($1x10^{14}$ GC/kg)	Dose Level 2 (Pivotal Dose) ($2x10^{14}$ GC/kg)		Total n = 13
Age Range (number dosed)		**4–11** Dose Evaluation (n = 3)	**1–3** Younger Boys (n = 3)	**4–11** Dose Evaluation/Expansion (n = 7)	**All Age Ranges**
SAE		0	0	0	0
AESI	Central Or Peripheral Neurotoxicity	0	0	0	0
	Drug-Induced Liver Injury[1]	0	0	0	0
	Thrombocytopenia[2]	0	0	0	0
Myocarditis[2]		0	0	0	0
Myositis[2]		0	0	0	0
The most common drug-related AEs reported are: nausea (n=3), vomiting (n=7), and fatigue (n=5)					

RGX-202 has been well-tolerated in Phase I/II patients at both dose levels with no SAEs or AESIs

Data cut data May 7, 2025

SAE – Serious Adverse Event; AESI – Adverse Events of Special Interest

[1]Based on recognized criteria in Duchenne gene therapy (SRP-9001 sponsor briefing document, FDA Ad. Comm. Mtg, 12 May 2023): GGT > 3 × ULN, or GLDH > 2.5 × ULN, or ALT > 3 × baseline

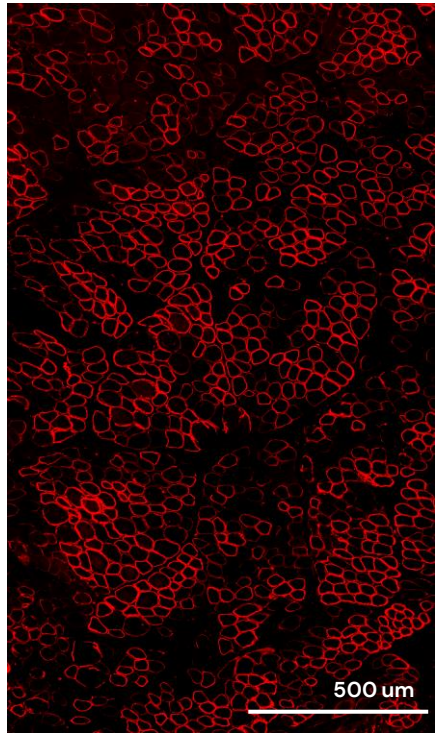
[2]Based on Common Terminology Criteria for Adverse Events (CTCAE) version 5

RGX-202: AFFINITY DUCHENNE New Phase I/II Interim Functional Data, June 2025

Biomarkers Support Consistent Robust Expression, Transduction, and Sarcolemmal Localization of RGX-202 Microdystrophin

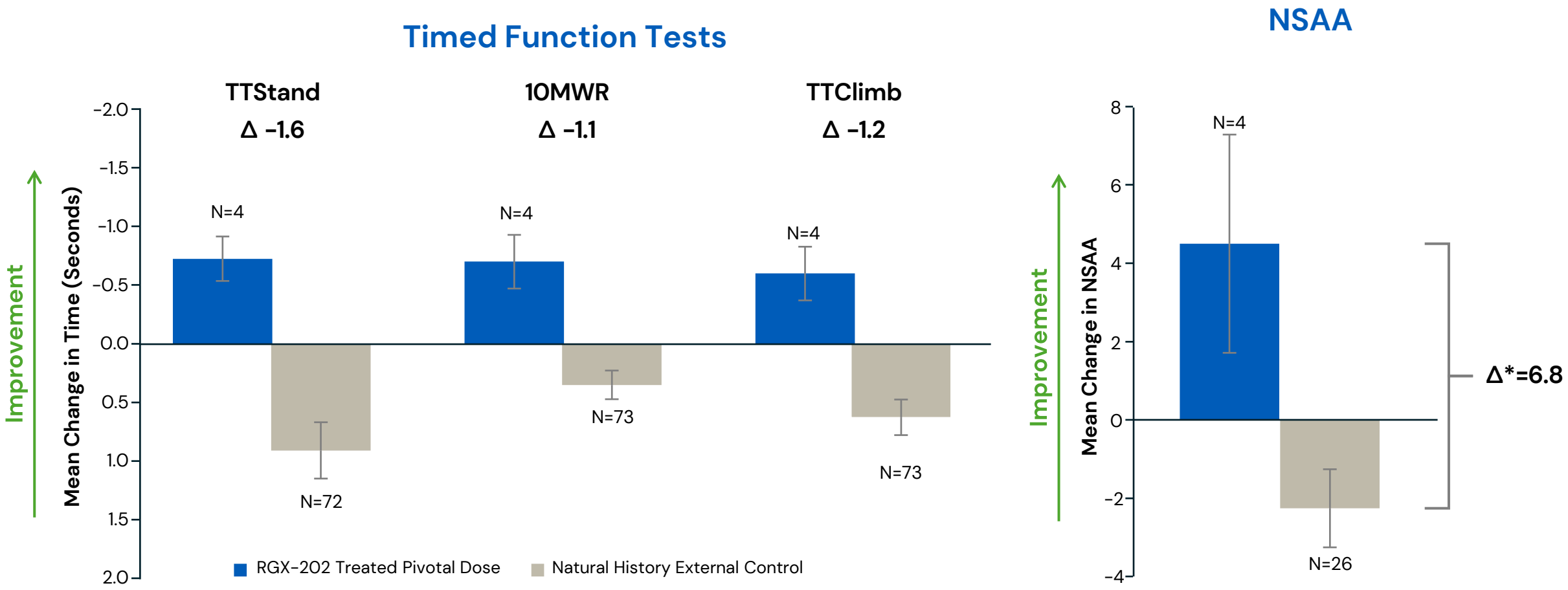
Mean at 12 Weeks (min, max)	Dose Level 1 $1x10^{14}$ GC/kg		Dose Level 2 (Pivotal Dose) $2x10^{14}$ GC/kg		
Age range at screening (number with data)	4–7 (2)	8–11 (1)	1–3 (2)	4–7 (2)	8–11 (5)
RGX-202 Microdystrophin[1] % (Western Blot)	**60.6** (37.8, 83.4)	**10.4**	**120.5** (118.6, 122.3)	**54.3** (31.5, 77.2)	**39.7** (20.8, 75.7)
VCN copies/nucleus (qPCR)	**9.8** (7.4, 12.1)	**5.4**	**24.8** (20.4, 29.1)	**30.1** (4.9, 55.4)	**17.8** (12.0, 30.7)
Positive Fibers[2] % (Immunofluorescence)	**79.3**[3]	**34.6**	**89.6** (82.1, 97.1)	**50.3** (29.4, 71.1)	**45.7** (21.3, 70.6)

RGX-202 Microdystrophin DL 2, 12 weeks



Data cut date May 7, 2025
[1]Microdystrophin expression adjusted for muscle content; % normal control
[2]Positive Fibers defined as change from baseline of RGX-202 microdystrophin & dystrophin positive fibers
[3]One sample could not be evaluated

Pivotal Dose Participants Demonstrate Improvement in Function and Exceed External Controls at 12 Months

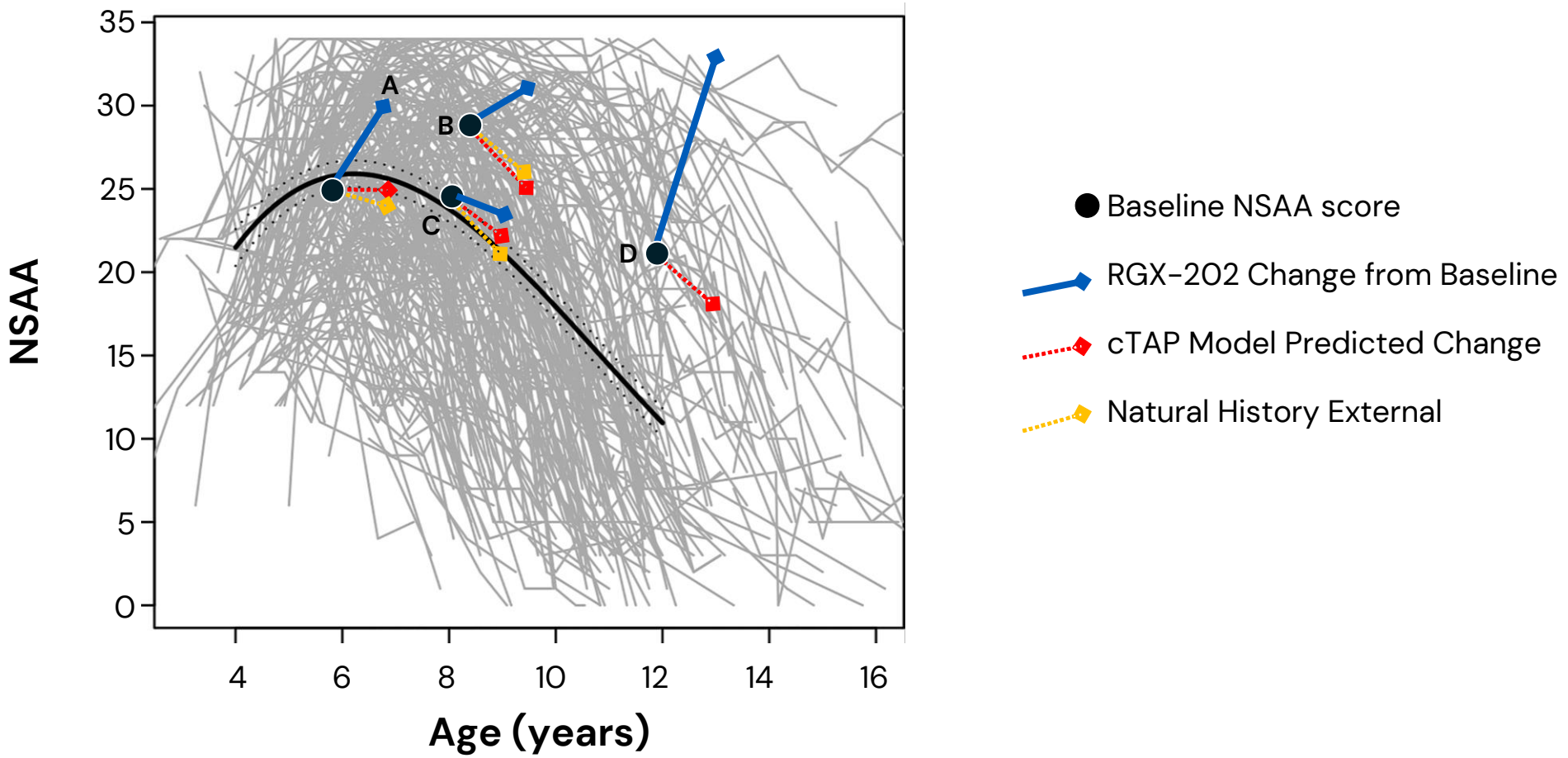


Data cut date May 7, 2025
Time to Stand (TTStand); 10M Walk Run (10MWR); Time to Climb (TTClimb)
Natural history datasets included 402 patients with steroid exposure from CINRG and the D-RSC Data Platform. The D-RSC Data Platform initiative is a public/private partnership funded by the Parent Project Muscular Dystrophy (PPMD) and launched in August of 2015 by Critical Path Institute (Cpath)
Mean of changes from baseline for EC was stratum-based, i.e., the values of individual matched EC subjects to a RGX-202 subject were averaged first before calculating the mean.
Error bar represents standard error.
*For NSAA, the EC matched subjects of one treated subject did not have data at Month 12. The delta was based on the mean of RGX-202 participants' changes from baseline minus stratum-based mean change from baseline of EC matched participants.

Adapted from : RGX-202: AFFINITY DUCHENNE New Phase I/II Interim Functional Data, June 2025

Pivotal Dose Participants Exceed Expected NSAA Trajectory Across Multiple Methods

NSAA Performance
Baseline to Month 12



Data cut date May 7, 2025
Graph adapted from Muntoni (2019) *PLoS ONE*
Muntoni, (2025) *PLoS One*
For NSAA, the EC matched subjects of Patient D did not have data at Month 12.