RGX-202: AFFINITY DUCHENNE®
Pivotal Trial and Interim Functional Data

November 2024

RGX-202 is an investigational product that has not been approved by the FDA. No conclusions regarding safety and efficacy can be made.

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Agenda

- **Welcome**
- **RGX-202 overview**
- **AFFINITY DUCHENNE® Pivotal Trial of RGX-202**
- **Phase I/II Data**
  - New biomarker data
  - First functional data
  - Clinic and caregiver videos
  - KOL discussion
- **Q&A**

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Seeking to improve lives through the curative potential of gene therapy

We pioneered the landscape of adeno-associated virus (AAV) gene therapies.

Thousands of patients have been treated with approved and investigational medicines built on our NAV® Technology platform.

We are advancing late-stage, potential first- and best-in-class gene therapies for patients with retinal and rare diseases.

Addressing multiple billion-dollar+ opportunities, with lead candidate in Duchenne muscular dystrophy.

With the expertise and end-to-end capabilities, REGENXBIO is leading the future of one-time treatments.

Fully-integrated manufacturing and fill-finish capabilities support multiple potential product launches.

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RGX-202: A Next-Generation, Investigational Gene Therapy

Accelerated Approval Pathway: Four pillars for delivering RGX-202 as next to market for Duchenne

Regulatory and Patients

Aligned with FDA on a path to **Accelerated Approval**; on track to file **BLA in 2026** and are committed to **data transparency with the patient community**

Robust Clinical Biomarkers

Consistent & robust levels of RGX-202 microdystrophin expression and transduction observed in target muscle providing the potential for **long-term, durable clinical outcomes**

Differentiated Safety

Combination of a differentiated construct, proactive immunosuppression regimen and high product purity have enabled a **preferred dose with encouraging safety profile**

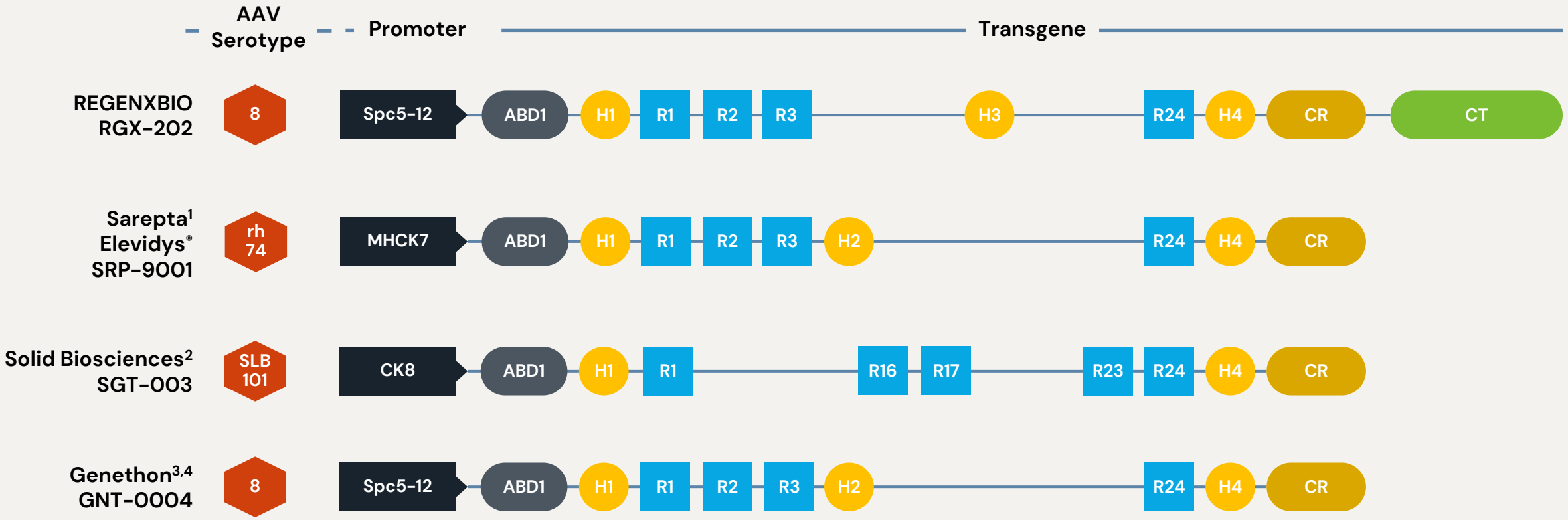
Positive Functional Outcomes

RGX-202 demonstrates functional improvements exceeding natural history benchmarks

RGX-202 NAVXpress™ Process Platform: In-house Manufacturing, High Yield, High Purity, Commercial Ready

RGX-202 is Designed for Improved Function in Duchenne

RGX-202 is the only microdystrophin gene therapy with the functional elements of the C-Terminal (CT) domain found in naturally occurring dystrophin

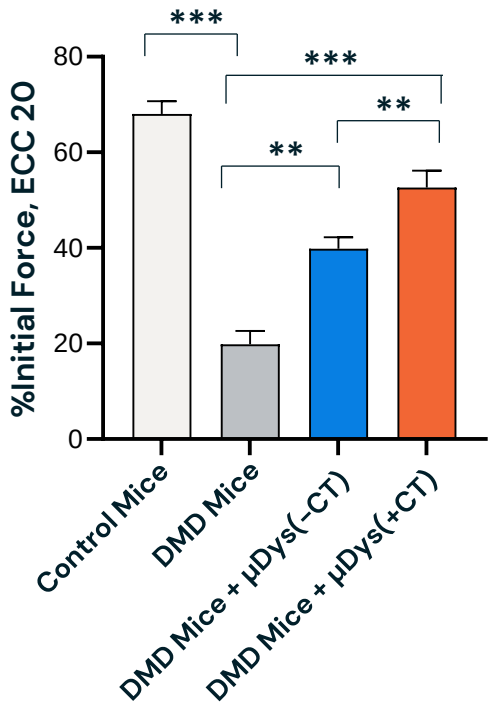


1. Harper (2002) Nat Med
2. https://investors.solidbio.com/Corporate Presentation, January 2024
3. Mbakam & Tremblay (2023) Expert Rev Neurother
4. Le Guiner (2017) Nat Comm

Role of the CT Domain in Preserving Muscle Health

Preclinical studies indicate the CT domain in RGX-202 microdystrophin enables muscle resilience

Microdystrophin+CT domain better protects the muscle against contraction-induced damage



How the CT Domain May Contribute to Improved Outcomes with RGX-202

Functional microdystrophin

- CT domain significantly enhanced restoration of the DAPC in *mdx* mice, more similar to natural dystrophin

Prolonged microdystrophin activity

- CT domain increased the half-life of RGX-202 which remains in muscle fibers longer to strengthen muscle

Muscle health

- CT domain in RGX-202 microdystrophin protected against contraction-induced damage enabling better muscle recovery

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DAPC – Dystrophin Associated Protein Complex
Foltz et al. Manuscript submitted

AFFINITY DUCHENNE® Trial Design

Pivotal Trial for Accelerated Approval Initiated

- Aligned with FDA on pivotal design and accelerated approval pathway
- **BLA expected 2026** using accelerated approval to include approximately 30 patients

Phase I/II

✓ **Dose Evaluation**
(Ages 4–11)

Dose Level 1
$1x10^{14}$ GC/kg
N=3

Dose Level 2
$2x10^{14}$ GC/kg
N=2

→

✓ **Expansion Cohort**
(Ages 4–11)

Dose Level 2
(N=5)

Younger Patient Cohort
(Ages 1–3)

Dose Level 2
(up to 5 patients)

Pivotal

Dose Level 2 Ambulatory
(patients aged 1+)
N ~ 30

Primary endpoint: Proportion of patients with ≥10% microdystrophin levels

Secondary endpoints: Timed function tests, including time to stand velocity, SV95C ages 1–3

Exploratory endpoint: NSAA, SV95C for 4+

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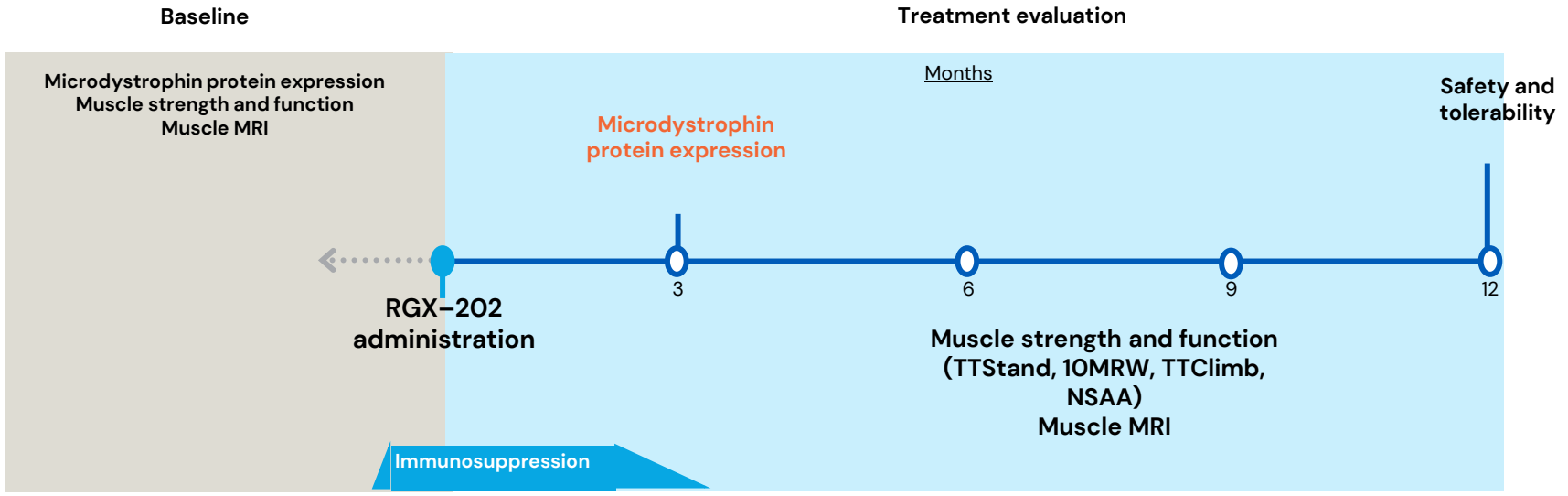
Phase I/II Data

Phase I/II AFFINITY DUCHENNE Study Overview

Key Eligibility Criteria

- **Boys aged 1 to 11 years** at screening
- **Genetically confirmed DMD** (mutations in exons 18 and above)
- **100-meter walk:** able to perform without assistive devices
- **No pre-existing antibodies** to the gene therapy (AAV8 capsid)

Administration and Assessments Timeline



North Star Ambulatory Assessment (NSAA); Time to Stand (TTStand); 10M Walk Run (10MWR); Time to Climb (TTClimb)

Key Baseline Demographics

Variable Mean (range)	Dose Level 1 $1x10^{14}$ GC/kg	Dose Level 2 $2x10^{14}$ GC/kg	
Age range at screening (number dosed)	**4–11** (n = 3)	**1–3** (n = 1)	**4–11** (n = 7)
Age at Dosing (yrs)	**7.1** (4.4–10.5)	**3.7**	**8.7** (5.8–12.1)
Weight (kg)	**24.3** (17.8–28.3)	**12.5**	**26.2** (17.3 – 35.5)
Time from Dosing (months)	**17.0** (13.9–19.4)	**1.6**	**7.0** (1.2–11.8)
Functional Outcomes			
NSAA	**20.3** (14.0–26.0)	Not completed*	**24.0** (13.0–30.0)
Time to Stand (sec)	**4.9** (2.9–6.8)	n/a†	**4.4** (3.7–5.4)
10 Meter Walk Run (sec)	**5.1** (3.9–6.2)	n/a†	**4.9** (4.2–6.0)
Time to Climb (sec)	**3.6** (2.1–5.2)	n/a†	**3.1** (2.1–4.6)

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Data cut data November 1, 2024
* Participant was uncooperative; functional baseline not obtained
† Boys 1–3 years old only complete the NSAA and Peabody Developmental Motor Scale, Third Edition (PDMS-3) at baseline

Interim Safety

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 Age Ranges
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
The most common drug-related AEs reported are anticipated with gene therapy: nausea (n=3), vomiting (n=6), and fatigue (n=5), all resolved					

RGX-202 has been well-tolerated in all patients at both dose levels with no SAEs or AESIs

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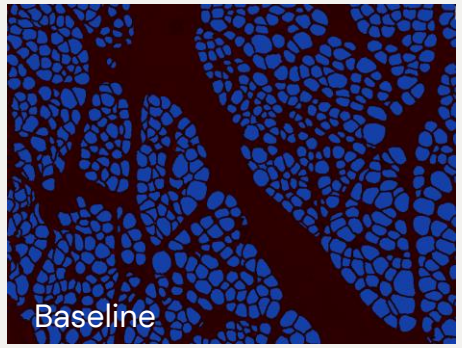
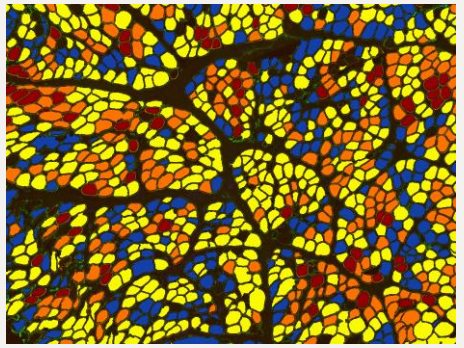
Data cut data November 1, 2024
SAE – Serious Adverse Event; AESI – Adverse Events of Special Interest
*based on Common Terminology Criteria for Adverse Events (CTCAE) version 5

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 $2x10^{14}$ GC/kg	
Age range at screening (number with data)	4–7 (2)	8–11 (1)	4–7 (1)	8–11 (5)
RGX-202 Microdystrophin* % (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)

Fiber Intensity †





RGX-202 DL2, 12 weeks

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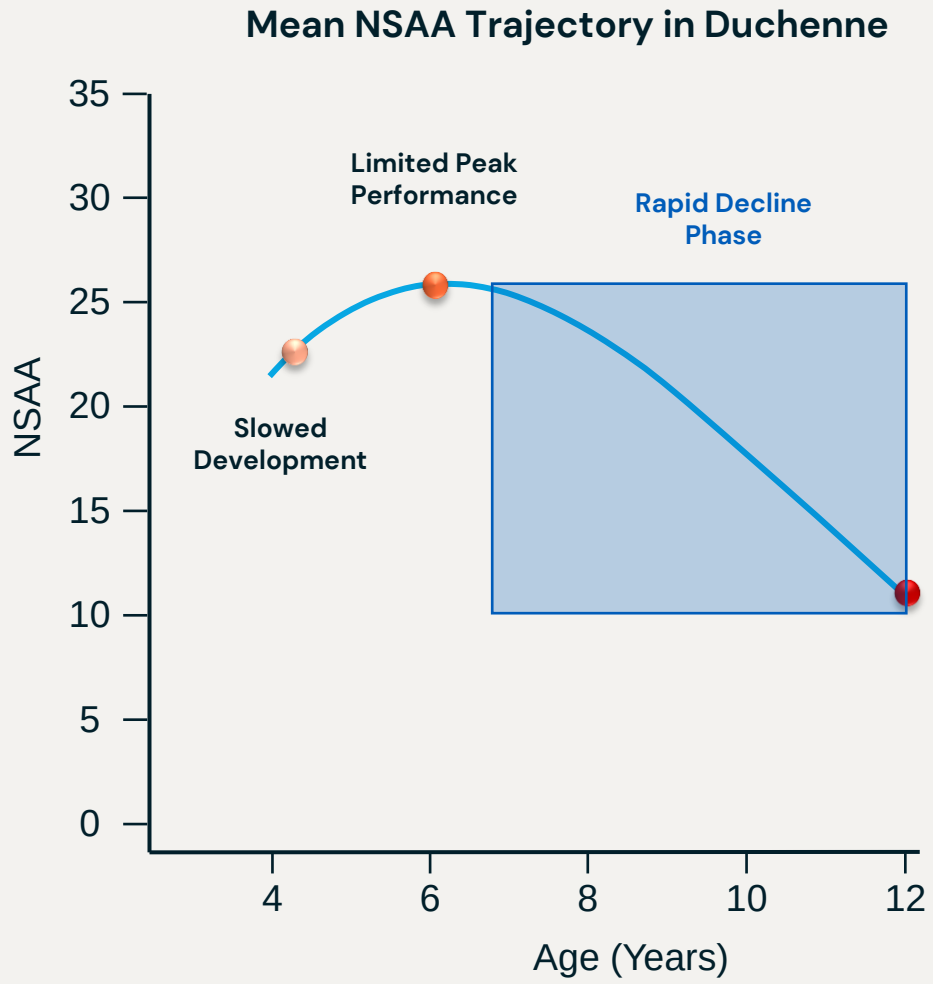
Data cut date November 1, 2024
* Microdystrophin expression adjusted for muscle content; % normal control
**Positive Fibers defined as change from baseline of RGX-202 microdystrophin & dystrophin positive fibers
*** One sample could not be evaluated
† Microdystrophin Fiber Intensity: Blue = Negative; Yellow = +1 (low) intensity; Orange = +2 (medium) intensity; Red = +3 (strong) intensity

RGX-202 Functional Data: Natural History Control Methodology



Functional Data at Clinically Meaningful Timepoints

- Dose level 1
  - N=3 at 12 months post-RGX-202 administration
- Dose level 2
  - N=2 at 9 months post-RGX-202 administration

Method for External Controls

Heterogeneity is present in baseline disease stage, rate of disease progression, and anticipated efficacy response

Matched controls from Natural History Dataset* enable comparison to RGX-202 for rate of disease progression and anticipated efficacy response.

Natural history control matching criteria:**

- Age
- Baseline function

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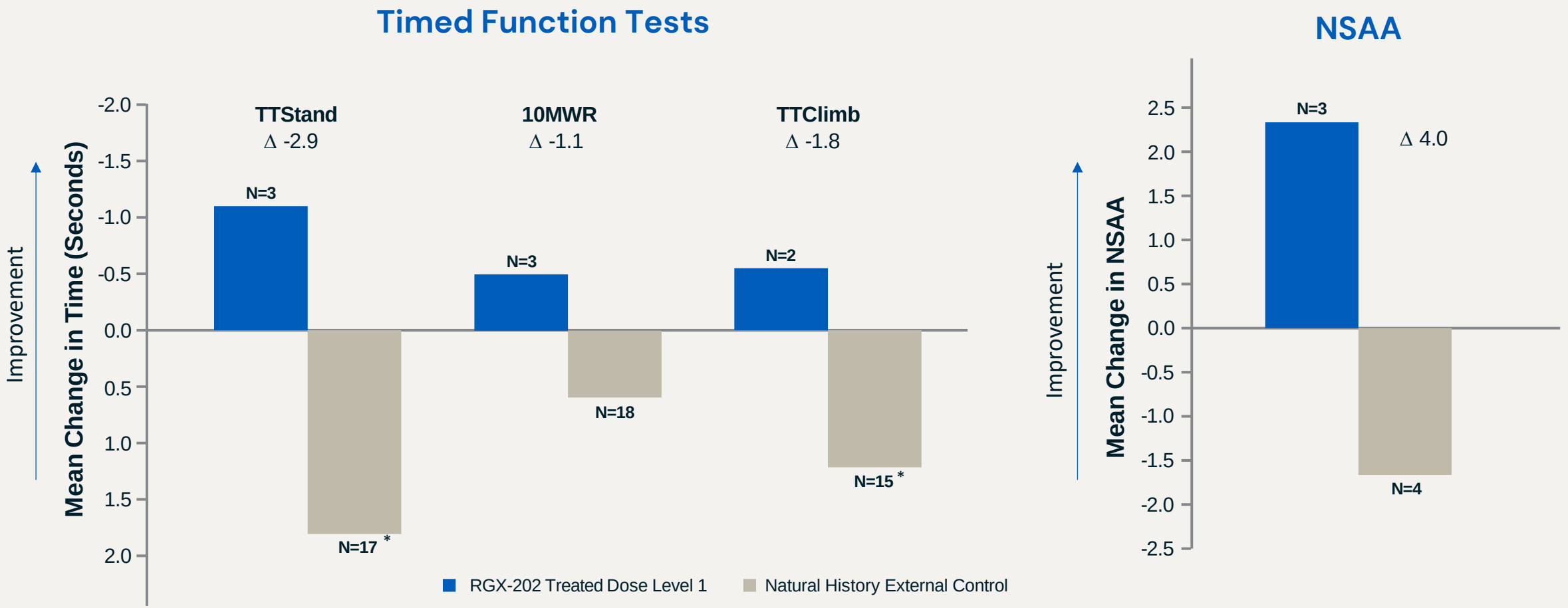
Graph adapted from Muntoni 2019

* Natural history datasets included 420 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).

** Criteria for matching:, TTSTAND, TTRW, and TTCLIMB . Group mean for external controls were weighted by the number of matched NH patient per each RGX- 202 treated participants.

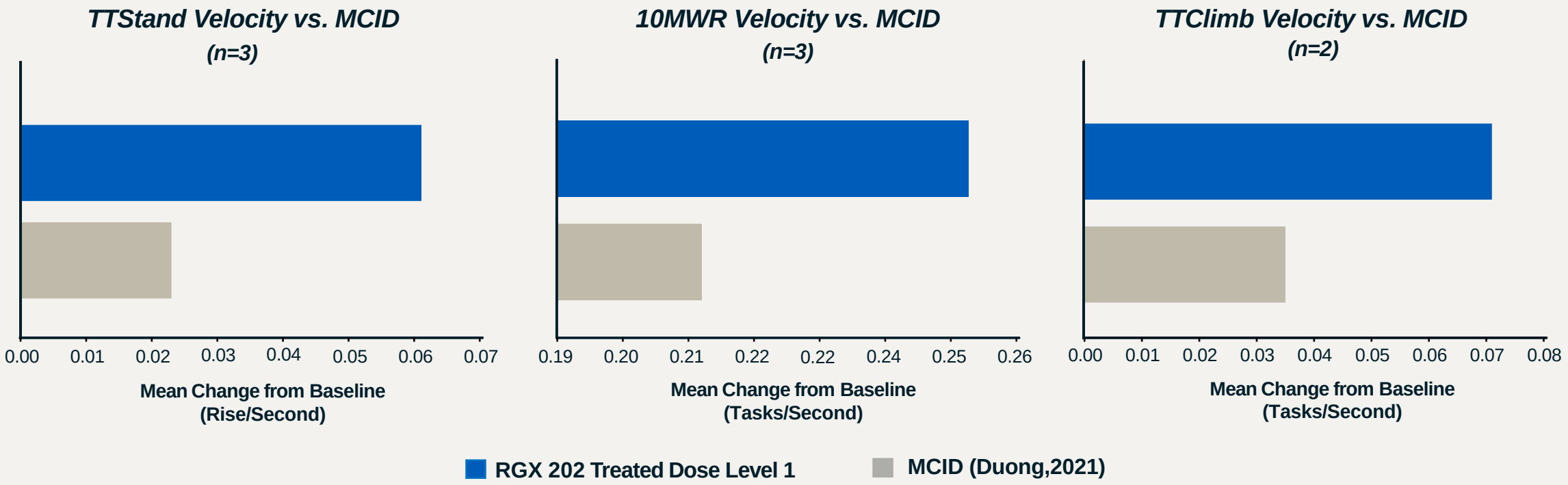
Dose Level 1 Participants Demonstrate Improvement in Function and Exceed External Controls at 12 months



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

Dose Level 1 Timed Task Velocity Changes Exceed MCID Benchmarks at 12 months

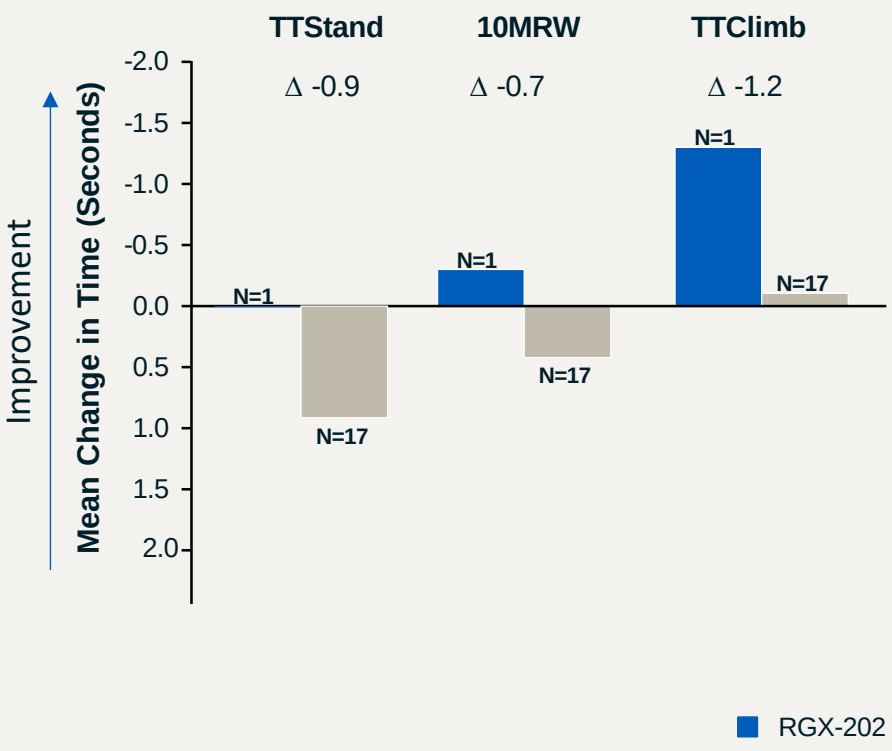
RGX-202 exceeds minimal clinically important difference (MCID) referenced by FDA in the approval of an available gene therapy in ambulatory boys*



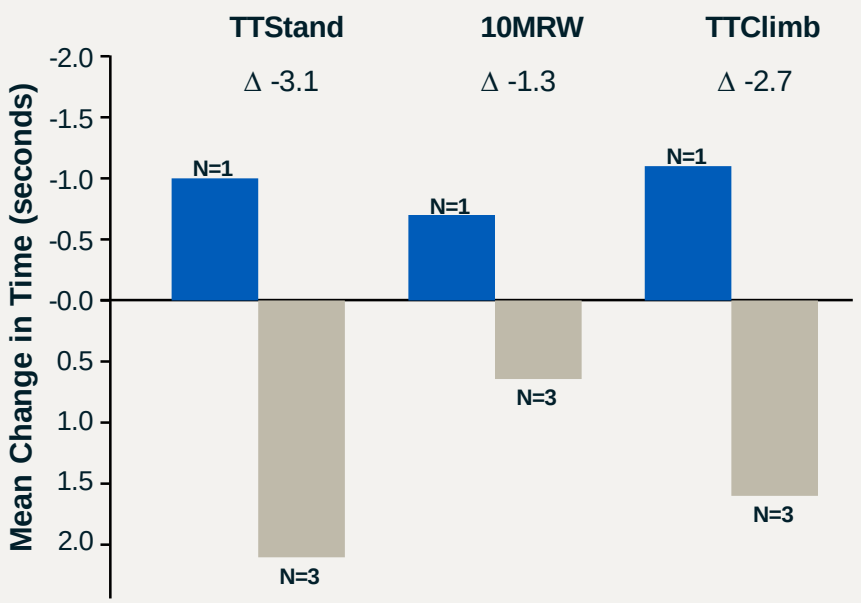
Data cut date November 1, 2024
Time to Stand (TTStand); 10M Walk Run (10MWR); Time to Climb (TTClimb)
*Accessed November 6, 2024: Center Director Decisional Memo, BLA125781/Amendment 34
Duong T, et al. 2021. The minimal clinical important difference (MCID) in annual rate of change of timed function test in boys with DMD. *Journal of Neuromuscular Diseases.* 2021; 939-948.

Pivotal Dose Participants Demonstrate Improvement in Function at 9 months

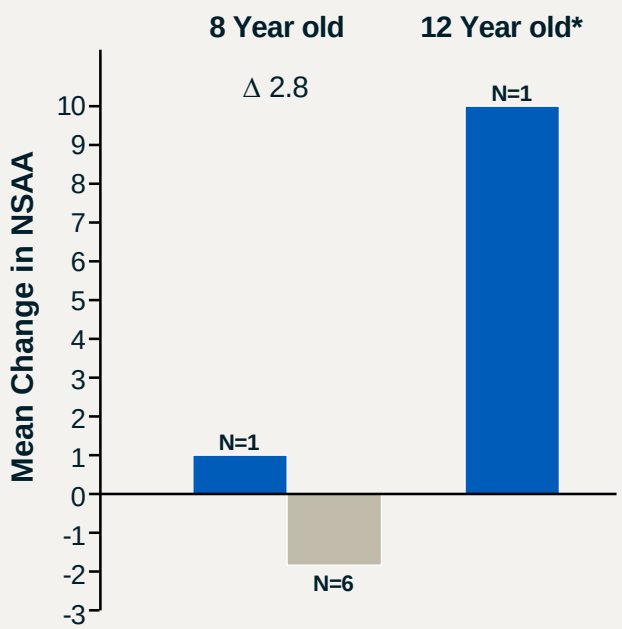
8 Year Old



12 Year Old



Individual NSAA



RGX-202 Treated Dose Level 2 Natural History External Control

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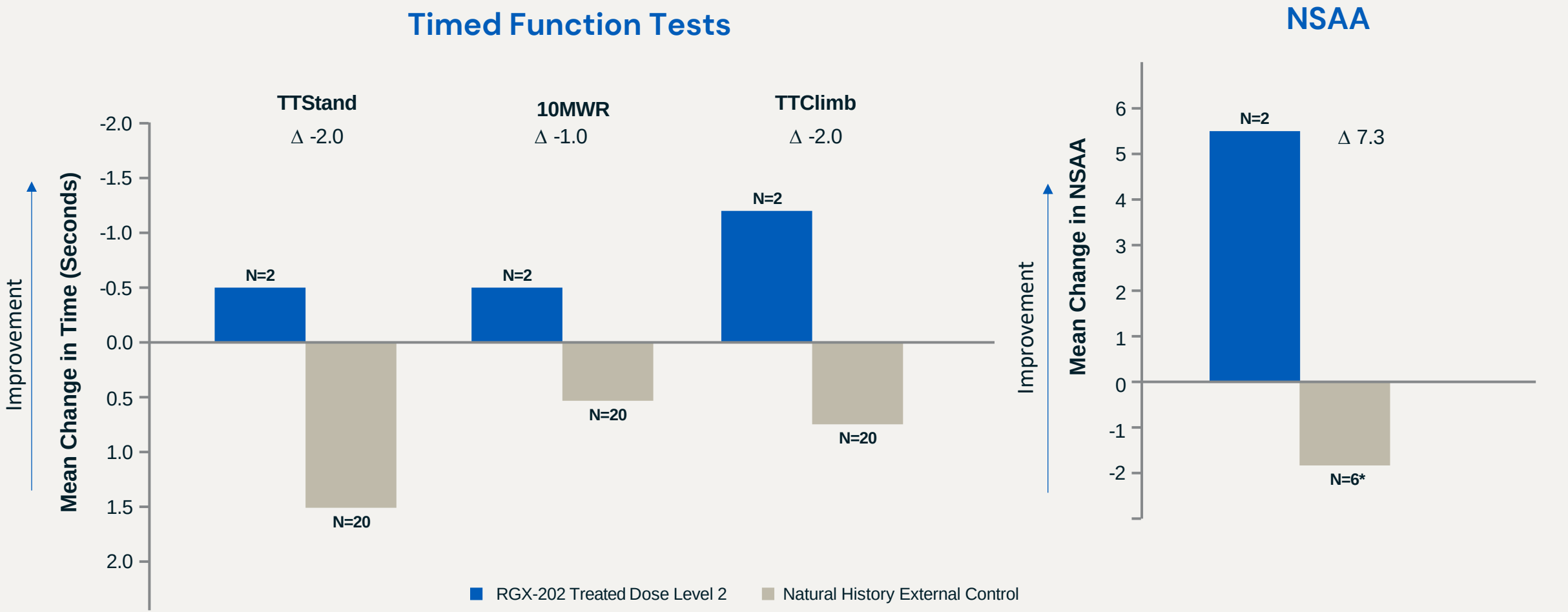
Data cut date November 1, 2024
Time to Stand (TTStand); 10M Walk Run (10MWR); Time to Climb (TTClimb)
*The 12 year old participant does not have any matched natural history external controls for NSAA

Pivotal Dose Participants Demonstrate Improvement in Function at 9 Months



Data cut date November 1, 2024
Time to Stand (TTStand); 10M Walk Run (10MWR); Time to Climb (TTClimb)
* For NSAA, one patient did not have matching natural history external controls

Caregivers Reported Improved Function

Caregivers reported improvements in the home and community environments as measured by PODCI

Improved skills included:

- Running
- Riding a bicycle/tricycle
- Climbing stairs
- Walking in the community
- Participating in recreational activities and sports with peers

Date cut date November 1, 2024
Pediatric Outcomes Data Collection Instrument (PODCI)
* All 5 participants had improved PODCI scores on at least one of the measures at 12 months (dose level 1) or 9 months (dose level 2) change from baseline

Phase I/II AFFINITY DUCHENNE: Interim Summary

Positive safety, biomarker and functional data demonstrate the potential of RGX-202 to be a differentiated, best-in-class gene therapy

RGX-202 has been well-tolerated in 11 patients across both dose levels with no SAEs or AESIs

Biomarkers support consistent robust expression, transduction, and sarcolemmal localization of RGX-202 microdystrophin

Participants treated with RGX-202:

- Demonstrated clinically meaningful improvement in functional outcomes at both dose levels
- Exceeded comparisons using NH external controls and MCID*

Evidence of altering the trajectory of disease

Data cut date November 1, 2024

* MCID (minimal clinically important difference) (Duong, 2021) compared to dose level 1 at 12 mo

Discussion

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