RGX-202: AFFINITY DUCHENNE®
New Phase I/II Interim Functional Data

June 2025

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Agenda

Welcome

RGX-202 therapeutic approach

Phase I/II data

- Safety and biomarker data
- New interim functional data
- Clinic and caregiver videos
- KOL discussion

Q&A

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RGX-202 Therapeutic Approach

Duchenne Muscular Dystrophy

A severe, progressive, degenerative muscle disease

Disease

- Duchenne is caused by mutations in the DMD gene which encodes for dystrophin, a protein involved in muscle cell structure and signaling pathways
- Affects 1 in 3,500 to 5,000 male births worldwide
- Estimated US population = ~15,000**

Progression

- Without dystrophin, muscles throughout the body degenerate and become weak, eventually leading to loss of movement and independence, trouble breathing, cardiomyopathy and premature death
- Degenerative disease trajectory: boys gain functional skills until ~6 years, then experience loss of ambulation and rapid decline*

Child has not participated in clinical trials of RGX-202

Unmet Need

Significant ongoing unmet need for a gene therapy to serve prevalent and incident markets with the potential to deliver a favorable safety and efficacy profile.

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* Muntoni 2019

** Parent Project Muscular Dystrophy. (2020, April 14). About Duchenne Muscular Dystrophy - Parent Project Muscular Dystrophy. https://www.parentprojectmd.org/about-duchenne/

Rapid progress toward delivering RGX-202 as next to market gene therapy for Duchenne

Preclinical POC

- Unique design of RGX-202 construct with CT-domain
- Established next-generation manufacturing
- Preclinical safety and efficacy data demonstrate promise

2019-2022

Initiated Phase I/II study

- AFFINITY DUCHENNE® dose escalation trial in patients aged 4+
- Safely escalated and expanded to dose level 2 (pivotal dose)

Jan 2023

Expanded enrollment

- Opened cohort for patients aged 1-4

Jun 2024

Positive initial Phase I/II functional data

- Demonstrated evidence of positively impacting disease trajectory

Opened pivotal (Phase III) trial

- ~30 patients aged 1+ at pivotal dose (dose level 2)

Nov 2024

Inclusion criteria expansion

- Expanded *DMD* mutation criteria

Pivotal >50% enrolled

- As of May 12, 2025

May 2025

We are here

Accelerating to market

- 2025: Complete pivotal enrollment
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Potential FDA Approval in 2027

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Differentiated therapeutic approach designed for improved outcomes

Only microdystrophin construct with CT domain

- Designed to improve function and preserve muscle health
- Delivered by proprietary NAV® AAV8 vector

Industry-leading manufacturing

- Product purity levels of more than 80% full capsids

Proactive, short-course immune modulation regimen

- Designed to counter safety concerns common with high-dose AAV gene therapy and to improve safety outcomes

Trial designed to show differentiation

- Clinical trial designed to demonstrate meaningful change in disease trajectory in pursuit of broad label
- Positive interim efficacy and safety outcomes reported in Phase I/II

AFFINITY DUCHENNE® New Interim Phase I/II Data

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

Phase I/II Demographics, Safety & Biomarkers

Phase I/II Interim 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 = 3)	**4–11** (n = 7)
Age at Dosing (yrs)	**7.1** (4.4-10.5)	**3.2** (2.3-3.7)	**8.7** (5.8-12.1)
Weight (kg)	**24.3** (17.8-28.3)	**11.4** (10.3-12.5)	**26.2** (17.3 – 35.5)
Time from Dosing (months)	**23.1** (20.0-25.5)	**4.0** (0.2-7.8)	**13.1** (7.3-18.0)
Functional Outcomes			
NSAA	**20.3** (14.0-26.0)	n/a†	**23.9** (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 date May 7, 2025
† Boys 1-3 years old complete the Peabody Developmental Motor Scale, Third Edition (PDMS-3) at baseline; NSAA collected but not applicable

Phase I/II Interim Safety

RGX-202 Treatment-Emergent Adverse Events		Dose Level 1 ($1x10^{14}$ GC/kg)	Dose Level 2 ($2x10^{14}$ 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	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: nausea (n=3), vomiting (n=7), and fatigue (n=5)					

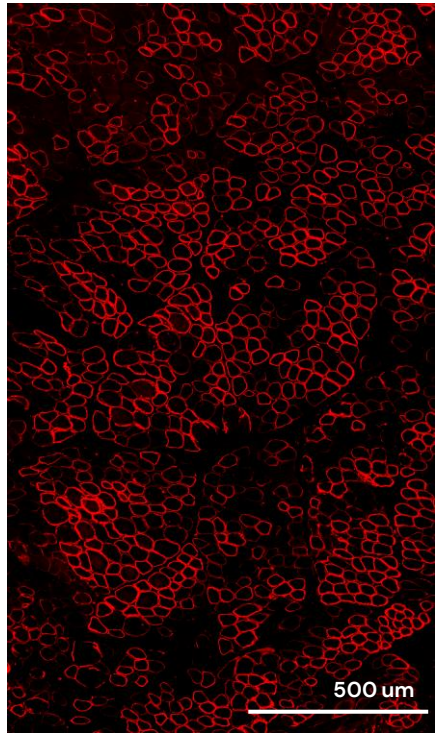
RGX-202 has been well-tolerated in Phase I/II patients at both dose levels with no SAEs or AESIs

Data cut data May 7, 2025
SAE – Serious Adverse Event; AESI – Adverse Events of Special Interest
*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)	1-3 (2)	4-7 (2)	8-11 (5)
RGX-202 Microdystrophin* % (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** % (Immunofluorescence)	**79.3****	**34.6**	**82.1****	**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
* 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

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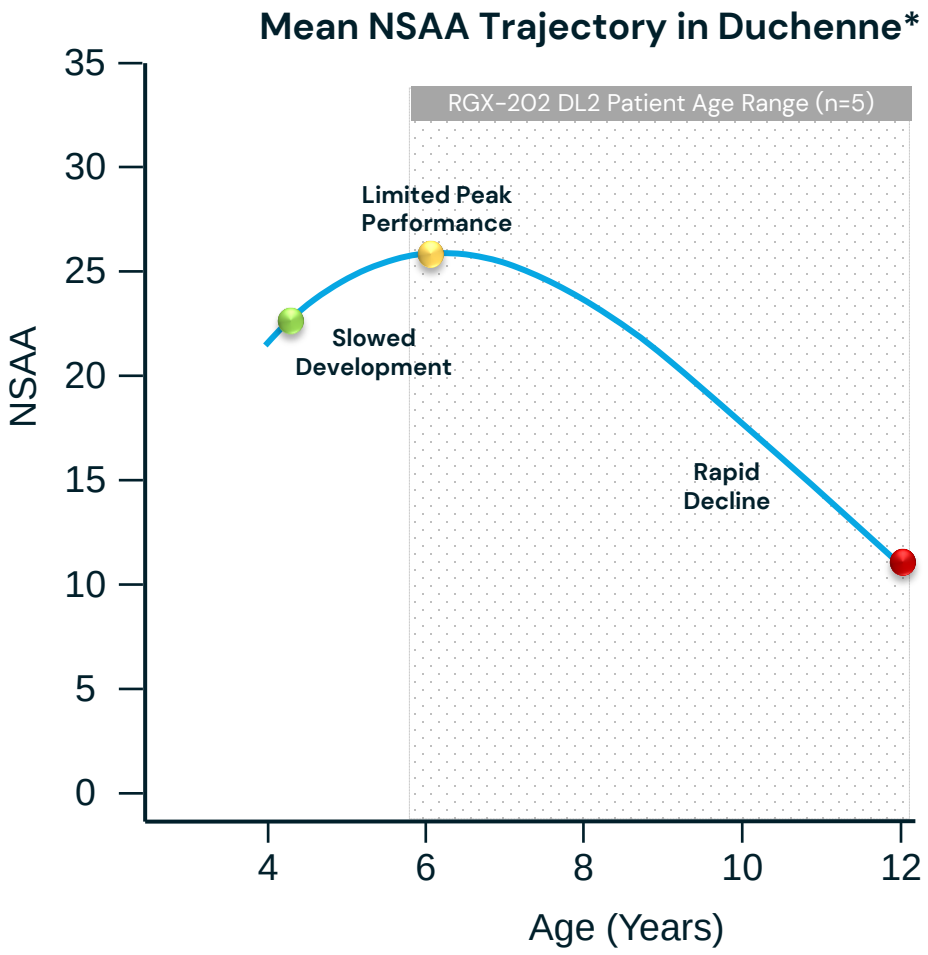
Phase I/II Dose Level 2 New Functional Data

Phase I/II Functional Data: Natural History Control Methodology

RGX-202 dose level 2 recipients expected to be in stable or decline phase of disease trajectory



Dose Level 2 Functional Data Set

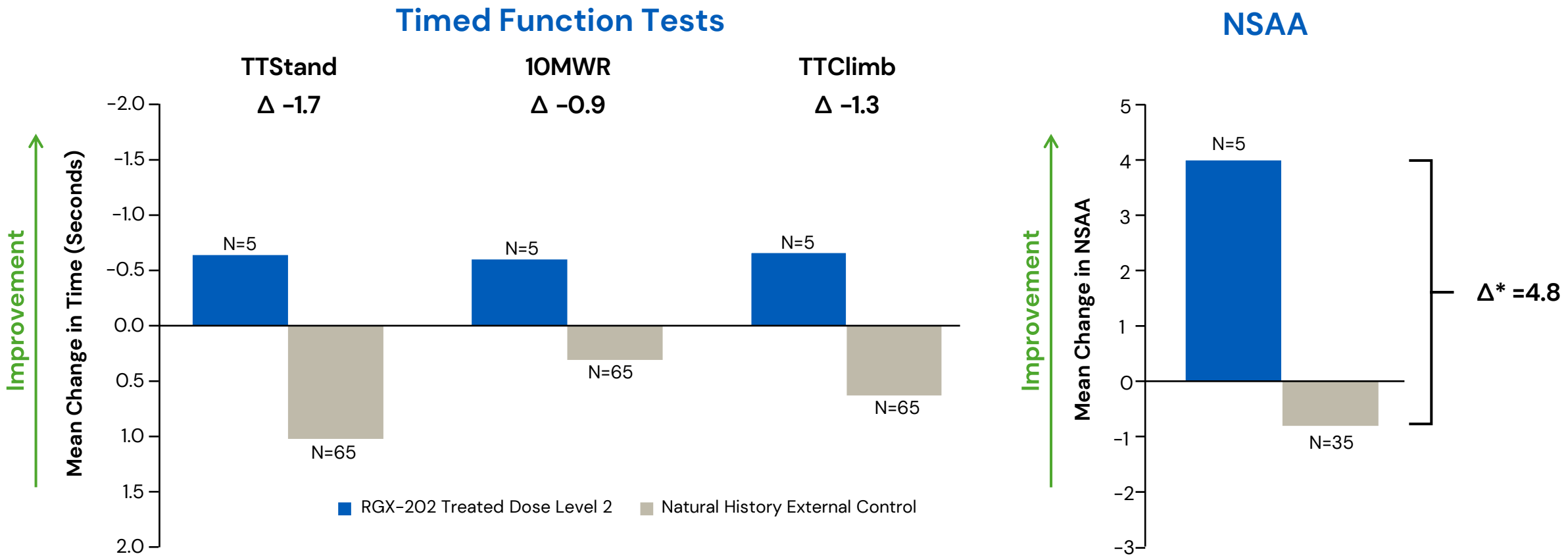
- **N = 5, aged 5.8 to 12.1 at dosing**
  - 9m post-dosing: n=5 (4 patients aged 8+ at dosing)
  - 12m post-dosing: n=4 of 5 (3 patients are 8+)
- **9- and 12-month timepoints: 6-9 months after immune modulation regimen ends**

Method for External Controls

- **Heterogeneity is present across baseline disease stage,** rate of disease progression, and anticipated efficacy response
- **Strictly-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***

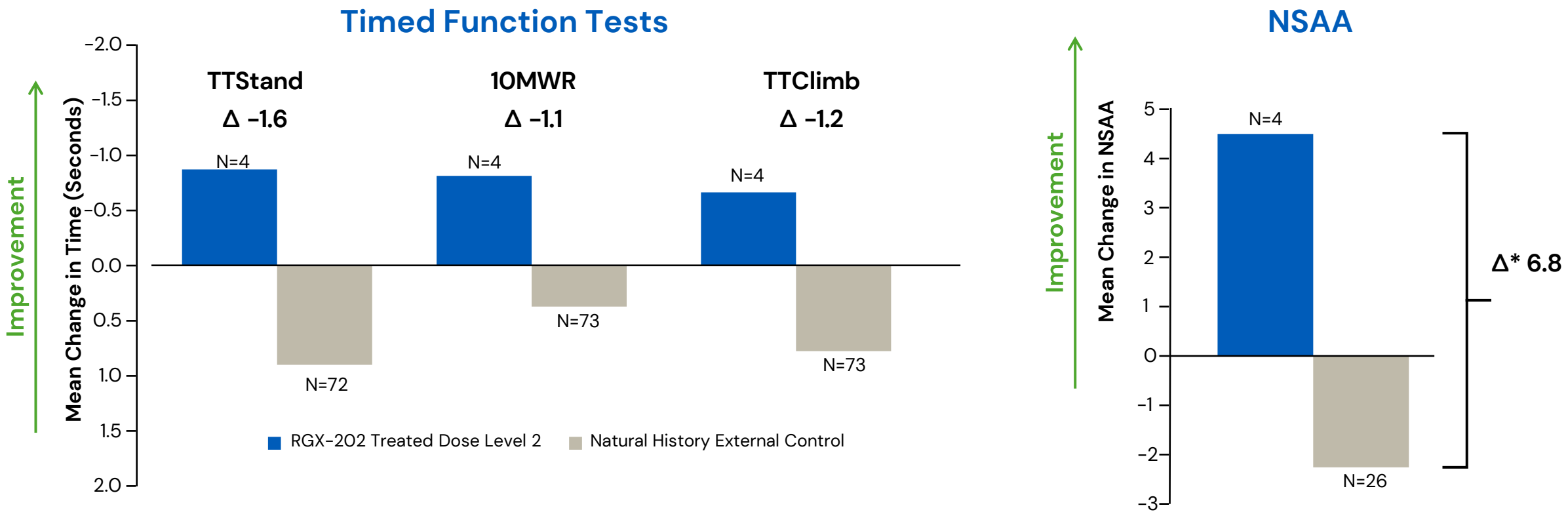
*Graph adapted from Muntoni 2019
** Natural history datasets included 402 patients with steroid exposure from CINRG and the D-RSC Data Platform. The D-RSC Data Platform initiative is a public/private partnership funded by the Parent Project Muscular Dystrophy (PPMD) and launched in August of 2015 by Critical Path Institute (CPath).
*** Time to Stand (TTStand); 10M Walk Run (10MWR); Time to Climb (TTClimb)

Dose Level 2 Participants Demonstrate Improvement in Function and Exceed External Controls at 9 Months



Data cut date May 7, 2025
Time to Stand (TTStand); 10M Walk Run (10MWR); Time to Climb (TTClimb)
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.
* For NSAA, the EC matched subjects of one treated subject did not have data at Month 9. 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.

Dose Level 2 Participants Demonstrate Improvement in Function and Exceed External Controls at 12 Months



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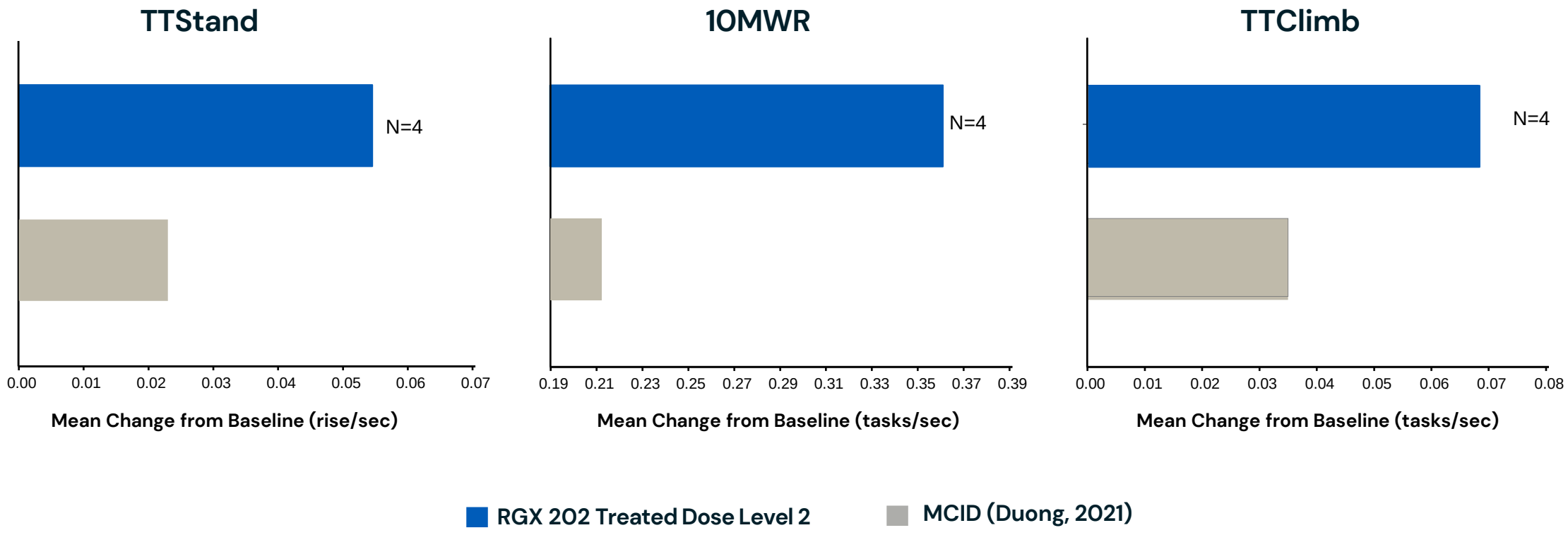
*For NSAA, the EC matched subjects of one treated subject did not have data at Month 12. The delta was based on the mean of RGX-202 participants' changes from baseline minus stratum-based mean change from baseline of EC matched participants.

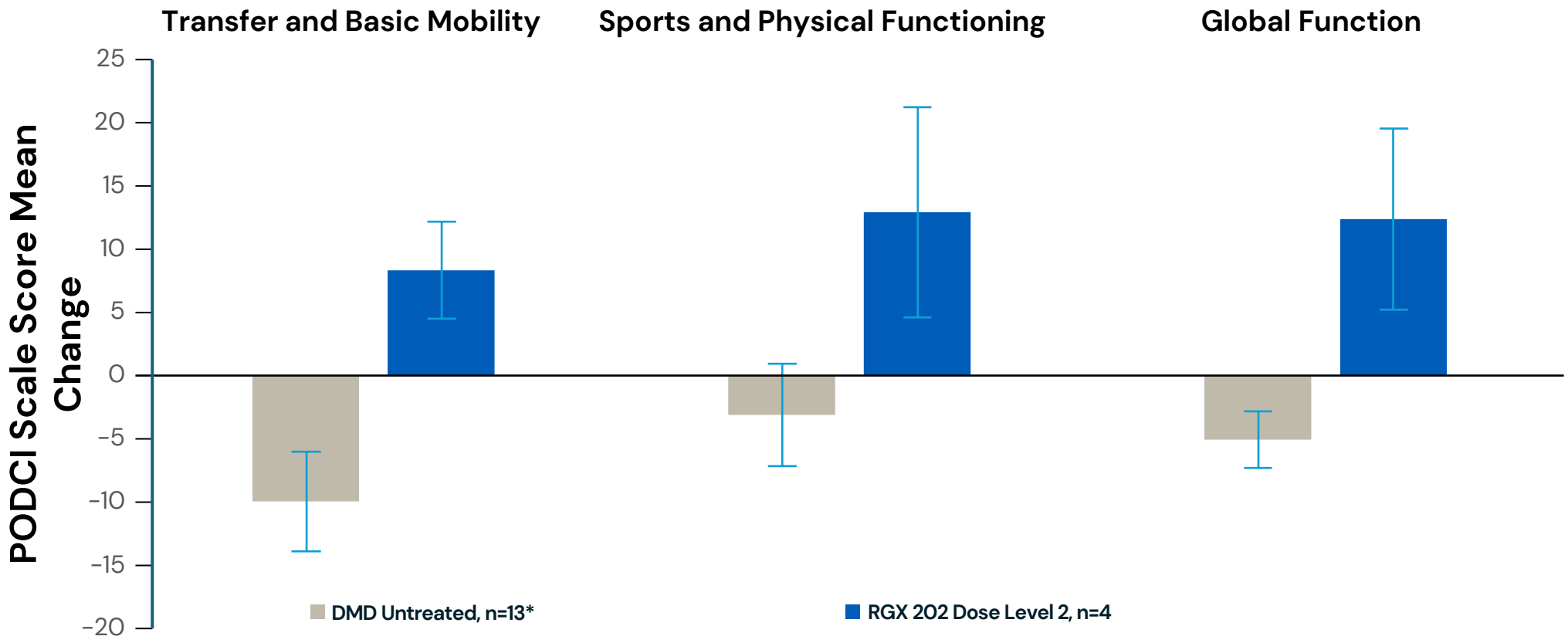
Dose Level 2 Timed Task Velocity Changes Exceed MCID Benchmarks at 12 months

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 May 7, 2025
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 Caregivers Reported Improved Function at 12 months



Caregivers reported improved function in the home and community as measured by key dimensions of the PODCI at 12 months compared to expected decline in natural history**

Date cut date May 7, 2025
Mean change from baseline
PODCI Scale Scores range from 0-100, with 100 being highest function
*Henricson (2013) PLoS: DMD Untreated
** McDonald (2010) J Child Neurol Boys with DMD experience decline in motor function over time as measured by three dimensions of the PODCI

Discussion

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AFFINITY DUCHENNE: Phase I/II Interim Summary

Well tolerated in 13 patients across both dose levels with no SAEs or AESIs
Differentiated therapeutic approach may contribute to positive safety profile

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

New functional data support consistent evidence of RGX-202 altering the trajectory of disease, showing boys treated with Dose Level 2:

- ✓ Demonstrated clinically meaningful improvement in function at 9 and 12 months
- ✓ Exceeded natural history external controls and MCID benchmarks
- ✓ Showed improved function in the home and community, as reported by caregivers

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Data cut date May 7, 2025

On track to deliver RGX-202 as next to market gene therapy for Duchenne

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