RGX-202, an investigational gene therapy for the treatment of Duchenne muscular dystrophy: interim clinical data

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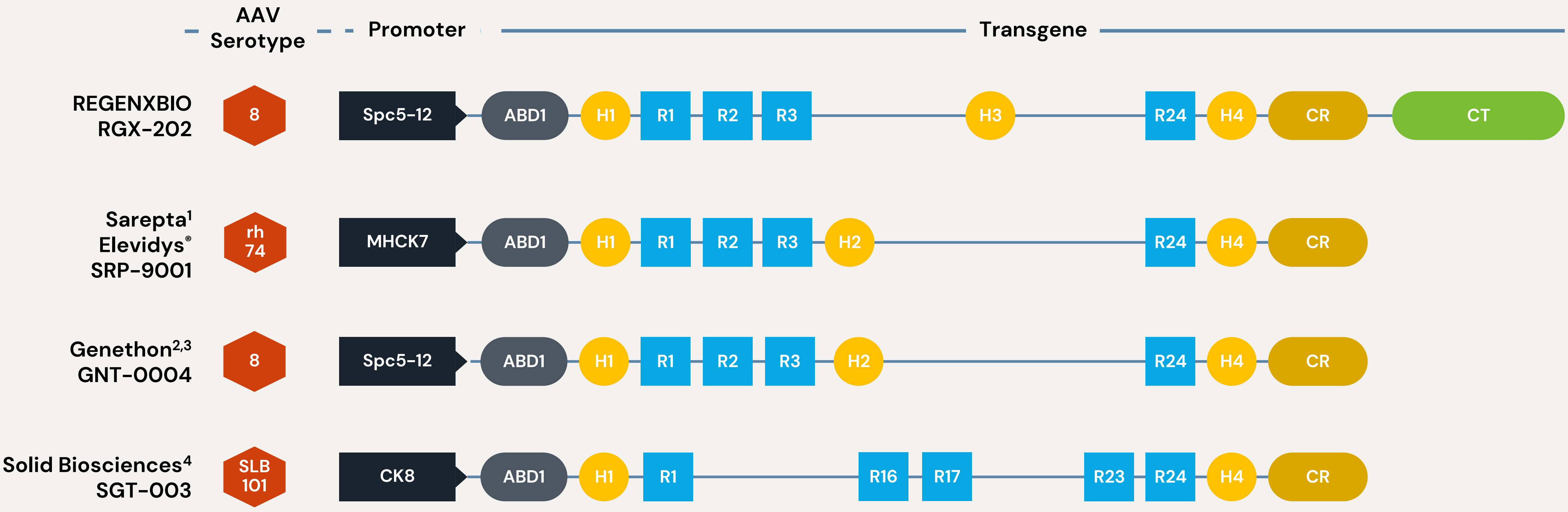
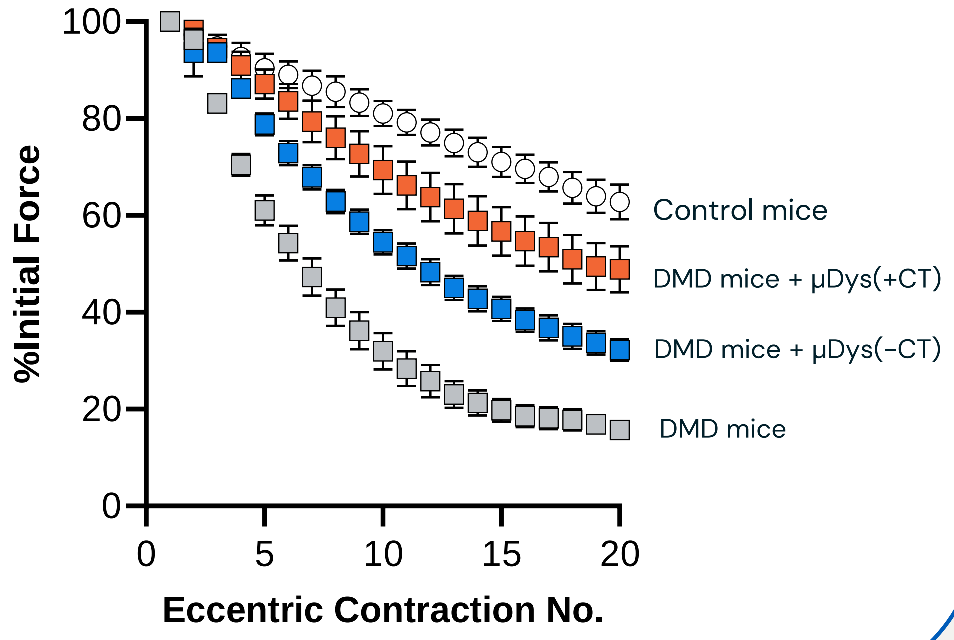
RGX-202 is the only microdystrophin gene therapy with the functional elements of the C-Terminal (CT) domain found in naturally occurring dystrophin



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

Preclinical studies indicate CT domain in RGX-202 microdystrophin preserves muscle health and enables muscle resilience

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



How the CT Domain May Contribute to Improved Outcomes

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 the RGX-202 microdystrophin, which remained in muscle longer*

Muscle health

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

Foltz (2025) MDA
* Data not shown

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Interim Phase I/II Data

Phase I/II Trial Overview

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	4+ yo
10 meter walk without assistance	100 meter walk without assistance
Stable dose on or off corticosteroids x 12 weeks	Stable dose of corticosteroids x 12 weeks
Weight >10kg	

✔ **Dose Level 1**
Dose Evaluation
$1x10^{14}$ GC/kg
n=3

→

✔ **Dose Level 2**
Dose Evaluation
$2x10^{14}$ GC/kg
n=2

→

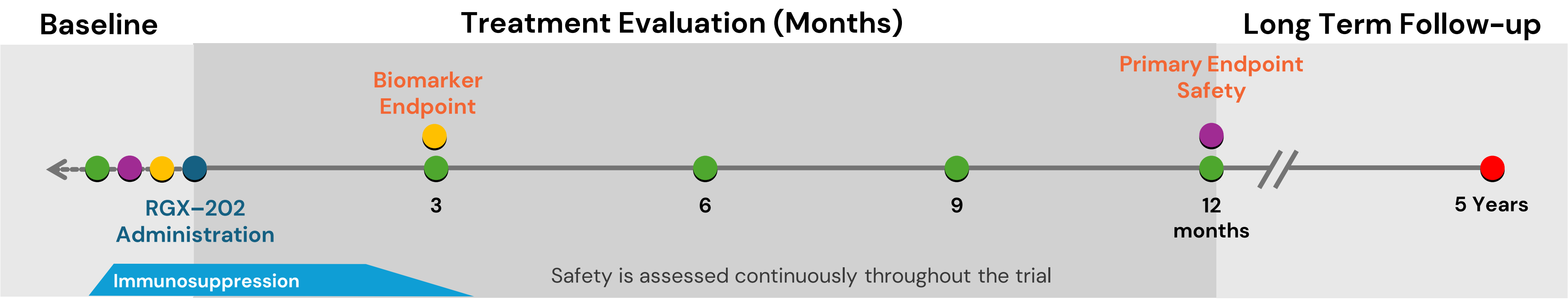
✔ **Dose Level 2**
Expanded Cohort
$2x10^{14}$ GC/kg
n= 5 patients

Dose Level 2
1-3 yr olds
$2x10^{14}$ GC/kg
(up to 5 patients)

✔ Fully enrolled

Phase I/II Trial Design

Administration and Assessments Timeline



Muscle biopsy	(yellow)	All:	RGX-202 microdystrophin, VCN, % positive fibers
Muscle Function	(green)	4+	TTStand, 10 MRW, TTClimb, NSAA
		1 to <4	PDMS-3
MRI	(purple)	4+	Skeletal and cardiac

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

Adapted from Dastgir (2024) Breakthroughs in Muscular Dystrophy, Chicago

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 = 2)	**4–11** (n = 7)
Age at Dosing (yrs)	**7.1** (4.4–10.5)	**3.0** (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)	**20.6** (17.5–23.1)	**3.4** (1.5,5.3)	**10.6** (4.9–15.5)
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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† Boys 1-3 years old complete the Peabody Developmental Motor Scale, Third Edition (PDMS-3) at baseline; NSAA collected but not applicable

Interim Safety

RGX-202 Treatment-Emergent Adverse Events		Dose Level 1 Dose Evaluation ($1x10^{14}$ GC/kg)	Dose Level 2 Younger Boys ($2x10^{14}$ GC/kg)	Dose Level 2 Dose Evaluation / Expansion ($2x10^{14}$ GC/kg)	Total n = 12
Age Range (number dosed)		4-11 (n = 3)	1-3 (n = 2)	4-11 (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=6), vomiting (n=3), and fatigue (n=5), all resolved					

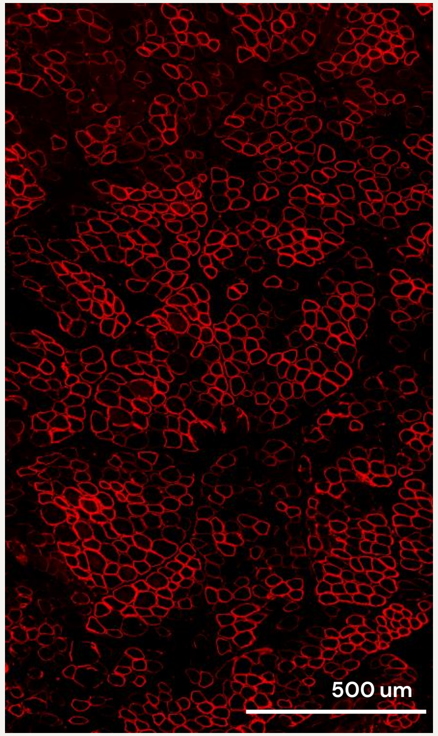
RGX-202 has been well-tolerated in all patients at both dose levels with no SAEs or AESIs

Data cut data February 21, 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 1×10^{14} GC/kg		Dose Level 2 2×10^{14} GC/kg		
Age range at screening (number with data)	4-7 (2)	8-11 (1)	1-3 (1)	4-7 (2)	8-11 (5)
RGX-202 Microdystrophin* % (Western Blot)	**60.6** (37.8, 83.4)	**10.4** (n/a)	**122.3** (n/a)	**54.3** (31.5, 77.2)	**39.7** (20.8, 75.7)
VCN copies/nucleus (qPCR)	**9.8** (7.4, 12.1)	**5.4** (n/a)	**20.4** (n/a)	**30.1** (4.9, 55.4)	**17.8** (12.0, 30.7)
Positive Fibers** % (Immunofluorescence)	**79.3***** (n/a)	**34.6** (n/a)	**82.1** (n/a)	**50.3** (29.4, 71.1)	**45.7** (21.3, 70.6)

RGX-202 Microdystrophin DL 2, 12 weeks



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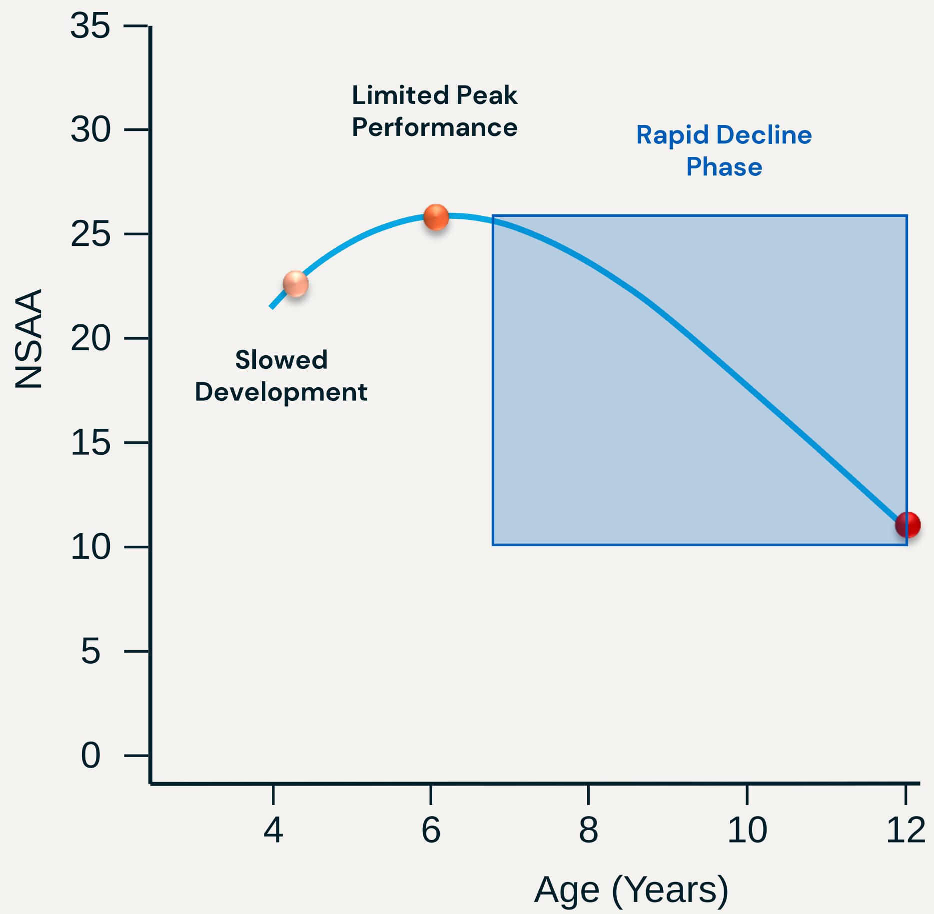
Data cut date February 21, 2025
* Microdystrophin expression adjusted for muscle content; % normal control
**Positive Fibers defined as change from baseline of RGX-202 microdystrophin & dystrophin positive fibers
*** One sample could not be evaluated

RGX-202 Functional Data: Natural History Control Methodology

Mean NSAA Trajectory in Duchenne



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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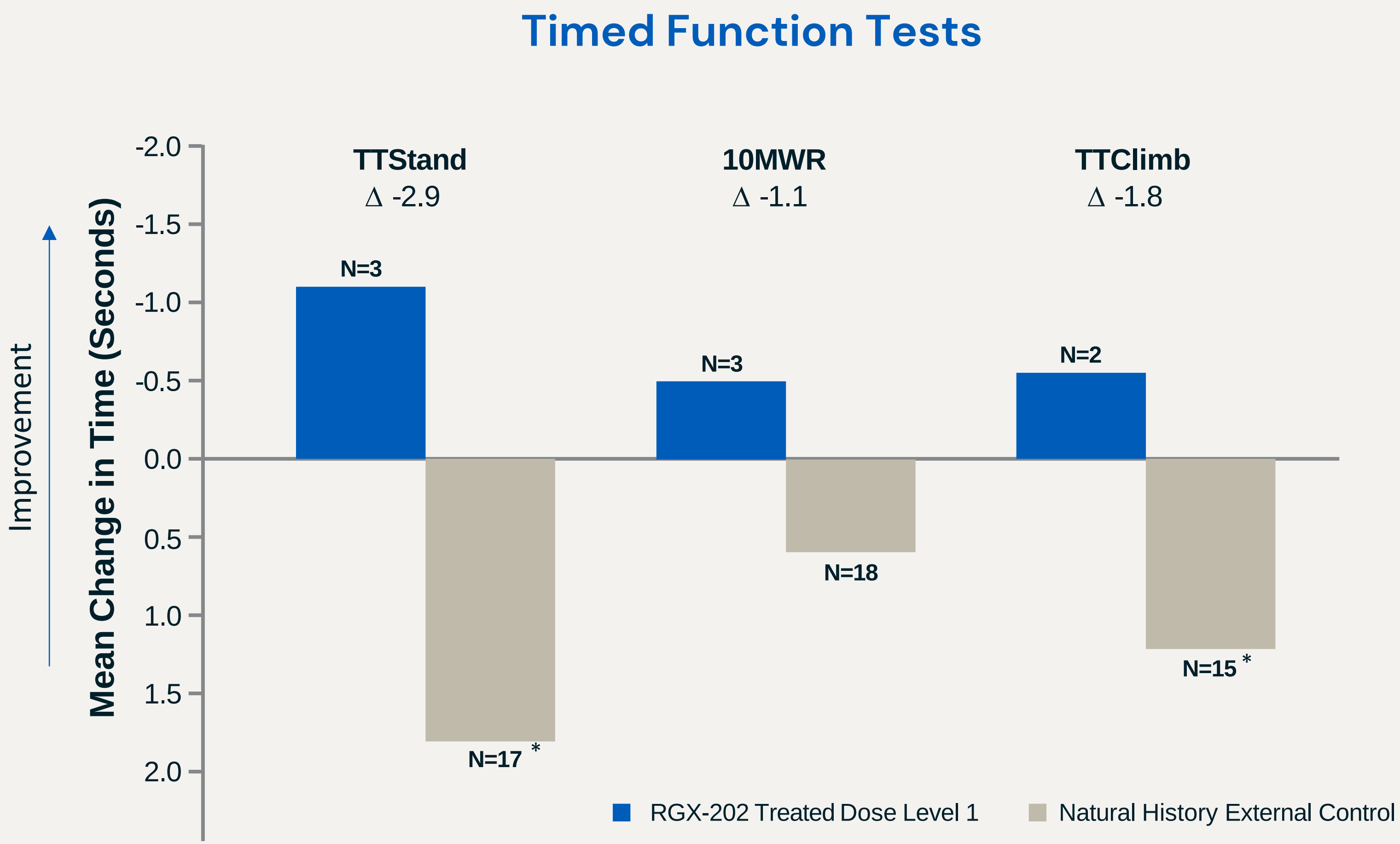
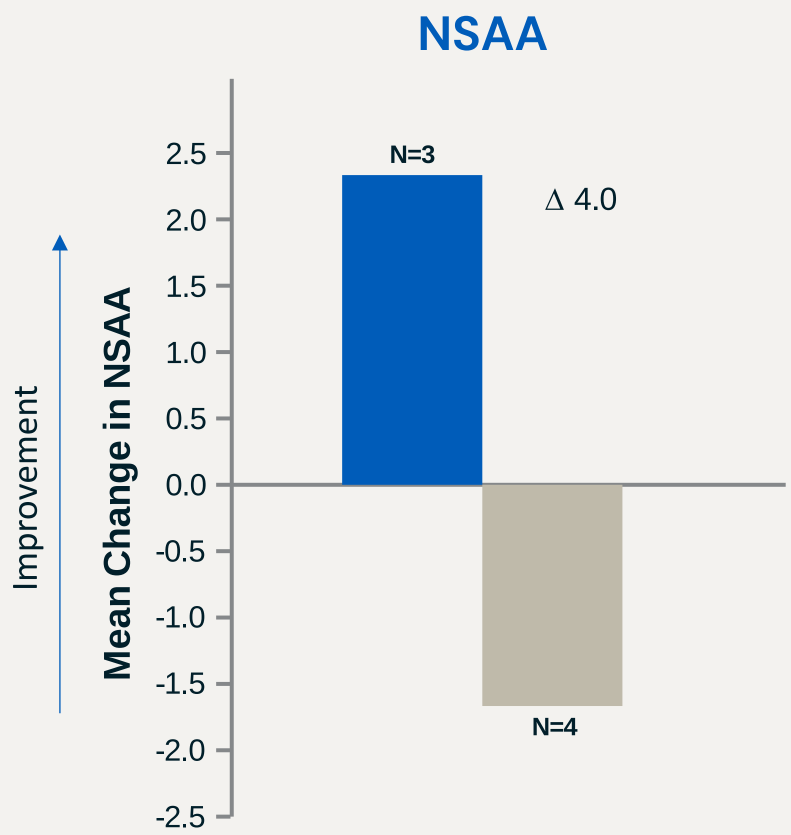
Graph adapted from Muntoni 2019

* Natural history datasets included 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).

** 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 participant.

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

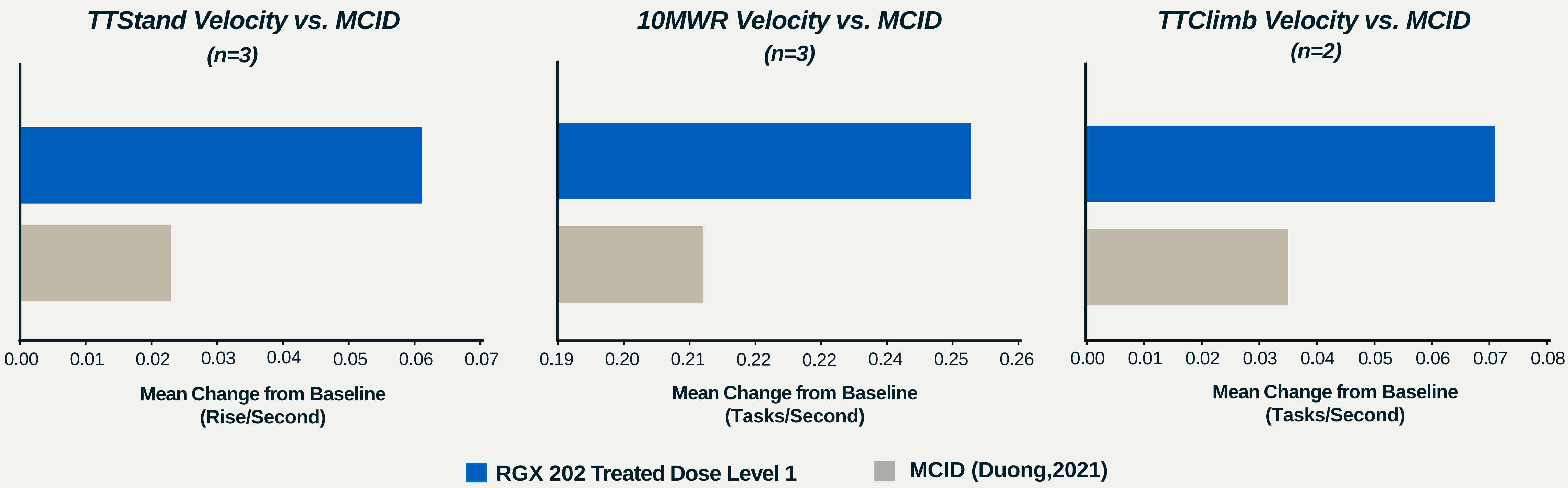




Data cut date November 1, 2024
Time to Stand (TTStand); 10M Walk Run (10MWR); Time to Climb (TTClimb)
*One NH EC patient did not have a TTStand and one RGX-202 patient did not have TTClimb so associated NH EC also removed

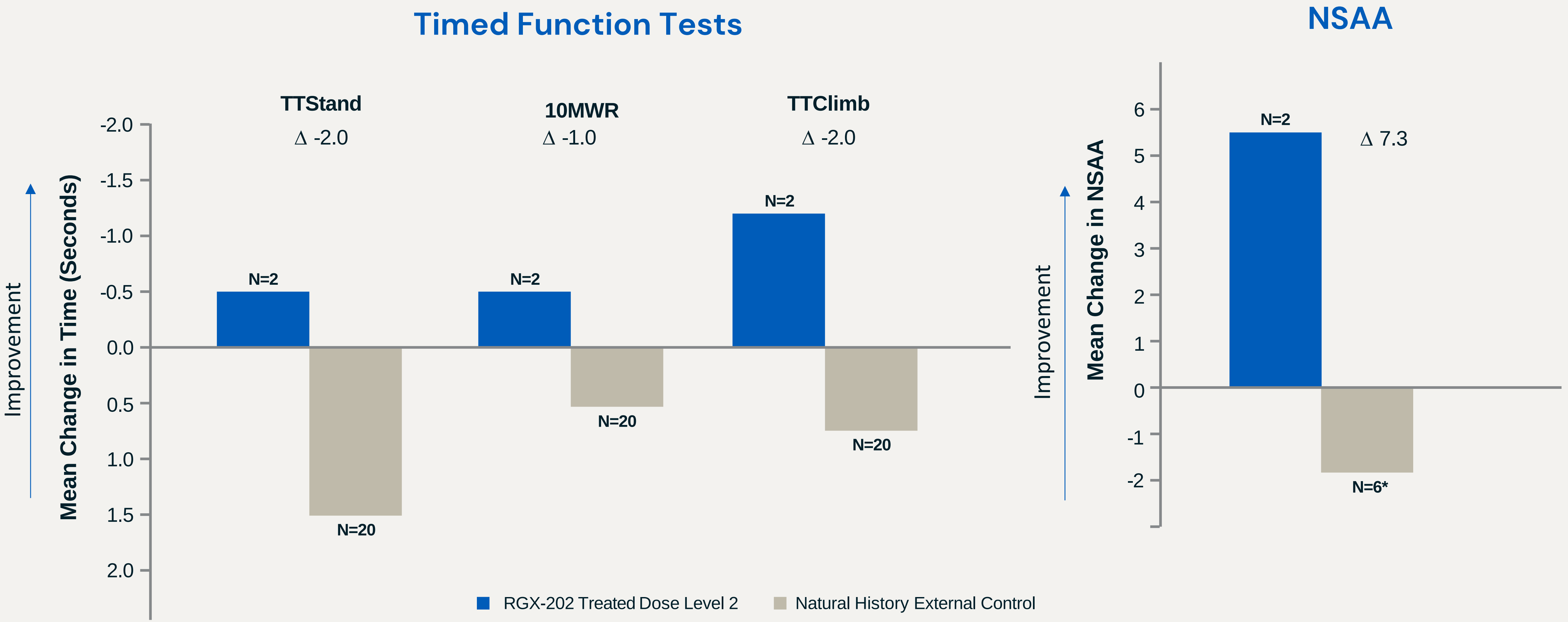
Dose Level 1 Timed Task Velocity Changes Exceed MCID Benchmarks at 12 months

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



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

Photo not representative of all patients

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 listed measures at 12 months (dose level 1) or 9 months (dose level 2) change from baseline

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Pivotal Trial Design

AFFINITY DUCHENNE Phase III Trial: Open & Enrolling

Key Eligibility Criteria (n = 30)

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

1 to <4yo	4+ yo
10 meter walk without assistance	100 meter walk without assistance
Stable dose on or off corticosteroids x 12 weeks	Stable dose of corticosteroids x 12 weeks
Weight >10kg	NSAA ≥ 16

Pivotal Endpoints

Primary Endpoint: Proportion of patients with ≥ 10% RGX-202 microdystrophin levels

Secondary Endpoints: Timed function tests (including vTTStand) 4+ yo; PDMS-3 & SV95C for 1 to <4 yo; safety

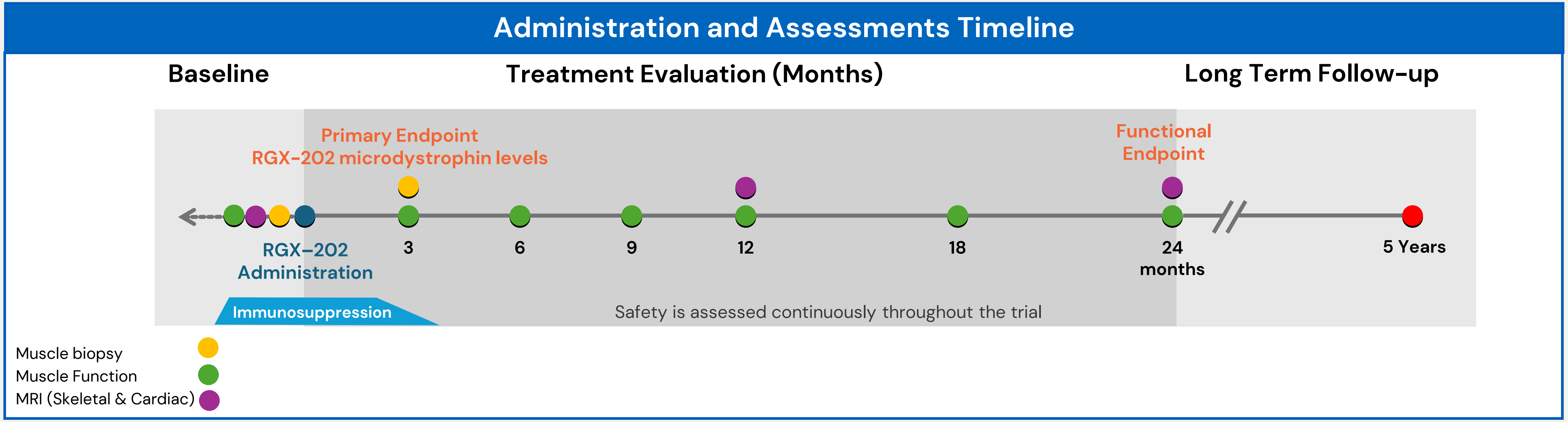
Exploratory Endpoints: NSAA, SV95C & MRIs for 4+ yo

Access ClinicalTrials.gov: AFFINITY DUCHENNE® for additional information

vTTStand: time to stand velocity
PDMS-3: Peabody Developmental Motor Scale, Third Edition

AFFINITY DUCHENNE Pivotal Trial Design

A multi-center, open-label pivotal trial



AFFINITY DUCHENNE: Phase I/II Interim Summary

Phase III trial open and enrolling

RGX-202 has been well-tolerated in 12 patients across both dose levels with no SAEs or AESIs[1]

Biomarkers support consistent robust expression, transduction, and sarcolemmal localization of RGX-202 microdystrophin[1]

Participants treated with RGX-202:

- Demonstrated clinically meaningful improvement in functional outcomes at both dose levels
- Exceeded comparisons using NH external controls and MCID*[2]

- Pivotal trial is active and recruiting ambulatory boys aged 1 and above
- REGENXBIO plans to use RGX-202 microdystrophin as a surrogate endpoint likely to predict clinical benefit to support accelerated approval

1. Data cut date February 21, 2025
2. Data cut date November 1, 2024
* MCID (minimal clinically important difference) (Duong, 2021) compared to dose level 1 at 12 mo

Acknowledgements

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