RGX-202, An Investigational Gene Therapy for the Treatment of Duchenne Muscular Dystrophy: Interim Phase I/II Clinical Data

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MDA 2026 Clinical & Scientific Conference
Orlando, FL
Wednesday, March 11, 2026

RGX-202 is an investigational product that has not been approved by any regulatory authority

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RGX-202: A Differentiated Therapeutic Approach

NOVEL CONSTRUCT

- NAV® AAV8 vector
- Muscle-specific promoter
- Only microdystrophin construct encoding C-Terminal domain

IMMUNE SUPPRESSION

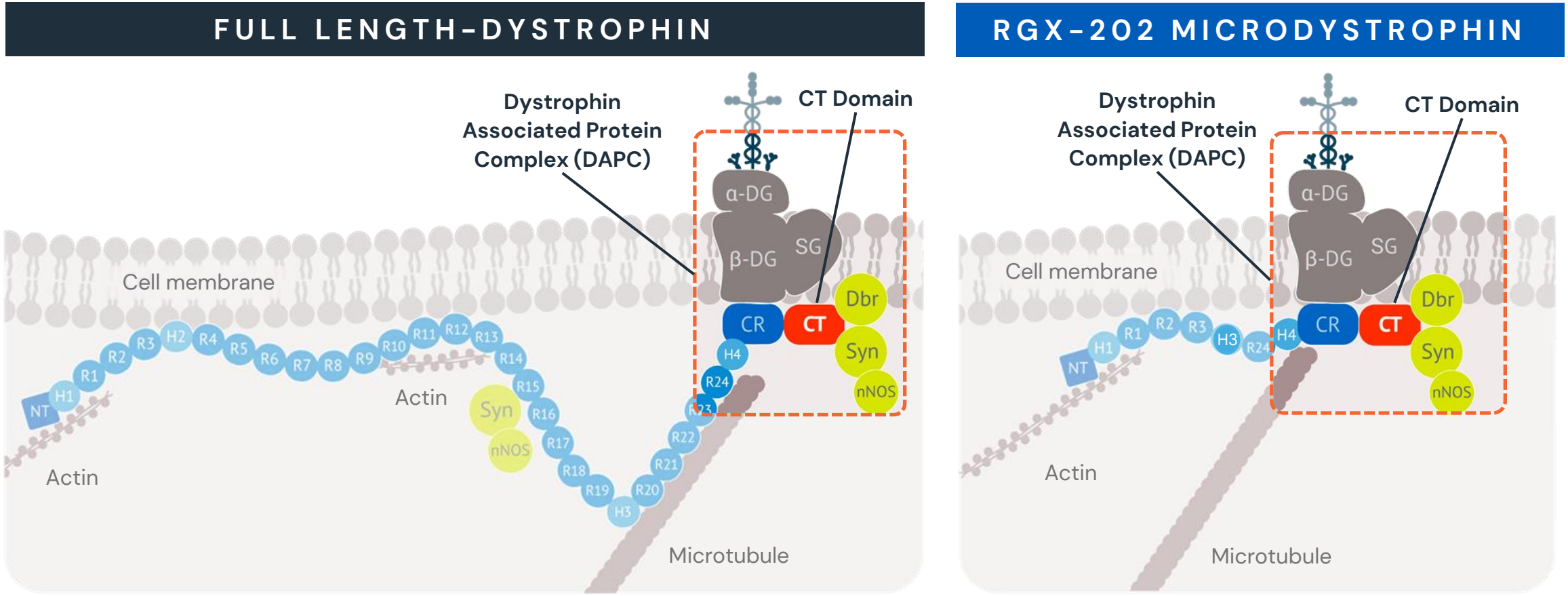
- Comprehensive, proactive immune suppression regimen implemented from the outset of the program

MANUFACTURING

- Leading purity levels (>80% full capsids) in Duchenne gene therapy allows for maximum therapeutic dose with lower capsid load

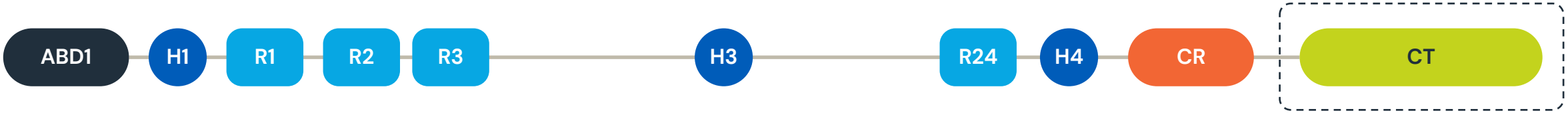
RGX-202 Contains Key Elements of Full-Length Dystrophin

Only microdystrophin construct with C-terminal (CT) domain



Syn: Syntrophin; Dbr: Dystrobrevin; CR: Cysteine rich; nNOS: Neuronal nitric oxide synthase; DG: Dystroglycan
H: Hinge; R: Repeat; NT: N-Terminal; CT: C-Terminal

Preclinical Studies Indicated the CT Domain in RGX-202 Microdystrophin Preserved Skeletal and Cardiac Muscle Health and Enabled Muscle Resilience



HOW THE CT DOMAIN MAY CONTRIBUTE TO IMPROVED OUTCOMES[1]

Prolonged microdystrophin (µDys) activity

The CT domain significantly enhanced restoration of the DAPC, stabilizing the µDys in muscle cells and potentially allowing it to accumulate at higher levels and act for extended periods of time[2]

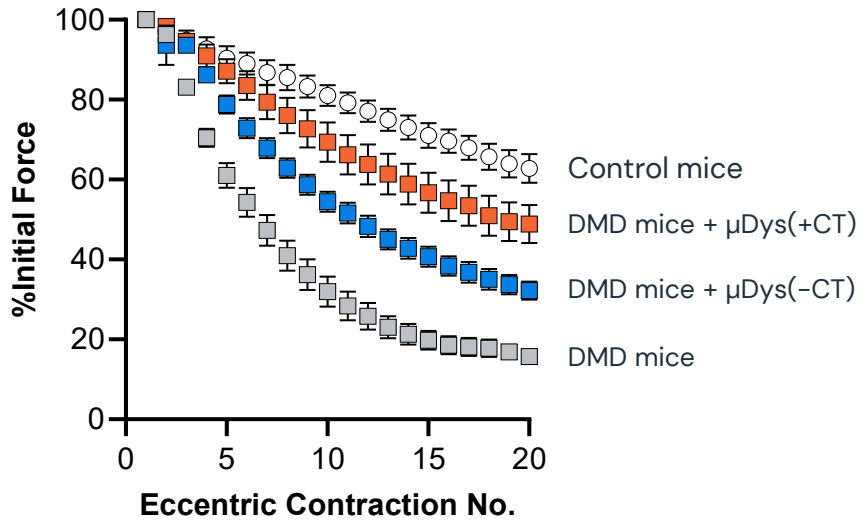
Skeletal Muscle health

CT domain in RGX-202 µDys protected against contraction-induced damage in DMD mice, enabling better muscle recovery

Cardiac Muscle health

RGX-202 µDys protected the against cardiomyopathy in a pharmacologically induced model[3]

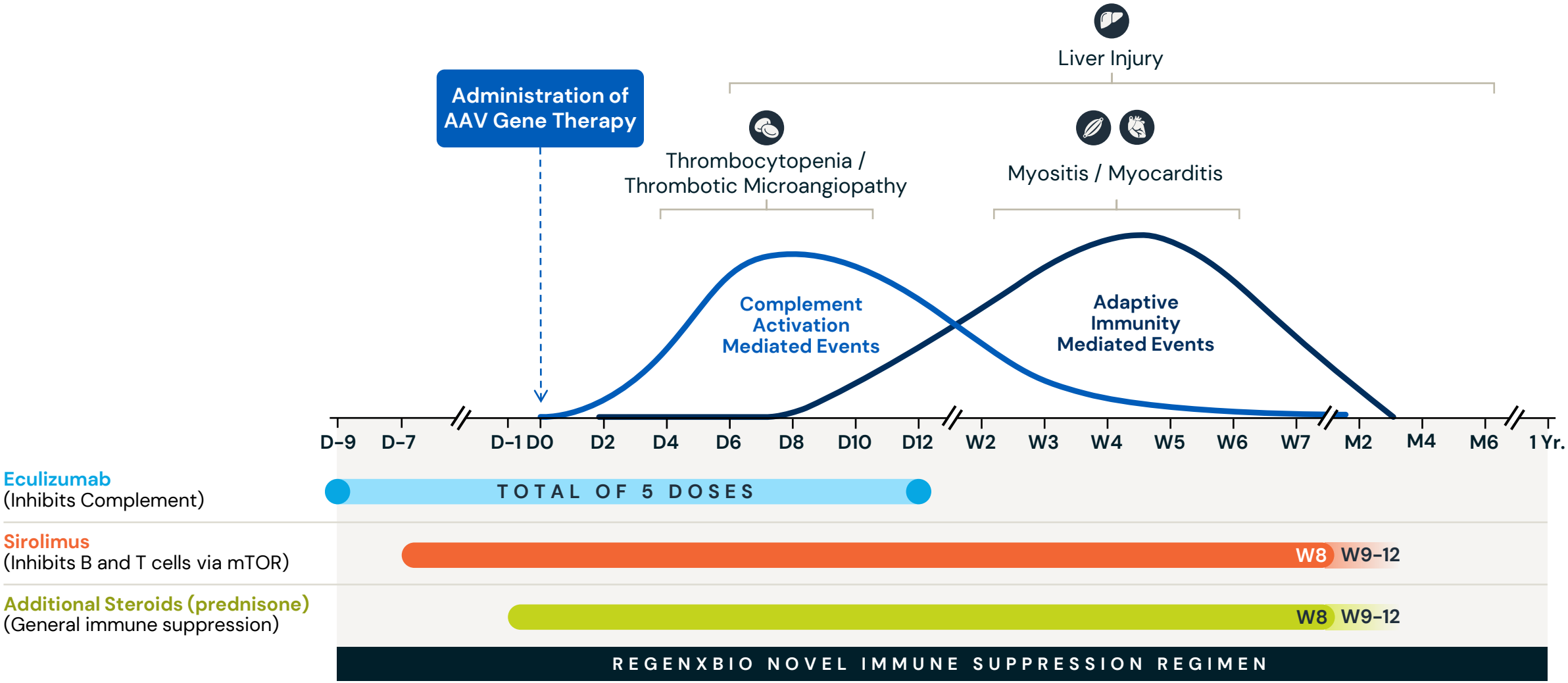
Microdystrophin+CT domain better protected the muscle against contraction-induced damage



[1] Foltz (2025) *Mol Ther Meth Clin Dev*
[2] Data not shown
[3] Foltz (2026) MDA Clinical & Scientific Conference, Orlando, FL

µDys: Microdystrophin; ABD: Actin-binding domain; H: Hinge; R: Repeat; CR: Cysteine rich; CT: C-Terminal

RGX-202 Immune Suppression Regimen



Adapted from Servais, Neuromuscular Disorders (2023) 33:884-896.

Duvuru, *Ped Neurol* (2024) 163:1-3. Laforet, *Hum Gene Ther* (2025) 36:64-76. Oskoui, *Neurology* (2025) 104:e213604. Salabarria, *J Clin Invest* (2024) 134(1):e173510. *Silver, Int J Card* (2024) 398:131617. Zaidman, *J Neuromusc Dis* (2024) 11:687-699.

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Interim Phase I/II Data

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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
- Perform supine to stand without assistance

4 to <12 yo

- 100-meter walk without assistance
- Time to stand ≥3 or <9 seconds
- Stable dose of corticosteroids x 12 weeks

Phase I/II Trial Endpoints

- **Primary Endpoint:** Safety
- **Biomarker Endpoint:** Microdystrophin expression
- **Secondary Endpoints:**

<4yo: PDMS-3

4 to <12 yo function (including TTStand, 10MWR, TTClimb, and NSAA)

Adapted from Pakola (2025) World Muscle Society, Vienna, Austria

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; SV95C: Stride velocity 95th centile

Phase I/II Interim Key Baseline Demographics

VARIABLE MEAN (range)	DOSE LEVEL 1 1X10^{14} GC/kg	DOSE LEVEL 2 (PIVOTAL DOSE) 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)
Mean age at last assessment (yrs)	**9.5** (6.9-13.0)	**4.0** (3.0-4.7)	**10.2** (7.3-14.1)
Time from Dosing (months)	**31.1** (28.0-33.5)	**12.0** (8.2-15.8)	**21.1** (15.3-26.0)
Weight (kg) **at dosing**	**24.3** (17.8-28.3)	**11.4** (10.3-12.5)	**26.2** (17.3 – 35.5)
BMI (kg/m2)	**20.4** (17.8-24.8)	**15.5** (14.5-16.1)	**18.8** (15.1-25.8)
BASELINE FUNCTION			
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)

Data cut date: January 5, 2026

† Boys 1-3 years old complete the Peabody Developmental Motor Scale, Third Edition (PDMS-3) at baseline; NSAA collected but not applicable Pakola (2025) World Muscle Society, Vienna. Austria

GC: Genome copies; BMI: Body mass index; NSAA: North Star Ambulatory Assessment

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Phase I/II Interim Safety

RGX-202 was well tolerated with no SAEs or AESIs up to 24 months

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	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 were: vomiting (n=7), fatigue (n=6), and nausea (n=4)

Data cut date: January 5, 2026

AESI criteria prospectively defined per protocol.
Drug-Induced Liver Injury: GGT > 3 × ULN, or GLDH > 2.5 × ULN, or ALT > 3 × baseline

SAE: Serious adverse event; AESI: Adverse event of special interest; GC: Genome copies

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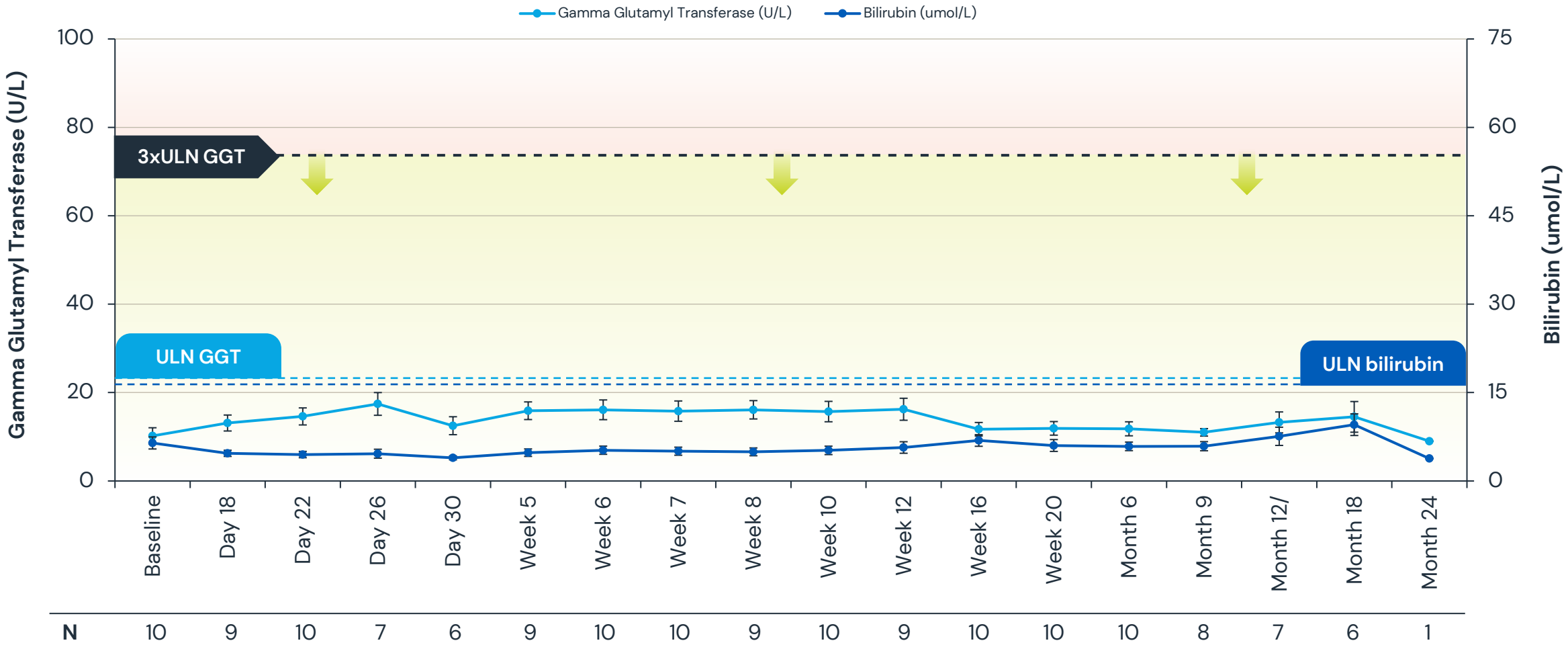
Pivotal Dose: Liver Safety Findings Up to 24 Months

Mean GGT and total bilirubin not exceeding ULN



Data cut date: January 5, 2026

Each point represents the mean +/- SEM of all subjects with an assessment windowed into that particular visit.
Due to constraints, not all counts are displayed beneath the figure.
Bilirubin ULN is 17.1 umol/L; GGT ULN is 24 U/L

GGT: Gamma glutamyl transferase; ULN: Upper limit of normal

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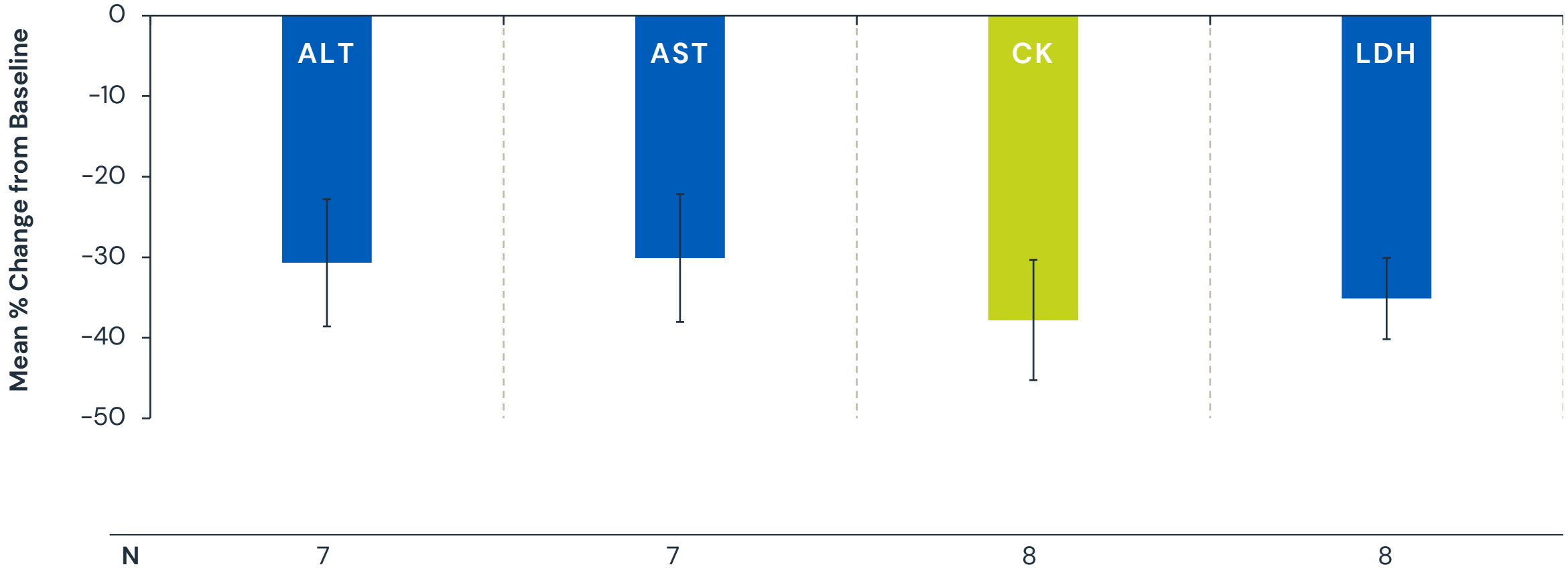
Pivotal Dose: Reductions in CK and Other Biomarkers Observed at 1 Year

MONTH 12



Data cut date: January 5, 2026

Bars represent mean +/- SEM

ALT: Alanine transaminase; AST: Aspartate transaminase; CK: Creatine kinase; LDH: Lactate dehydrogenase

Phase I/II Biomarkers Supported Consistent Robust Expression, Transduction, and Sarcolemmal Localization of RGX-202 Microdystrophin

WEEK 12 BIOPSY		RGX-202 Microdystrophin[1] % (Western Blot)	VCN copies/nucleus (qPCR)	Positive Fibers[2] % (Immunofluorescence)
DOSE LEVEL 1 $1X10^{14}$ GC/kg	4–7 (2)	60.6 (37.8, 83.4)	9.8 (7.4, 12.1)	79.3[3]
	8–11 (1)	10.4	5.4	34.6
DOSE LEVEL 2 (PIVOTAL DOSE) $2X10^{14}$ GC/kg	1–3 (3)	97.3 (51.2, 122.3)	24.8 (20.4, 29.1)	76.7 (50.8, 97.1)
	4–7 (2)	54.3 (31.5, 77.2)	30.1 (4.9, 55.4)	50.3 (29.4, 71.1)
	8–11 (5)	39.7 (20.8, 75.7)	17.8 (12.0, 30.7)	45.7 (21.3, 70.6)

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[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

VCN: Vector copy number; qPCR: Quantitative polymerase chain reaction; GC: Genome copies

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AFFINITY DUCHENNE® External Control Methodology

External Data Sources

- FOR-DMD
- BioMarin PRO-DMD-01 (CureDuchenne)
- CINRG DNHS
- cPATH / D-RSC

STEP 1

Filter EC Participants by Key Entry Criteria

- Stable dose of corticosteroid for 12 weeks
- Aged ≥ 4 and ≤ 1 + the maximum age of treated group (13)
- TTSTAND >3 and < 9 Seconds
- TTRW within +/- 1 sec of the treated group (3.2-7.0 seconds)

STEP 2

Further Balance Baseline Covariates of RGX and EC Group at Individual Patient Level

SAP Primary Method: *Propensity-Score Weighting

- Age
- NSAA
- TTSTAND
- TTRW

cTAP (Collaborative Trajectory Analysis Project)

- A cross-validated, longitudinal prognostic model that uses baseline age and motor function measures to predict up to 5-year NSAA trajectories in ambulatory steroid-treated boys with DMD.

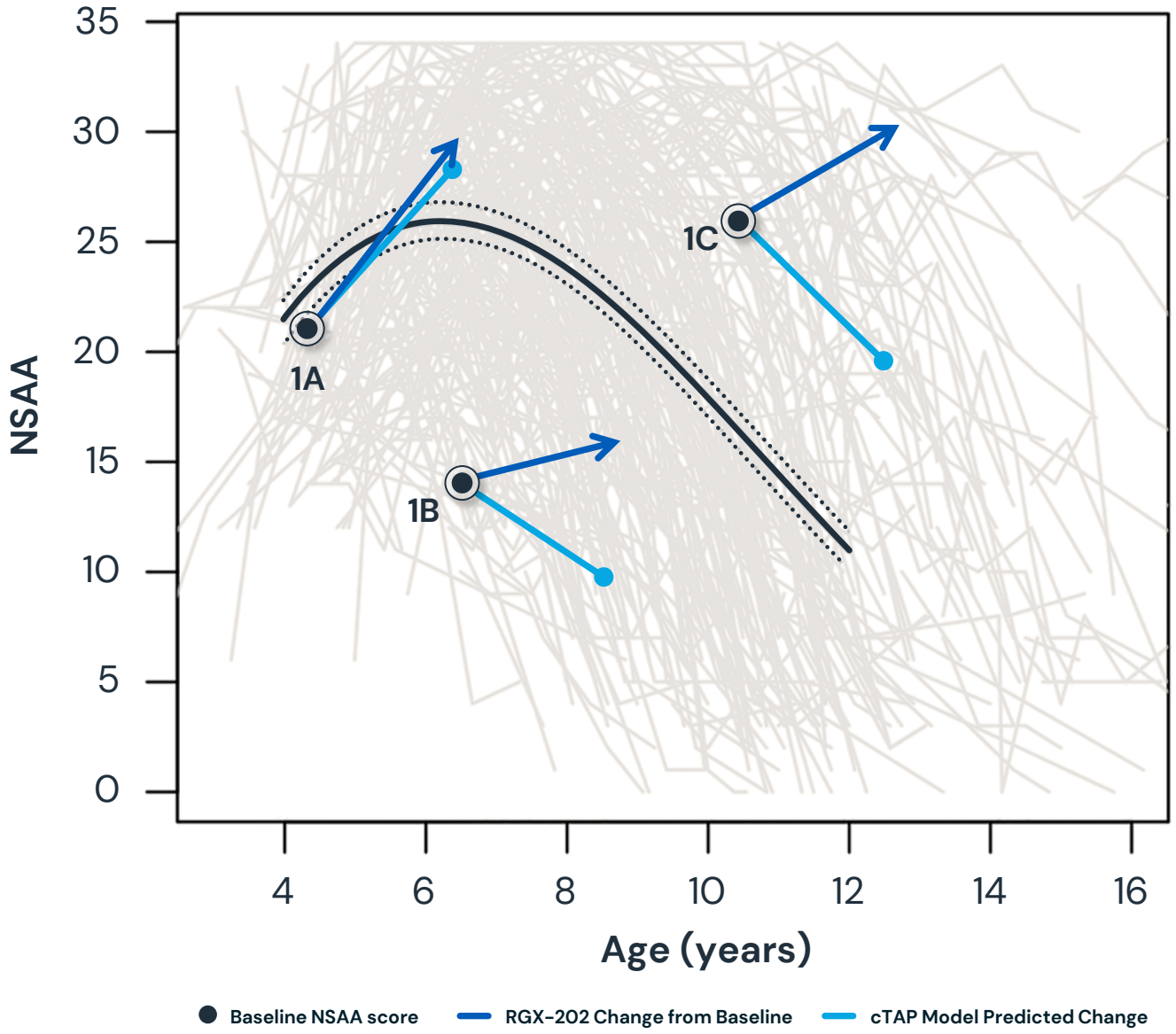
MULTIPLE, VALIDATED METHODS TO DETERMINE EXPECTED TRAJECTORY

*Propensity-score weighting method mimics a randomization setting for RGX-202-1101 study by taking an EC group with similar entry criteria and balancing baseline age and function. It assigned higher weights to patients in the EC group with greater similarity to RGX-202 treated patients.
FOR-DMD, Finding the Optimum Regimen for Duchenne Muscular Dystrophy; NSAA, North Star Ambulatory Assessment; TTSTAND, Time to stand; TTRW, time to run/walk 10 meters.
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)

Muntoni F, Signorovitch J, Goemans N, Manzur AY, Done N, Sajeev G, Li J, Akbarnejad H, Sharma A, Ward SJ, Niks EH, Servais L, Mercuri E, Guglieri M, Straub V, de Groot I, Ridout D; PRO-DMD-01 study investigators; Association Française contre les Myopathies; NorthStar Clinical Network; McDonald C. Predicting trajectories of the north star ambulatory assessment total score in Duchenne muscular dystrophy. PLoS One. 2025 Jun 27;20(6):e0325736. doi: 10.1371/journal.pone.0325736. PMID: 40577272; PMCID: PMC12204569.

Dose level 1: NSAA Outcomes at 2 Years

NSAA performance exceeded expected disease trajectory



Data cut date: January 5, 2026

Fig 1. NSAA total score trajectories for individual patients by age (in grey) and the fitted mean and 95% confidence interval (in black).
Each grey line represents NSAA total scores from an individual patient plotted versus age; the population mean and its 95% confidence bands are shown in black.

NSAA, North Star Ambulatory Assessment.

Muntoni F et al. (2019) Categorising trajectories and individual item changes of the North Star Ambulatory Assessment in patients with Duchenne muscular dystrophy. PLoS ONE 14(9): e0221097. https://doi.org/10.1371/journal.pone.0221097.g001

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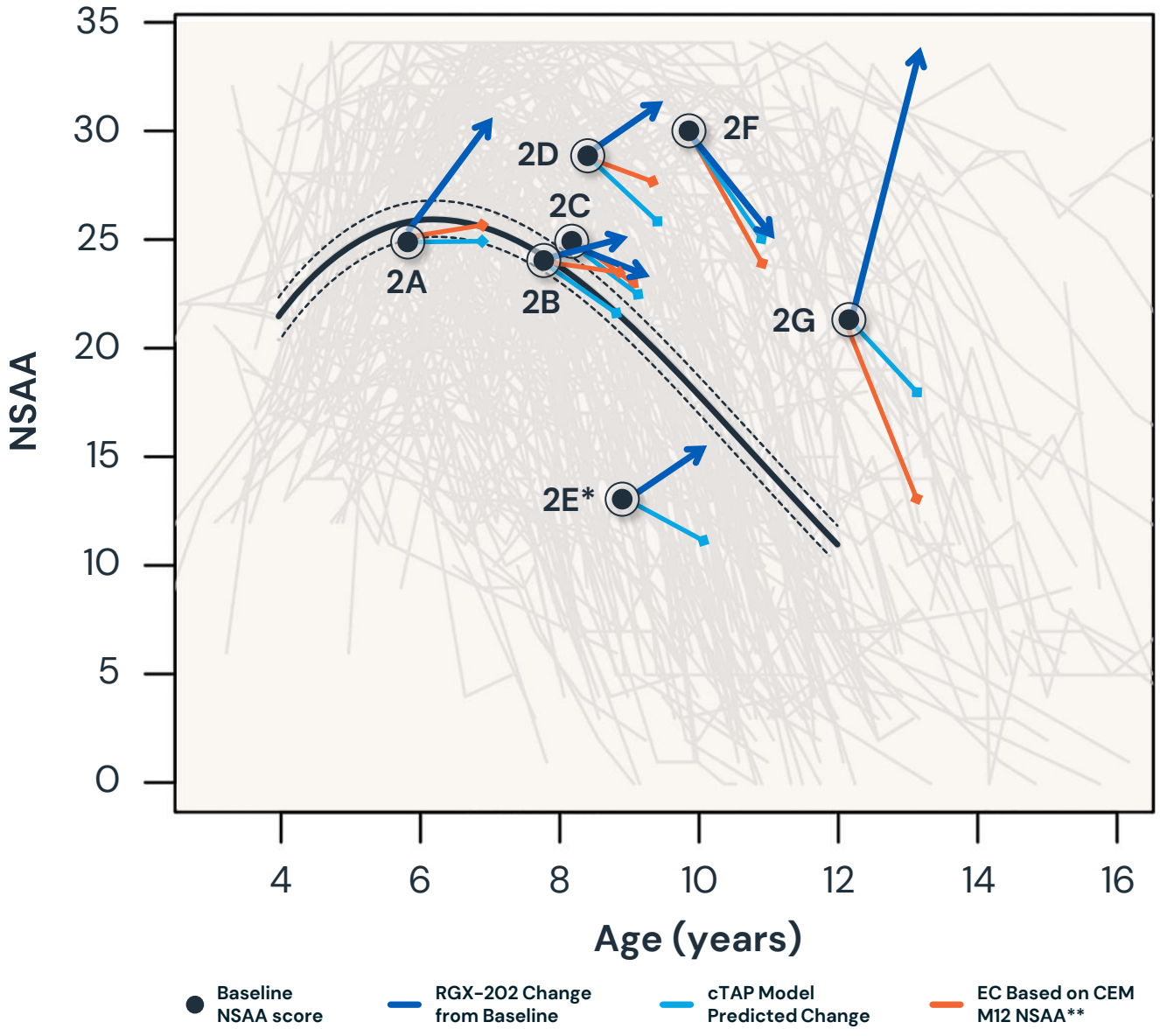
Pivotal Dose: NSAA Outcomes at 1 Year

NSAA performance exceeded external controls and expected disease trajectory



Data cut date: January 5, 2026

Fig derived from Muntoni et al. NSAA total score trajectories for individual patients by age (in grey) and the fitted mean and 95% confidence interval (in black). Each grey line represents NSAA total scores from an individual patient plotted versus age; the population mean and its 95% confidence bands are shown in black.

NSAA, North Star Ambulatory Assessment; CEM: Coarsened exact matching; M12: Month 12

Muntoni F et al. (2019) Categorising trajectories and individual item changes of the North Star Ambulatory Assessment in patients with Duchenne muscular dystrophy. PLoS ONE 14(9): e0221097. https://doi.org/10.1371/journal.pone.0221097

*2E Month 12 collected approximately Month 10.8

**Coarsened exact matching based on: Age +/- 1 year, NSAA +/-2, TTSTAND +/- -.5 seconds; TTRW +/- 1 sec.

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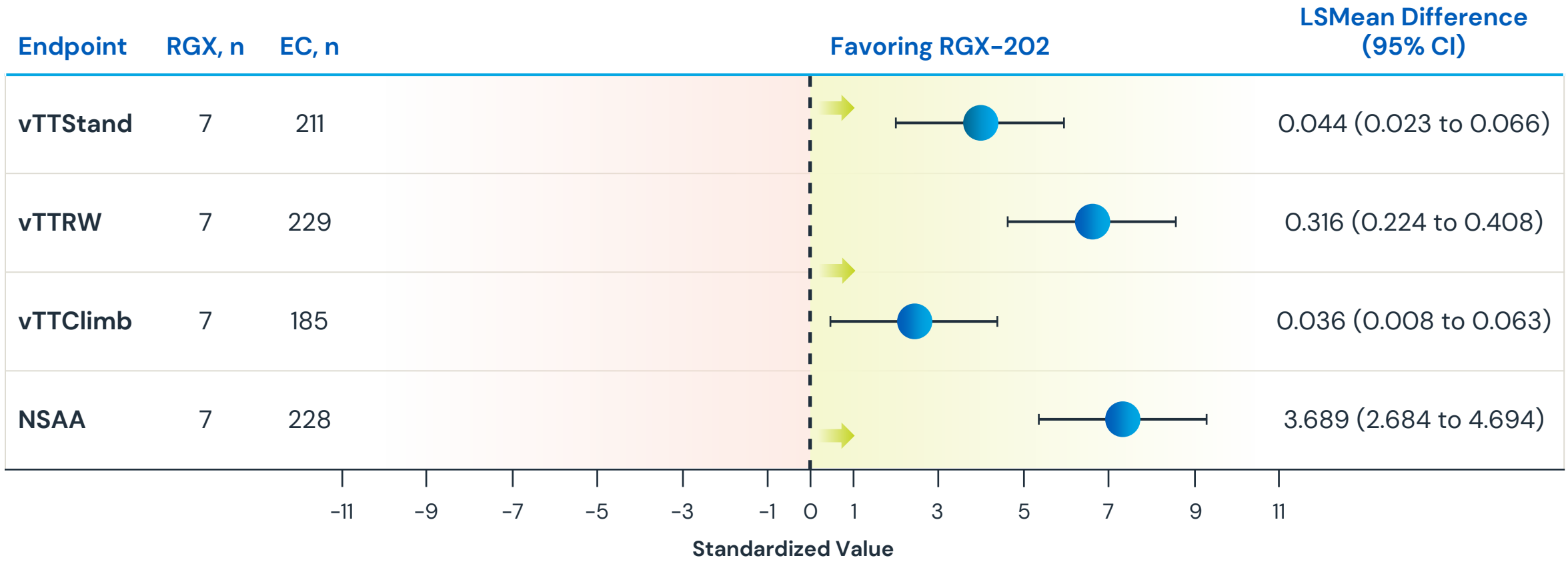
Pivotal Dose: Functional Improvements at 1 Year Compared with External Controls

Exceeded external controls using propensity score weighting

Endpoint	RGX, n	EC, n	LSMean Difference (95% CI)
vTTStand	7	211	0.044 (0.023 to 0.066)
vTTRW	7	229	0.316 (0.224 to 0.408)
vTTClimb	7	185	0.036 (0.008 to 0.063)
NSAA	7	228	3.689 (2.684 to 4.694)



Data cut date: January 5, 2026

V: velocity; TTStand: Time to Stand; TTRW: Time to Run and Walk; TTClimb: Time to Climb; NSAA: North Star Ambulatory Assessment; EC: External controls

Least Square Mean (LSMean) differences were estimated using a mixed model for repeated measures (MMRM), comparing the change from baseline for RGX versus external controls (EC), adjusting for age at dosing and baseline functional test score. To ensure that a favorable RGX effect appears to the right side of zero in the forest plot, data transformations were applied. Specifically, the values of timed functional tests were multiplied by -1. The plot also standardized the values of different parameters with different units by graphing the standardized effect size (LSM and 95% CI divided by standard error).

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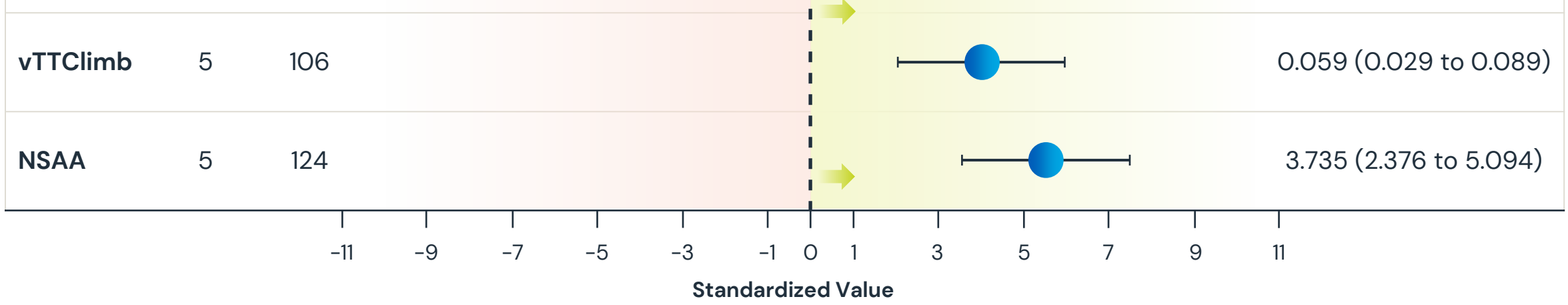
Pivotal Dose: Functional Improvements at 1 Year Compared with External Controls in Participants Aged 8+ (n=5)

Exceeded external controls using propensity score weighting

Endpoint	RGX, n	EC, n	LSMean Difference (95% CI)
vTTStand	5	115	0.059 (0.030 to 0.089)
vTTRW	5	126	0.297 (0.174 to 0.420)
vTTClimb	5	106	0.059 (0.029 to 0.089)
NSAA	5	124	3.735 (2.376 to 5.094)



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Cardiac Data

Cardiac MRI is the Gold Standard in DMD

Superior accuracy and reproducibility[1]

- Cardiac MRI (cMRI) provides accurate and reproducible measurements of ejection fraction (EF)
- cMRI is not dependent on acoustic windows, which may be poor in participants with DMD
- Small longitudinal changes in EF are detected more reliably than with ECHO

Early detection of myocardial disease[3,4]

- Global strain parameters correlate with rate of cardiac disease progression
- cMRI identifies myocardial fibrosis using late gadolinium enhancement (LGE)
- Fibrosis often appears before EF declines

Better risk stratification[2]

- Presence and extent of LGE correlates with future EF decline, ventricular arrhythmias, and adverse outcomes

Cardiac MRI enables earlier detection and more accurate tracking of ventricular function and myocardial fibrosis in DMD compared to ECHO

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[1] Brunklaus et al. *Eur J Paediatr Neurol.* 2015
[2] Birnkrant et al. *Lancet Neurol.* 2018.
[3] Hor and Tonnis. *Journal of Cardiovascular Magnetic Resonance.* 2024
[4] Earl CC et al. *Journal of Cardiovascular Magnetic Resonance*, 2025

MRI: Magnetic resonance imaging; ECHO: Echocardiography

Pivotal Dose: Cardiac Function Remained Stable Through 1 Year

	BASELINE	12 MONTHS
Subjects (N)	**7**	**7**
Age Mean (range)	**8.7*** (5.8–12.1)	**9.7** (6.8–13.1)
Left Ventricular Ejection Fraction Mean (range) Median	**61.7 %** (54–72**) 60%	**61.6%** (57–74) 60%
Global Circumferential Strain*** Mean (range) Median	**-20.4 %** (-22% to -19%) -20.4 %	**-20.9 %** (-23% to -17%) -21.5%
Late Gadolinium Enhancement (LGE)	***1 participant with fibrosis***	***No change from baseline***

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*Age at dosing
**One participant met LVEF criteria at baseline by ECHO of >55%; later cMRI had measure of 54
*** More negative strain values are better.

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AFFINITY DUCHENNE® Confirmatory Trial

Currently Enrolling

Key Eligibility Criteria

- **Boys aged 1+ years** at screening
- **Genetically confirmed DMD:** except those with deletions or point mutations in exons 8, 9, and/or 10
- **No pre-existing antibodies** to the gene therapy (AAV8 capsid)

Aged 1 to <4yo

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

Aged 4+

- 100-meter walk without assistance
- Stable dose of corticosteroids x 12 weeks
- NSAA ≥ 16
- Time to stand ≥3 and <7 seconds

PROACTIVE IMMUNE SUPPRESSION REGIMEN

Adapted from Pakola (2025) World Muscle Society, Vienna, Austria

AFFINITY DUCHENNE® Phase I/II Trial Interim Results

Phase I/II Interim Data Summary

- **RGX-202 was well-tolerated**, with **no SAEs or AESIs** observed
- Robust expression, transduction and localization of RGX-202 microdystrophin
  - All participants demonstrated **microdystrophin expression levels above 10%** at Week 12 (pivotal trial endpoint)
- Functional improvements observed in both dose cohorts
  - Dose level 1 **NSAA exceeded expected disease trajectory** at 2 years
  - Pivotal dose showed functional improvements at 1 year **exceeding external controls and expected disease trajectory on NSAA and external controls on timed function tests**, including older boys (aged 8+)
- **Cardiac function remained stable** at 1 year based on MRI

Next Steps

- **Pivotal Phase III enrollment complete**
- **Currently enrolling confirmatory trial (n=~30) ambulatory boys aged 1+**

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SAE: Severe adverse event; AESI: Adverse event of special interest; NSAA: North Star Ambulatory Assessment; MRI: Magnetic resonance imaging

Adapted from Pakola (2025) World Muscle Society, Vienna, Austria

Acknowledgements

We Thank the Participants and their Families

Phase I/II Investigators

Aravindhan Veerapandiyan, M.D., Arkansas Children's Hospital

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