Gene Therapy Today and Tomorrow:

An Introduction to Gene Therapy

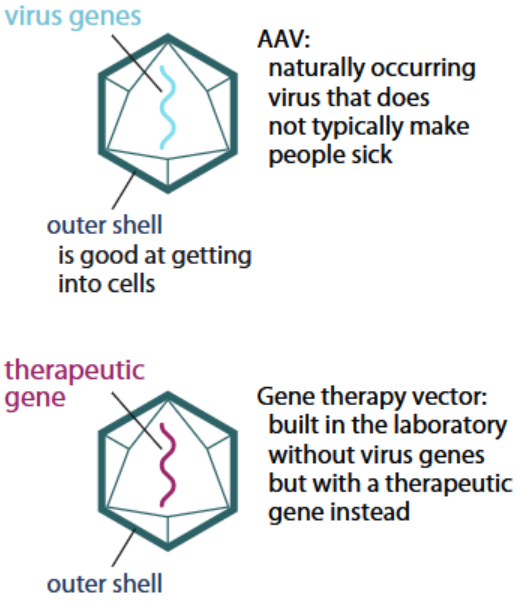
Parent Project Muscular Dystrophy

The Components of Gene Therapy

1. **Transgene –** genetic material to modify or replace the disease-causing variant, or treat other aspects of the disease

2. **Promoter –** Controls where in the body the transgene active

3. **Vector –** The shuttle for transporting the transgene/promoter across the body



What is Being Delivered to Treat the Disease?

1. **Modify a genetic variant –** genes that can change the DNA sequence such as **CRISPR/Cas9** or other gene editing sequences

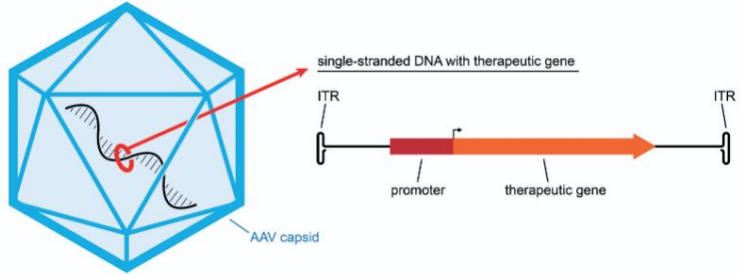
2. **Provide a replacement copy of the gene –** supplying another modified copy of the gene to restore protein production such as **micro-dystrophin**

3. **Deliver a different gene to treat disease –** using genes that can address other aspects of the disease, such as **SERCA2** for the heart or act as a surrogate for the disease-causing gene

PPMD

How is the therapy delivered to cells?

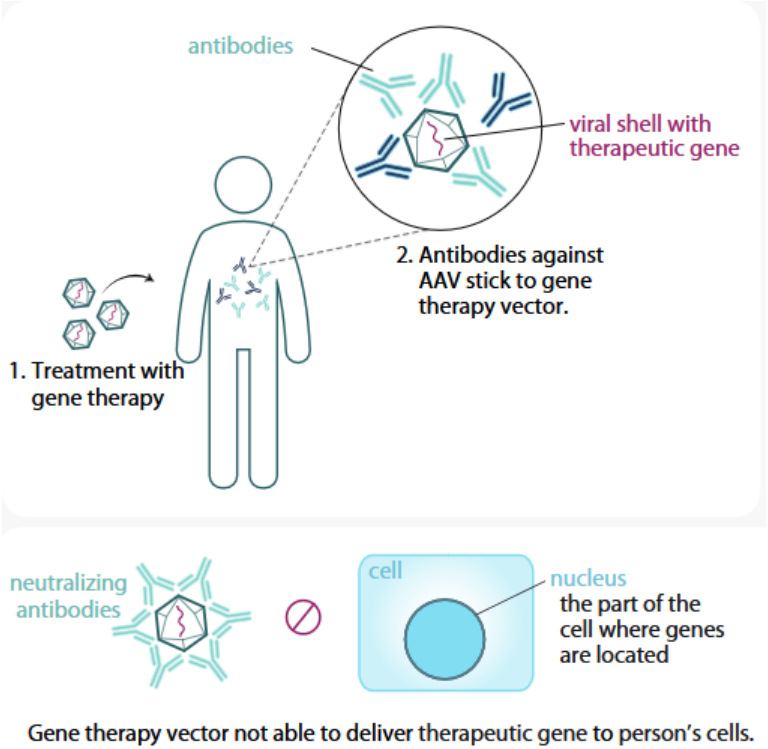
- In Duchenne this has primarily been through the use of **Adeno-Associated Virus (AAV)**
- AAV is a small virus with serotypes (variants such as AAV8, AAVrh74, AAV9, etc) that favor muscle tissues
- For Duchenne gene therapy is administered Intravenous (IV) or Intrathecal (IT) to ensure body-wide distribution – to get to skeletal and cardiac tissues
- While effective at delivering transgenes to tissues there <u>are limitations to AAV</u>
    - Safety-risks at high doses
    - Limitation on size of the transgene that can fit in the vector
    - Pre-existing antibodies
    - High antibody production after administration that prevent patients from receiving a second dose



- Research is ongoing to explore delivery with non-viral vectors (e.g. lipidnano particles) which may address some of these issues. But they may have their own challenges

Pre-existing Antibodies

- Pre-existing antibodies can prevent some patients from being able to receive the gene therapy
- Additionally, patients who have received gene therapy will have high antibody production following administration that prevent patients from receiving a second dose
- Strategies to circumvent pre-existing antibodies are being explored
  - Plasma exchange, drugs that destroy or block antibodies
- Approaches that work for low level pre-existing antibodies may not work for redosing because of the difference in amount of antibodies



Potential Risks and Uncertainties of Gene Therapy

- Immune Response and Hospitalization
- Risk of death
  - 5 reported deaths related to AAV Gene Therapy in Duchenne across multiple programs and different AAV vectors
- Not being able to participate in other trials
  - We are seeing some companies allow post-gene therapy treated patients to join studies
- Variability in expression and functional improvement for an individual
- How long the benefit will last is still being studied
- One-time dose: No timeline for if or when re-dosing will be possible

Benefits of Dystrophin-restoration Gene Therapy

- May help stabilize the muscle membrane
- May slow down rate of muscle being replaced with fatty tissue
- May lessen downstream effects of disease (e.g. inflammation)
- May improve an individual's motor function
- May protect the heart
- While not a cure, it could alter progression of disease – delay major disease milestones

PPMD

Educational resources about Gene Therapy (Ongoing Research, Approved and Investigational Products) can be found on PPMD's Website

Solid Biosciences

SGT-003: Solid's Next-Generation Gene Therapy Candidate for Duchenne Muscular Dystrophy

Parent Project Muscular Dystrophy

SGT-003: Solid's Next Generation AAV Gene Therapy for Duchenne

Optimized Transgene

Solid's microdystrophin uniquely includes the nNOS binding domain with the goal of better protecting muscles from damage[1]

Next-Generation Capsid

Solid's capsid was designed to improve delivery to cardiac and skeletal muscle and to result in lower levels in the liver[2]

Improved Manufacturing Process

Solid's manufacturing process focuses on maintaining a high full/empty capsid ratio to limit the total viral load administered[3]

SGT-003's optimized transgene and next-generation capsid were selected to deliver a unique microdystrophin to muscles while also de-targeting the liver

nNOS: neuronal nitric oxide synthase

1. Lai Y, et al. J Clin Invest. 2009;119(3):624-635. 2. Flanigan K, et al. ASGCT 2026 Annual Meeting oral presentation. 3. Data on file. Solid Biosciences. 2026.

SGT-003 is an investigational therapy and is not available for commercial use in any region

INSPIRE DUCHENNE: Study Overview

- Single-dose (1.0E14 vg/kg), open-label, Phase 1/2 study
- Actively enrolling: US, Canada, Italy, and the UK
- Patients < 12 years of age with a confirmed diagnosis of Duchenne
- Potential for further enrollment of older and non-ambulatory patients (Cohorts 4 and 5)
- Prophylactic prednisone regimen alone used as immunomodulation

Primary Endpoints:

- Incidence of treatment-emergent adverse events through Day 360
- Change from baseline of microdystrophin protein levels at Day 90

Secondary Endpoints:

- Microdystrophin protein levels and distribution at Days 90 and 360
- TTR, 10MWR, 4SC, NSAA, 6MWT, SV95C at Days 360 and 540

Exploratory Endpoints:

- % predicted FVC, PEF, FEV1; Bayley-4; PODCI

KEY ELIGIBILITY CRITERIA

Age:	Cohort 1: Aged 4 to <7 years Cohort 2: Aged 7 to <12 years Cohort 3: Aged 0 to <4 years
***DMD* Genetic Variant Exclusions:**	Any deletion in exons 1 to 11, 42 to 45, or 57-69, inclusive
Ambulation:	Cohorts 1, 2: Required Cohort 3: N/A
Additional Function:	Cohorts 1, 3: N/A Cohort 2: TTR and 10MWR criteria
Antibodies:	Negative for AAV9 antibodies
Prior Treatments:	No history of gene therapy ≥12-week washout from exon-skipping, vamorolone, and/or givinostat
Steroid Regimen:	Cohorts 1, 2: Stable daily oral steroids (prednisone/deflazacort) for ≥12 weeks Cohort 3: N/A

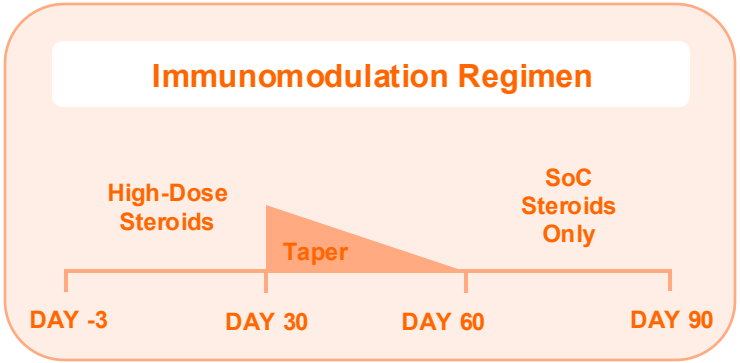
4SC: 4-stair climb; 6MWT: 6-minute walk test; 10MWR: 10-meter walk/run; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; IV: intravenous; N/A: not applicable; NSAA: North Star Ambulatory Assessment; PEF: peak expiratory flow; PODCI: pediatric outcomes data collection instrument; SV95C: stride velocity 95th centile; TTR: time to rise.
INSPIRE DUCHENNE: NCT06138639

INSPIRE DUCHENNE: Safety and Enrollment Update

Cohorts	Eligible Age Range (years)	Ages at Enrollment (years)	Weights for Dosing (kg)	Participants Enrolled (n)
1-3	0 to <12	1 to 10	9.9 to 39.7	46[1]

SGT-003 Participants With Treatment-Related SAEs	n (%)
Serious Adverse Events (SAEs)	1 (2.2)[2]

SGT-003 Participants With Treatment-Related AEs		n (%)
Most Common Treatment-Related Adverse Events (AEs)	Nausea	31 (67.4)
	Vomiting	27 (58.7)
	Decreased appetite	15 (32.6)
	Thrombocytopenia	13 (28.3)
	Abdominal Pain	8 (17.4)

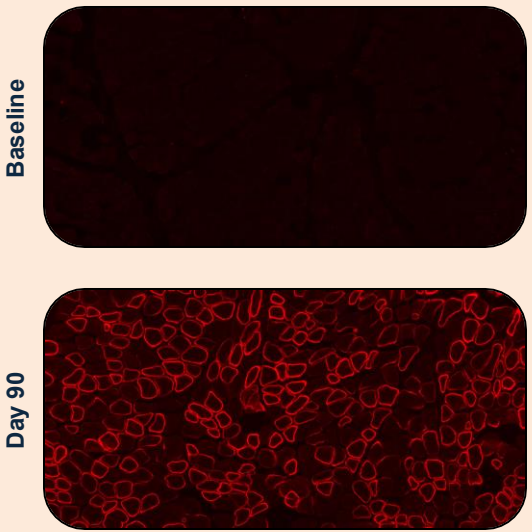


SGT-003 has been generally well tolerated using a steroid-only prophylactic immunomodulation regimen

AE: adverse event; SAE: serious adverse event
1. Flanigan K, et al. ASGCT 2026 Annual Meeting oral presentation. 2. One (n=1) previously reported CTCAE Grade 3 SAE of immune-mediated myositis. The myositis was not associated with muscle pain or weakness and has resolved.

Robust Transduction and Expression After SGT-003

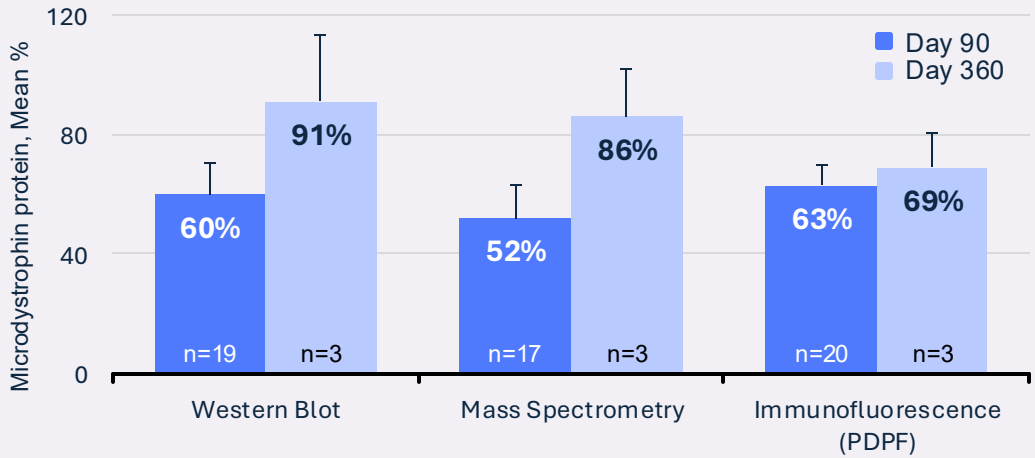
EXAMPLE SGT-003 MUSCLE BIOPSY MICRODYSTROPHIN STAINING



VECTOR GENOME COPIES/NUCLEUS (MEAN)

Day 90 (N=20)	Day 360 (N=3)
11	12

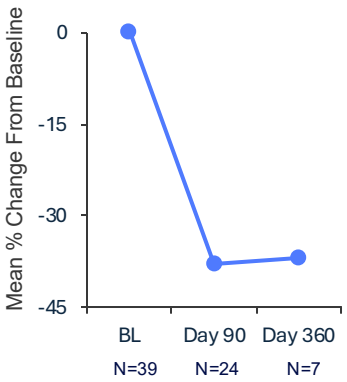
SGT-003 MICRODYSTROPHIN EXPRESSION[1,2,3]



PDPF: percent dystrophin positive fibers. 1. Values are means ± standard error of the mean. 2. Western blot and mass spectrometry baselines were 0% mean normal dystrophin, immunofluorescence is based on a manual count. 3. Western blot, mass spectrometry and immunofluorescence assays are conducted by multiple external vendors; at the time of this analysis, complete results from one western blot sample (from participant 20) and three mass spectrometry samples (from participants 15,16 and 20) had not been received. Data cutoff February 23, 2026. Veerapandiyan A, et al. MDA 2026 Clinical and Scientific Conference oral presentation.

Improved Muscle Integrity Observed After SGT-003

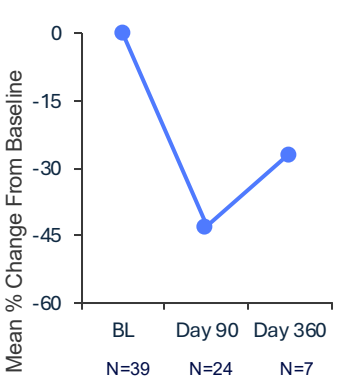
SERUM CK % Change From Baseline[1]



38% at Day 90

37% at Day 360

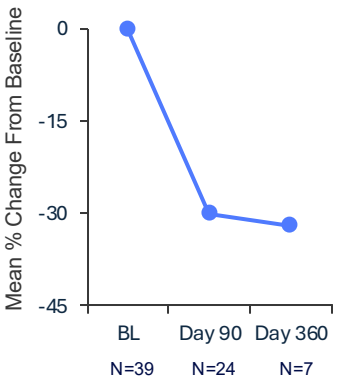
SERUM ALT % Change From Baseline[1]



43% at Day 90

27% at Day 360

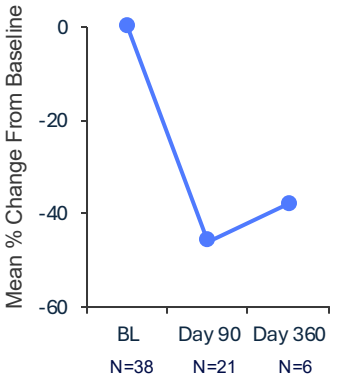
SERUM AST % Change From Baseline[1]



30% at Day 90

32% at Day 360

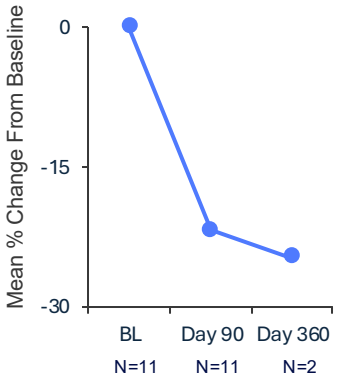
SERUM LDH % Change From Baseline[1,2]



46% at Day 90

38% at Day 360

SERUM Titin % Change From Baseline[1,2]



22% at Day 90

25% at Day 360

Improved muscle integrity may support slower disease progression and better long-term clinical outcomes[3-5]

1. Data cutoff February 23, 2026. Veerapandiyan A, et al. MDA 2026 Clinical and Scientific Conference oral presentation. 2. Certain data from a subset of participants were not available at the time of analysis. 3. Siddique Ahmed Khan M, et al. *Int J Sci Res.* 2016;5(11):156-157. 4. Voleti S, et al. *Pediatr Cardiol.* 2020;41(6):1173-1179. 5. Oshida N, et al. *Sci Rep.* 2019;9(1):19498.

IMPACT DUCHENNE: Study Overview (Newly Enrolling)

- Single-dose (1.0E14 vg/kg), placebo-controlled, Phase 3 study
- n=80 total participants, randomized 1:1 to SGT-003 or placebo
- Placebo participants receive SGT-003 after 18 months if still meeting antibody and safety criteria
- Actively enrolling: Australia, Canada
- Planned sites pending regulatory approval: EU, UK, and US
- Prophylactic prednisone regimen alone used as immunomodulation

Primary Endpoint:

- Change from baseline in time to rise (TTR) velocity for SGT-003 treated patients compared to placebo at Day 540 (18 months)

Key Secondary Endpoints:

- 10MWR, 4SC, NSAA, SV95C at Day 540

Additional Endpoints:

- Safety, pulmonary function, cardiac function, patient-reported outcomes

KEY ELIGIBILITY CRITERIA

Age:	7 to <12 years
***DMD* Genetic Variant Exclusions:**	Any deletion in exons 1 to 11, 42 to 45, or 57-69, inclusive
Functional Criteria:	TTR and 10MWR criteria
Antibodies:	Negative for AAV9 antibodies
Prior Treatments:	No history of gene therapy 6-month washout from exon-skipping, vamorolone, and/or givinostat
Steroid Regimen:	Stable daily oral steroids (prednisone/deflazacort) for at least 6 months

TTR: time to rise; 4SC: 4-stair climb; 10MWR: 10-meter walk/run; NSAA: North Star Ambulatory Assessment; SV95C: stride velocity 95th centile.
IMPACT DUCHENNE: NCT07160634

Thank You to Participating Families and Study Teams!

If you are interested in learning more about these SGT-003 studies, please email clinicaltrials@solidbio.com or scan either QR code for the most up-to-date information on enrollment status, details on study eligibility, and clinical trial sites.

INSPIRE DUCHENNE

IMPACT DUCHENNE

REGENXBIO

RGX-202

Parent Project Muscular Dystrophy

RGX-202 is an investigational therapy and hasn't been approved by any regulatory authority.

REGENXBIO Forward-Looking Statements

This presentation includes "forward-looking statements," within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements express a belief, expectation or intention and are generally accompanied by words that convey projected future events or outcomes such as "believe," "may," "will," "estimate," "continue," "anticipate," "assume," "design," "intend," "expect," "could," "plan," "potential," "predict," "seek," "should," "would" or by variations of such words or by similar expressions. The forward-looking statements include statements relating to, among other things, REGENXBIO's future operations, clinical trials, costs and cash flow. REGENXBIO has based these forward-looking statements on its current expectations and assumptions and analyses made by REGENXBIO in light of its experience and its perception of historical trends, current conditions and expected future developments, as well as other factors REGENXBIO believes are appropriate under the circumstances. However, whether actual results and developments will conform with REGENXBIO's expectations and predictions is subject to a number of risks and uncertainties, including the outcome of REGENXBIO's collaboration with AbbVie and other factors, many of which are beyond the control of REGENXBIO. For a summary of certain of these risks and uncertainties, refer to the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of REGENXBIO's Annual Report on Form 10-K for the year ended December 31, 2025 and comparable "risk factors" sections of REGENXBIO's Quarterly Reports on Form 10-Q and other filings, which have been filed with the U.S. Securities and Exchange Commission (SEC) and are available on the SEC's website at www.sec.gov. All of the forward-looking statements made in this presentation are expressly qualified by the cautionary statements contained or referred to herein. The actual results or developments anticipated may not be realized or, even if substantially realized, they may not have the expected consequences to or effects on REGENXBIO or its businesses or operations. Such statements are not guarantees of future performance and actual results or developments may differ materially from those projected in the forward-looking statements. Readers are cautioned not to rely too heavily on the forward-looking statements contained in this presentation. These forward-looking statements speak only as of the date of this presentation. Except as required by law, REGENXBIO does not undertake any obligation, and specifically declines any obligation, to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

PP
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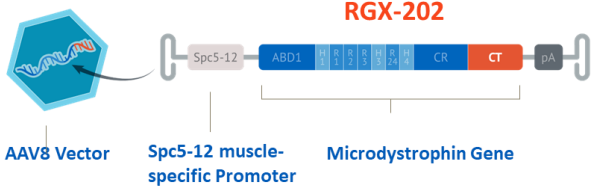
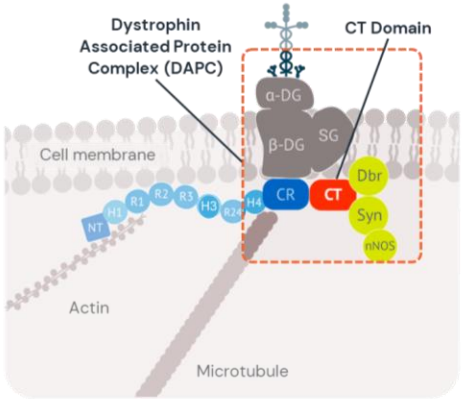
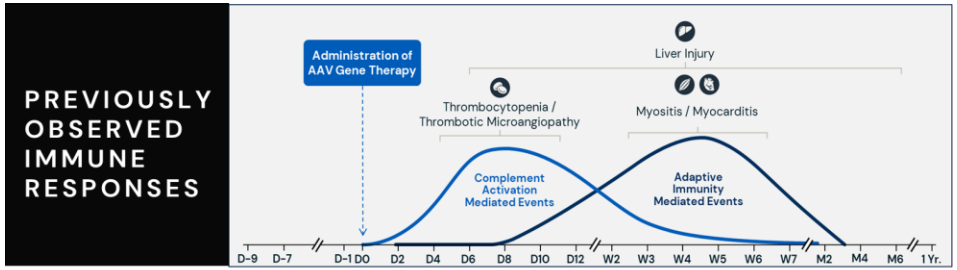
About RGX-202





- RGX-202 is an investigational gene therapy for DMD
- The RGX-202 microdystrophin gene uniquely includes the C-Terminal (CT) Domain, which has been shown in animal studies to protect muscle and improve muscle's ability to repair itself[1]
- The AAV8-based RGX-202 vector is designed to express the transgene in skeletal muscle and the heart
- RGX-202 is administered as a single IV infusion, and is given along with a short-course of proactive immune suppressive and antibiotic medications prior to and for several weeks afterward



CT: C-Terminal; DAPC: Dystrophin-associated protein complex; AAV: Adeno-associated virus; IV: intravenous

[1] Foltz (2025) Mol Ther Meth Clin Dev

AFFINITY DUCHENNE® Pivotal Study

Key Eligibility Criteria

- **Ambulatory boys aged ≥1 year** 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)

Pivotal Dose: $2x10^{14}$ GC/kg

1 to <4 years

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

≥4 years

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

PROACTIVE IMMUNE SUPPRESSION REGIMEN

Pivotal Study Endpoints

- **Primary Endpoint:**
  Proportion of patients with >10% RGX-202 microdystrophin expression at Week 12
- **Secondary Endpoints:**
  - **≥4 years:**
    Velocity and time of Timed Function Tests; NSAA; Safety
  - **1 to <4 years:**
    PDMS-3 & SV95C for 1 to <4 years; Safety
- **Exploratory Endpoints:**
  - **≥4 years:** SV95C & MRIs

PIVOTAL TOPLINE DATA

Biomarker:
N=30*

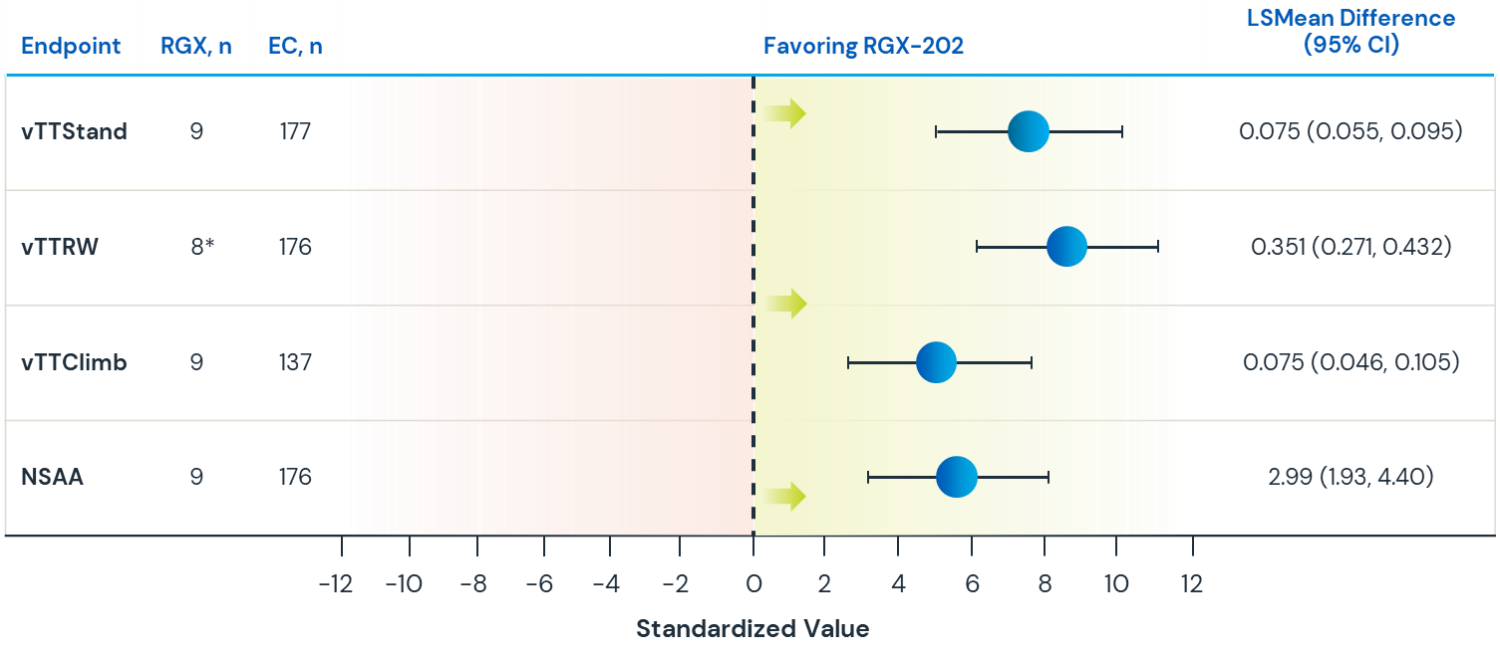
Interim Functional Data:
N=9 participants aged 4+ who reached 12 months post-treatment

Interim Safety:
N=31

Data cut date: April 16, 2026; Presented at the American Society of Gene & Cell Therapy 2026 Annual Meeting, Boston, MA
NSAA: North Star Ambulatory Assessment PDMS-3: Peabody Developmental Motor Scale, Third Edition; SV95C: Stride velocity 95th centile; MRI: Magnetic resonance imaging
*30 of 31 total participants have Week 12 biopsy available for evaluation; one participant refused muscle biopsy at Week 12

Participants Exceeded External Controls on All Functional Measures at 1 Year

- Functional improvements vs. external controls using propensity score weighting
- Older participants (aged 8+, n=5) showed improvement at similar levels as the full group (n=9)



Data cut date: April 16, 2026; Presented at the American Society of Gene & Cell Therapy 2026 Annual Meeting, Boston, MA

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

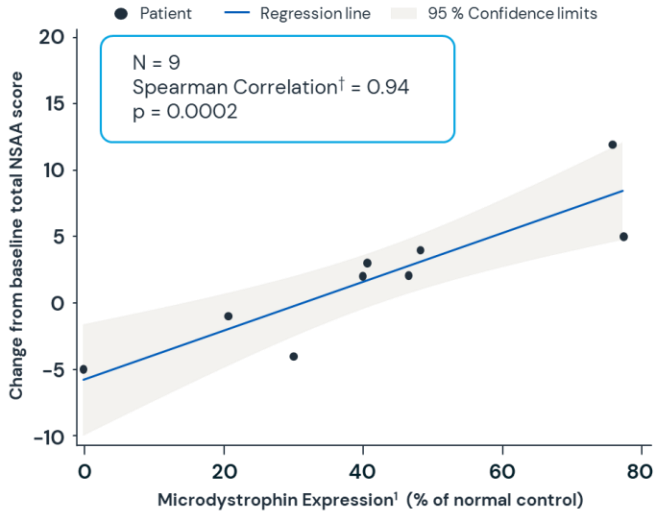
Least Square Mean (LSMean) differences were estimated using a mixed model for repeated measures (MMRM), comparing the change from baseline for RGX versus external controls (EC), adjusting for age at dosing and baseline functional test score. To ensure that a favorable RGX effect appears to the right 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).

*TTRW data for one (n=1) participant had missing data at Week 52, result was determined to be invalid due to participant behavior.

Primary Endpoint Met With High Statistical Significance

RGX-202 microdystrophin expression correlated with functional improvement at 1 year

WEEK 12 BIOPSY Mean ± SD	RGX-202 Microdystrophin[1] by western blot (% of normal control)	VCN copies/nucleus (qPCR)	Positive Fibers[2] by immunofluorescence (%)
Aged 1 to <4 (N=10)	**115.2** ± 81.0	**19.6** ± 10.7	**79.3** ± 17.4
Aged 4 to 7 (N=9)	**58.0** ± 37.2	**21.9** ± 16.4	**45.7** ± 31.5
Aged ≥8 (N=11)	**41.6** ± 24.5	**17.7** ± 7.0	**55.0** ± 20.7
Overall (N=30)	**71.1** ± 60.6	**19.6** ± 11.4	**60.6** ± 26.7



- 28 of 30* participants (93%) achieved microdystrophin expression >10% at Week 12 (p<0.0001)
  - 80% of participants achieved >40% microdystrophin expression
- Strong statistically significant correlation between RGX-202 microdystrophin expression at Week 12 and interim functional improvement at 1 Year (NSAA)

Data cut date: April 16, 2026; Presented at the American Society of Gene & Cell Therapy 2026 Annual Meeting, Boston, MA

[1] Microdystrophin expression assessed at Week 12 visit; adjusted for muscle content; % normal control

[2] Positive Fibers defined as change from baseline of RGX-202 microdystrophin & dystrophin positive fibers. Data available for 23 participants (N=8 for aged 1-4, N=7 for aged 4-7, N=8 for aged 8+) as of data cut date.

*30 of 31 total participants have Week 12 biopsy available for evaluation; one participant refused muscle biopsy at Week 12

†Additionally, regression model was used to visualize the linear relationship between microdystrophin expression and change from baseline in NSAA function. To support linear relationship of figure results, Pearson correlation coefficient was also calculated (r=0.88[p= 0.0016] for change from baseline, r=0.84[p= 0.0048] for difference from cTAP), p-values accounted for potential confounding effect of age at dosing and baseline function are 0.0132 (Left) and 0.0027 (Right).

Pivotal Study: Interim Safety

- RGX-202 was well tolerated
- No drug-related thrombocytopenia, myositis, or neurotoxicity reported

TR-SAEs	Aged <4 Years N = 11, n (%)	Aged ≥4 Years N = 20, n (%)	Overall N = 31, n (%)
Subacute myocarditis[1]	0	1 (5.0)	1 (3.2)
Liver injury[2]	0	1 (5.0)	1 (3.2)
TR-TEAEs *	**5** (45.5)	**19** (95.0)	**24** (77.4)
Vomiting	4 (36.4)	15 (75.0)	19 (61.3)
Fatigue	3 (27.3)	8 (40.0)	11 (35.5)
Nausea	1 (9.1)	9 (45.0)	10 (32.3)
Abdominal pain	0	7 (35.0)	7 (22.6)
Pyrexia	1 (9.1)	3 (15.0)	4 (12.9)

1. 8-year-old participant (23kg weight at dosing) with premature stop codon in exon 60 presented with subacute myocarditis onset 33 days after dosing presenting with normal troponin I and mild elevation of high-sensitivity troponin I (<2x ULN), mild chest and abdominal pain, and no evidence of fibrosis on cardiac MRI. Fully resolved with no sequelae 49 days after onset, and most recent follow up cardiac MRI confirms no heart muscle fibrosis and no change in Ejection Fraction (65%).
2. 10-year-old participant (34kg weight at dosing) with exon 3-7 duplication presented with asymptomatic liver injury diagnosed based on laboratory assessment 43 days after dosing, with GGT peak elevation 123 U/L (2x ULN by local lab, 5x ULN by central lab). Abdominal ultrasound and bilirubin levels were normal. Fully resolved with no sequelae 46 days after onset.

Data cut date: April 16, 2026; Presented at the American Society of Gene & Cell Therapy 2026 Annual Meeting, Boston, MA

AE: Adverse event; TR-SAE: Treatment-related serious adverse event; TR-TEAE: Treatment-related treatment-emergent adverse event; GGT: Gamma glutamyl transferase; MRI: Magnetic resonance imaging; ULN: Upper limit of normal

*TR-TEAEs listed are those affecting >= 10% of participants

AFFINITY DUCHENNE® Study Current Status

- AFFINITY DUCHENNE® Confirmatory Study enrollment expected to be completed in mid-2026.

- Key Eligibility Criteria:
  - Ambulatory 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)

Program Next Steps

- Expect to complete enrollment of the confirmatory portion of the AFFINITY DUCHENNE® study by mid-2026.

- Plan to initiate the BLA submission to the US FDA using the accelerated approval pathway in the 3rd quarter of this year, and complete it in the first quarter of 2027. This would enable potential accelerated approval in the second half of 2027.