Building the World's Leading Muscle Disease Company

COMPANY OVERVIEW | NOVEMBER 2024

Sarah, *living with DM1*

Forward-Looking Statements & Disclaimer

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OUR MISSION

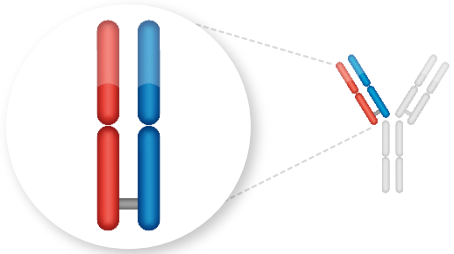
Life-transforming therapies

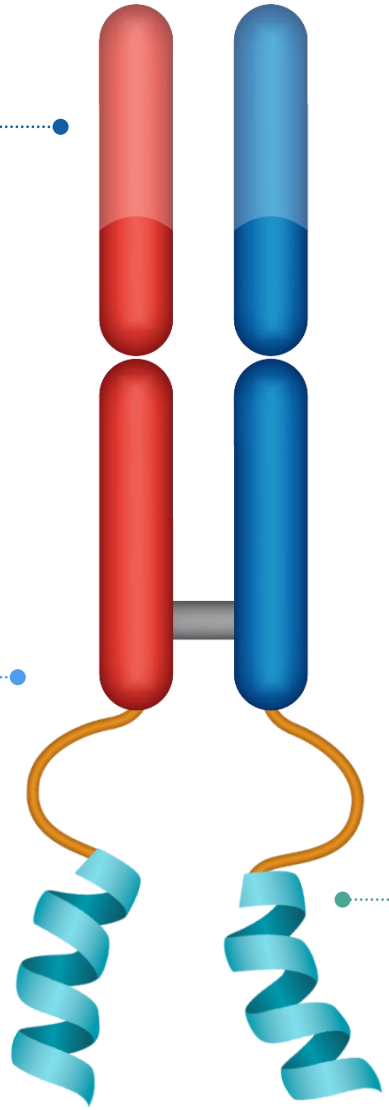
for patients with serious muscle diseases

Dyne FORCE™ Platform: Modern Oligo Therapeutics for Muscle Diseases

ANTIBODY

Proprietary Fab targets TfR1 to enable muscle delivery



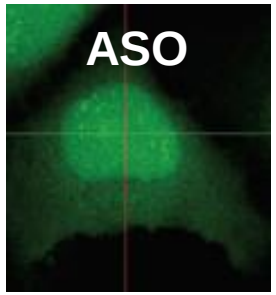


LINKER

Clinically validated, enables precise conjugation of multiple payloads to a single Fab

PAYLOAD

Modularity enables rational selection of payload to target the genetic basis of disease

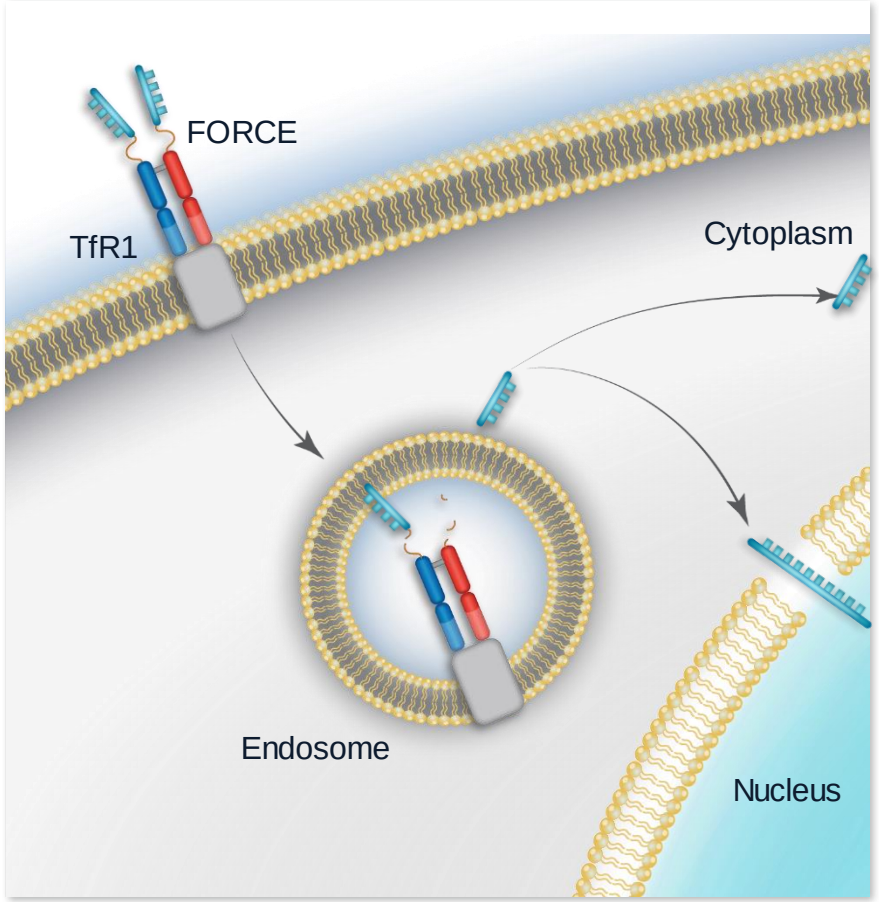


Nuclear localization

Cytoplasmic localization

Adapted from Ohrt T., et al. *Nucleic Acids Res* 2006;34:1369.

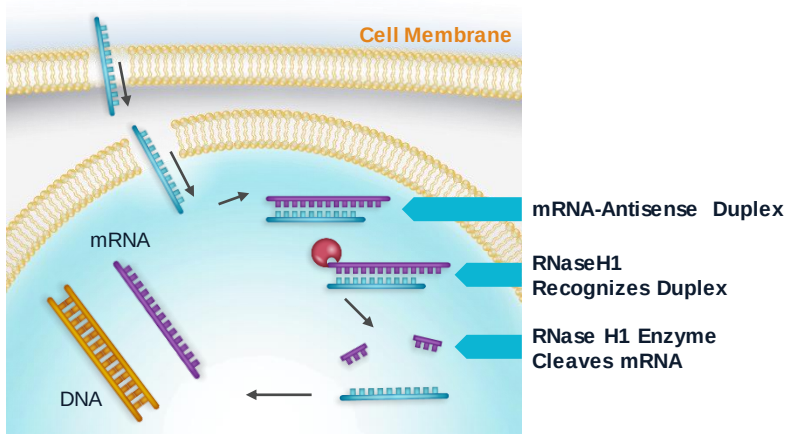
FORCE Platform Harnesses Cell Biology to Modify Disease



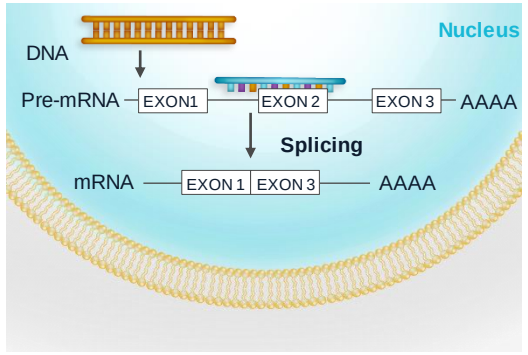
- Harnesses natural mechanism of TfR1 receptor-mediated delivery to transport therapeutics across the cell membrane
- Achieves endosomal escape without any membrane-destabilizing agents
- Distinctive pharmacokinetic profile creates opportunity for durable target engagement and wide therapeutic index

Rationally Select Payload to Target Genetic Basis of Disease

ASO acts in the nucleus and cytoplasm

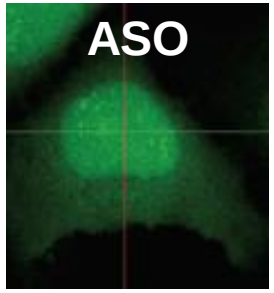


Splice-modulating ASO

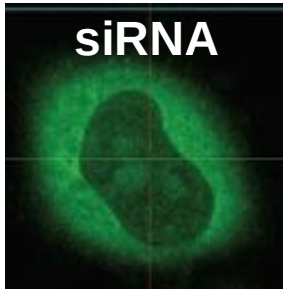


Single-Stranded Antisense

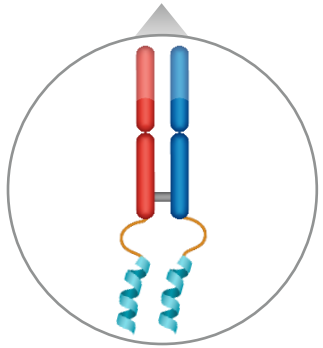
Subcellular distribution of ASO and siRNA



Nuclear localization

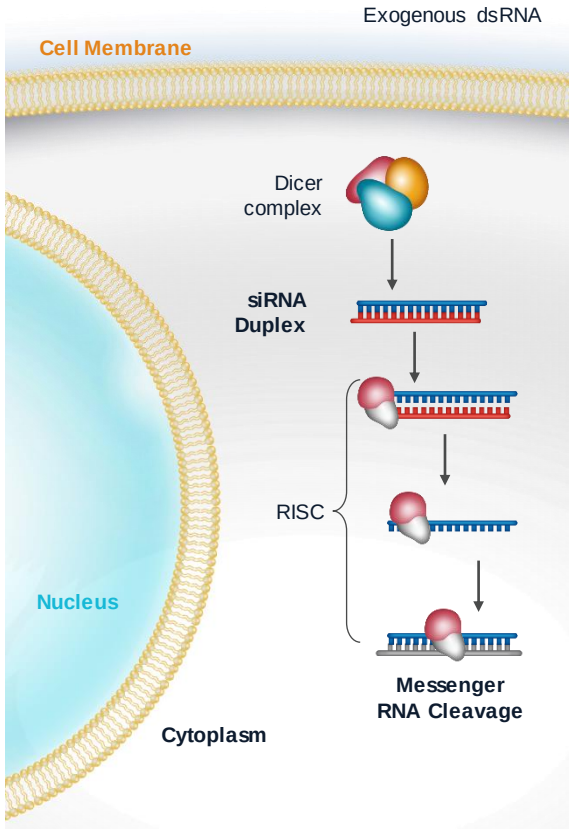


Cytoplasmic localization



FORCE delivers **ASO** payload for nuclear targets, **siRNA** payload for cytoplasmic targets

siRNA acts in the cytoplasm



Double-Stranded Antisense (siRNA)

Adapted from Ohrt T., et al. *Nucleic Acids Res* 2006;34:1369.

FORCE Platform Designed to Deliver Significant Advantages

Targeted Muscle Delivery

Leverages TfR1 expression on skeletal, cardiac and smooth muscle

Targets Genetic Basis of Disease

Rationally select payloads to match target biology

Redosable Administration

Potential for individualized patient titration and longer-term efficacy

Enhanced Tolerability

Targeted delivery limits systemic drug exposure

Extended Durability

Potential for prolonged disease-modifying effects, enabling less frequent dosing

Reduced Development and Manufacturing Costs

A single Fab and linker utilized across all programs

Advancing Robust Portfolio Focused on Muscle Diseases

DISEASE	TARGET	DISCOVERY / PRECLINICAL / PHASE 1/2	ESTIMATED PATIENTS
Myotonic Dystrophy Type 1 (DM1)	DMPK	**DYNE-101**	US: **>40,000** Europe: **>74,000**
Duchenne Muscular Dystrophy (DMD)	Exon 51	**DYNE-251**	US: **~12,000-15,000** Europe: **~25,000**
	Exon 53		
	Exon 45		
	Exon 44		
	Other Exons		
Facioscapulohumeral Muscular Dystrophy (FSHD)	DUX4	**DYNE-302**	US: **~16,000-38,000** Europe: **~35,000**

Pipeline Expansion Opportunities

- **Rare Skeletal**
- **CNS**
- **Cardiac**
- **Metabolic**

Achieving the Promise of FORCE to Deliver for Patients

ACHIEVE

Potential first-in-class DM1 therapy with differentiated efficacy and safety profile

- ✓ Dose-dependent muscle delivery and compelling splicing correction consistent across patients
- ✓ Meaningful improvements in multiple clinical endpoints, including myotonia, muscle strength, timed functional assessments and patient reported outcomes
- ✓ Early indication of durable effect beyond monthly dosing supports exploration of Q8W dosing
- ✓ Deepening of response with longer time on therapy
- ✓ Favorable safety profile to date[1]; 6.8 mg/kg Q8W cohort fully enrolled

DELIVER

Potential best-in-class DMD exon skipping franchise with differentiated efficacy and safety profile

- ✓ Dose-dependent increase in muscle delivery and dystrophin expression
  - 3.7% unadjusted and 8.7% muscle content adjusted dystrophin in 20 mg/kg Q4W cohort at 6 months
  - Improvements in multiple functional outcomes, including NSAA and SV95C, in multiple cohorts[2]
- ✓ Favorable safety profile to date[3]; enrolling 20 mg/kg Q4W registrational cohort

Pursuing Expedited Approvals, including Accelerated Approval in the U.S., for Both Programs

1. DYNE-101 data as August 20, 2024. 2. NSAA: North Star Ambulatory Assessment; SV95C: Stride Velocity 95th Centile. 3. DYNE-251 data as of August 21, 2024.

Developing Transformative Therapies for People Living with DM1

Overview

- Mutation in the *DMPK* gene
- Onset at any point, depending on DM1 phenotype
- Life expectancy of 45 - 60 years

Clinical Presentation

- Myotonia
- Muscle weakness
- Cardiac arrhythmia
- Pulmonary abnormalities
- CNS manifestations

Population

- >40,000 (US)
- >74,000 (Europe)

NO approved therapies

OUR APPROACH

Disease-Modifying Nuclear *DMPK* Knockdown

Targeting toxic gain of function *DMPK* RNA to potentially **stop or reverse** disease progression

Phase 1/2 Clinical Trial to Evaluate DYNE-101 in Patients with DM1

ACHIEVE

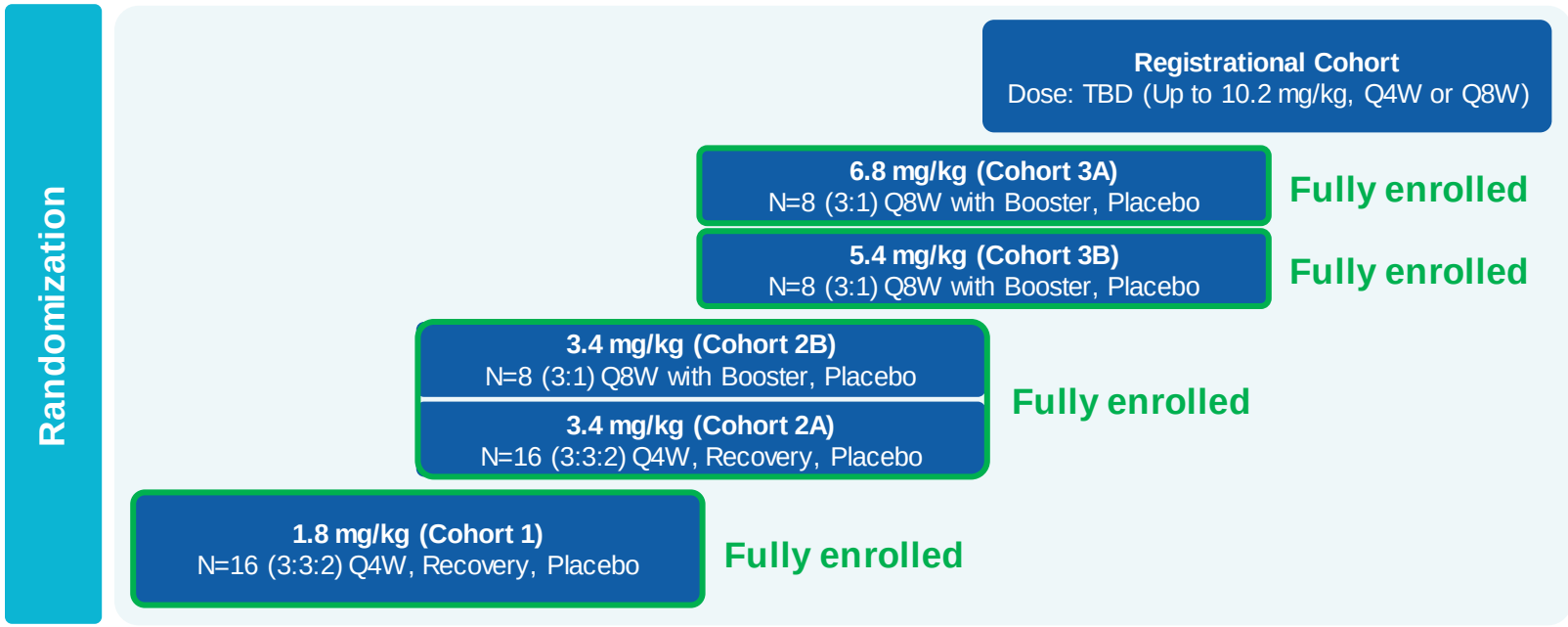
Population	Primary Endpoints	Additional Endpoints	Stages of ACHIEVE
• Adult patients living with DM1 • Ages 18 to 49 years	• Safety and tolerability	• Pharmacokinetics • Change from baseline of: – Splicing – *DMPK* RNA expression – Multiple assessments of muscle strength and function – Patient-reported outcomes, including DM1-ACTIV^{C} and MDHI	• Multiple Ascending Dose (MAD): 24 weeks • Open-Label Extension (OLE): 24 weeks • Long-Term Extension (LTE): 96 weeks

Additional endpoints include select secondary and exploratory endpoints. DM1-ACTIV^{C}: Myotonic Dystrophy type 1 Activity and participation scale. MDHI: Myotonic Dystrophy Health Index.

ACHIEVE Trial Design

ACHIEVE

Global, Randomized, Placebo-Controlled Stage Evaluating Once Monthly or Less Frequent Administration of DYNE-101 in Adult Patients Living with DM1



MAD Study Details

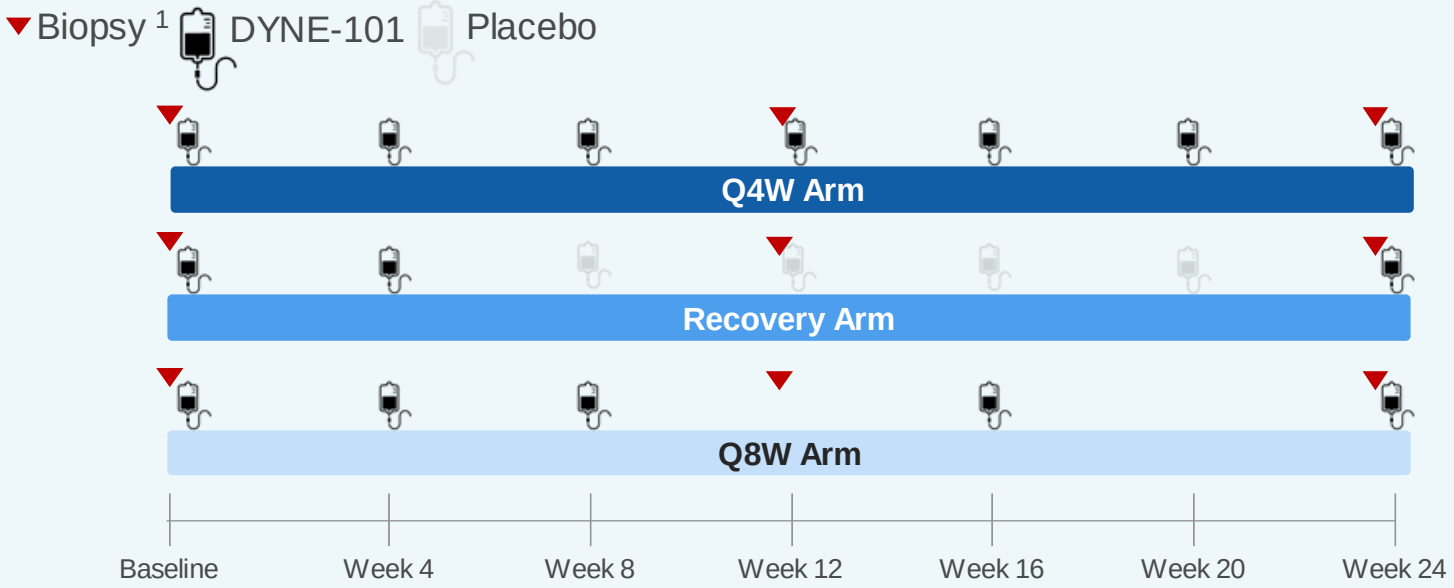
- IV administration of DYNE-101 or placebo every 4 weeks or every 8 weeks
- Muscle biopsies: Baseline, 12 weeks, 24 weeks
- Patients in MAD study escalated to highest tolerable dose in OLE and LTE

Global Strategy & Adaptive Trial Design To Enable Rapid Achievement of Potentially Registrational Clinical Data

Doses provided refer to ASO component of DYNE-101. Recovery cohort Q4W x 2 doses then placebo for the remainder of the 24W placebo-controlled period. Q8W with booster includes Q4W x 3 doses then Q8W dosing. Study protocol allows for dosing up to 10.2 mg/kg.

Dosing Schedules for Treatment Arms

ACHIEVE



1. Needle biopsies taken from alternating TA muscles prior to dosing at baseline, Day 85, and Day 169.

Note: Represents dosing during 24-week multiple ascending dose (MAD) stage. Patients in MAD study escalated to highest tolerable dose in 24-week OLE and 96-week LTE.

ACHIEVE Baseline Participant Characteristics

Mean(SD) or n(%)	1.8 mg/kg Q4W (N=16) [1]	3.4 mg/kg Q4W (N=16) [1]	5.4 mg/kg Q8W (N=8) [2]
Age (years)	34.6 (10.4)	34.3 (7.6)	39.6 (7.0)
Female n(%)	7 (43.8%)	3 (18.8%)	5 (62.5%)
BMI (kg/m^2)	22.4 (5.3)	23.8 (3.8)	21.7 (2.7)
CASI	0.62 (0.26)	0.67 (0.20)	0.79 (0.14)
CTG Repeats	375 (217)	527 (241)	586 (294)
vHOT (sec) (middle finger)	11.2 (4.3)	8.0 (5.7)	10.1 (6.2)
QMT Total (% predicted)	49.6 (10.9)	47.8 (10.6)	45.8 (16.1)
10M-RWT (sec)	3.5 (0.8)	3.6 (0.7)	4.7 (2.1)
5 Times Sit to Stand (sec)	9.33 (2.02)	10.05 (3.03)	12.28 (5.96)
DM1-ACTIV^c Total	43 (7)	42 (7)	44 (6)
MDHI Total	25 (20)	25 (20)	16 (9)

1. Q4W, recovery, and placebo arms are reported together for baseline characteristics. 2. Q8W and placebo arms are reported together for baseline characteristics.

DYNE-101 Safety Profile Is Favorable to Date

Summary of Treatment Emergent Adverse Events (TEAEs)[1]

TEAE Category	Participants with ≥1 TEAE – n (%)					
	1.8 mg/kg Q4W+Rec. N=16	3.4 mg/kg Q4W+Rec. N=16	3.4 mg/kg Q8W N=8	5.4 mg/kg Q8W N=8	6.8 mg/kg Q8W N=8	Overall (N=56)
Any TEAE	16 (100%)	16 (100%)	8 (100%)	8 (100%)	7 (88%)	55 (98%)
Any related TEAE	8 (50%)	8 (50%)	2 (25%)	3 (38%)	5 (63%)	26 (46%)
Any serious TEAE	4 (25%)	0	1 (13%)	0	0	5 (9%)
Any serious related TEAE	0	0	0	0	0	0
Any TEAE leading to withdrawal	0	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0	0

Most TEAEs Were Mild or Moderate in Intensity

- 6 serious TEAEs unrelated to study drug
  - Atrioventricular block first degree (1) [2]
  - Pneumonia (2 events in same participant)
  - Pulmonary embolism (1) [3]
  - Hyponatremia (1)
  - Influenza (1)
- Most common TEAEs (≥20% participant incidence)[4]
  - Nasopharyngitis (32%)
  - Procedural pain (29%)
  - Infusion-related reaction (21%)

Additional Safety Data

- Liver enzyme elevations have been observed in a minority of participants
  - No impact on liver function (bilirubin or coagulation)
  - Interpretation is complicated by underlying disease and elevated baseline values up to ~2.5x greater than the upper limit of normal
- No participants have demonstrated persistent related anemia or thrombocytopenia

~680 Doses Administered to Date Representing Over 55 Patient-Years of Follow-Up[1]

1. Data as of August 20, 2024; 2. Transient worsening of atrioventricular (AV) block in a participant with ongoing medical history of first-degree AV block; 3. Attributed to risk factors for pulmonary embolism; 4. All cohorts combined; preferred terms are reported

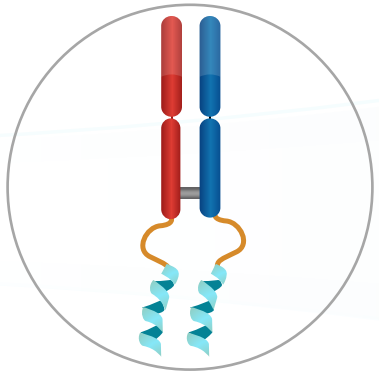
DYNE-101 Designed to Address the Foundational Spliceopathy of DM1 to Enable Comprehensive Functional Improvement

Robust Delivery

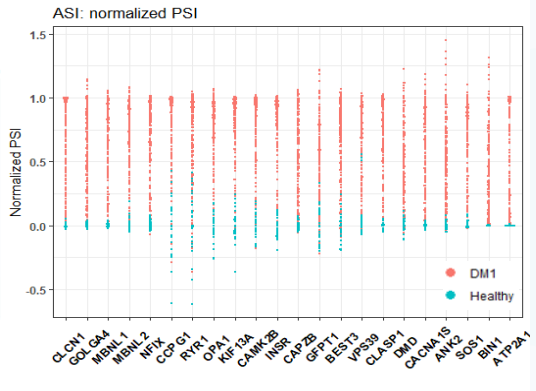
Validated Biomarker

Early Indicator of Functional Improvement

Broad Functional Improvement



FORCE Platform



Splicing

Myotonia

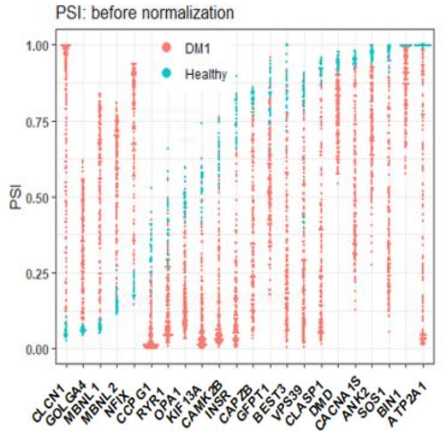
Muscle Strength:
Quantitative Muscle Testing

Functional Assessments:
10-Meter Walk / Run;
5x Sit to Stand

Patient Reported Outcomes:
Myotonic Dystrophy Health Index (MDHI); DM1-ACTIV[c]

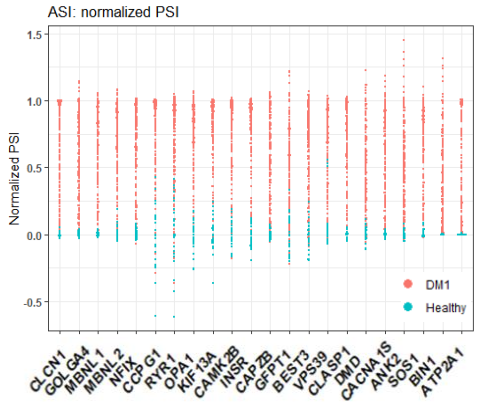
DMCRN NHS Enabled Establishment of Composite Alternative Splicing Index (CASI) as Biomarker Correlating with Clinical Function in DM1

PSI = Percent Spliced In



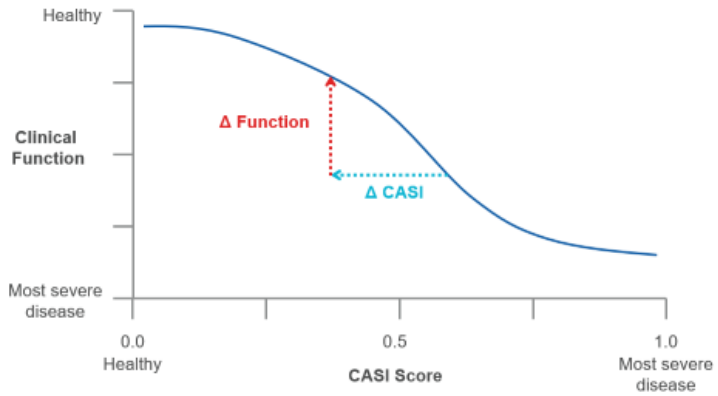
Targeted sequencing reads to calculate Percent Spliced In (PSI) of specific exons

ASI: Alternative Splicing Index



Normalize to reference PSI from healthy controls and patients from DM1 natural history studies [1]

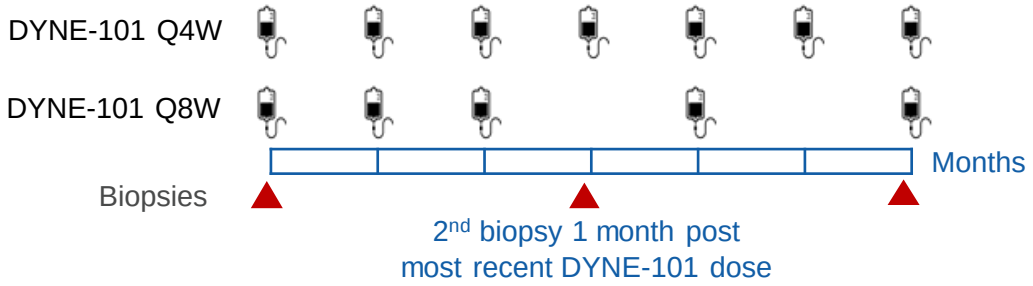
CASI: Composite Alternative Splicing Index

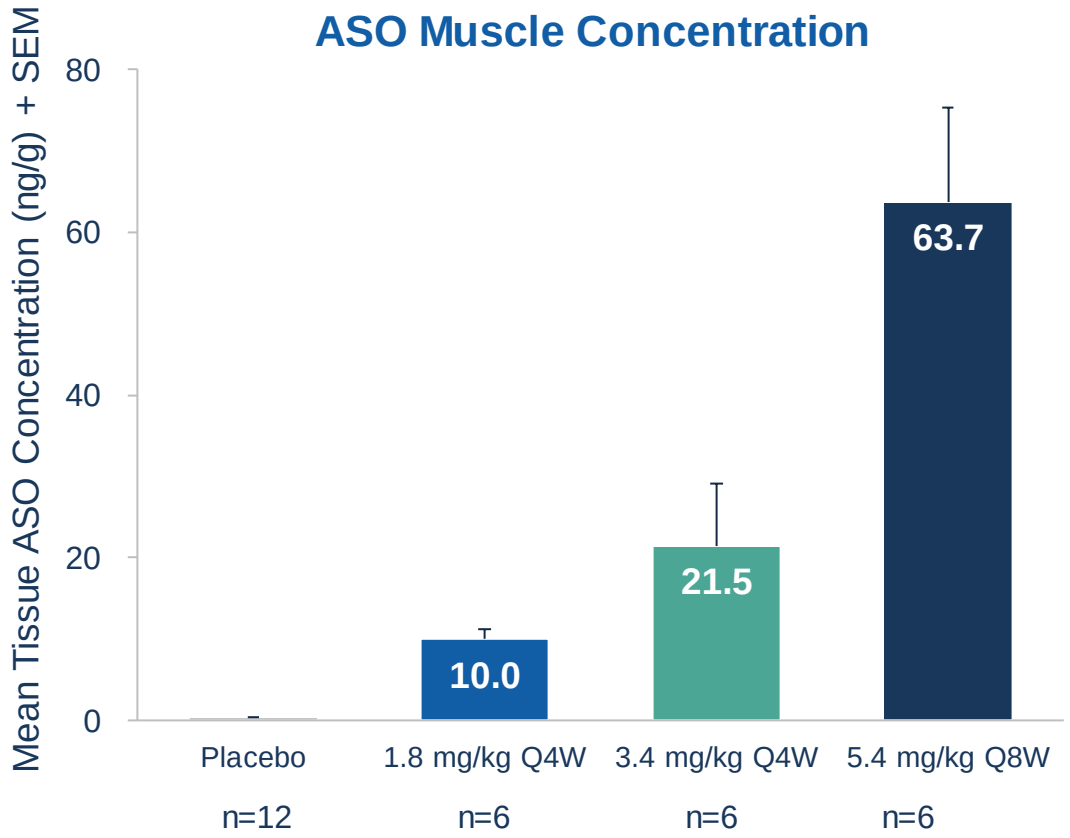


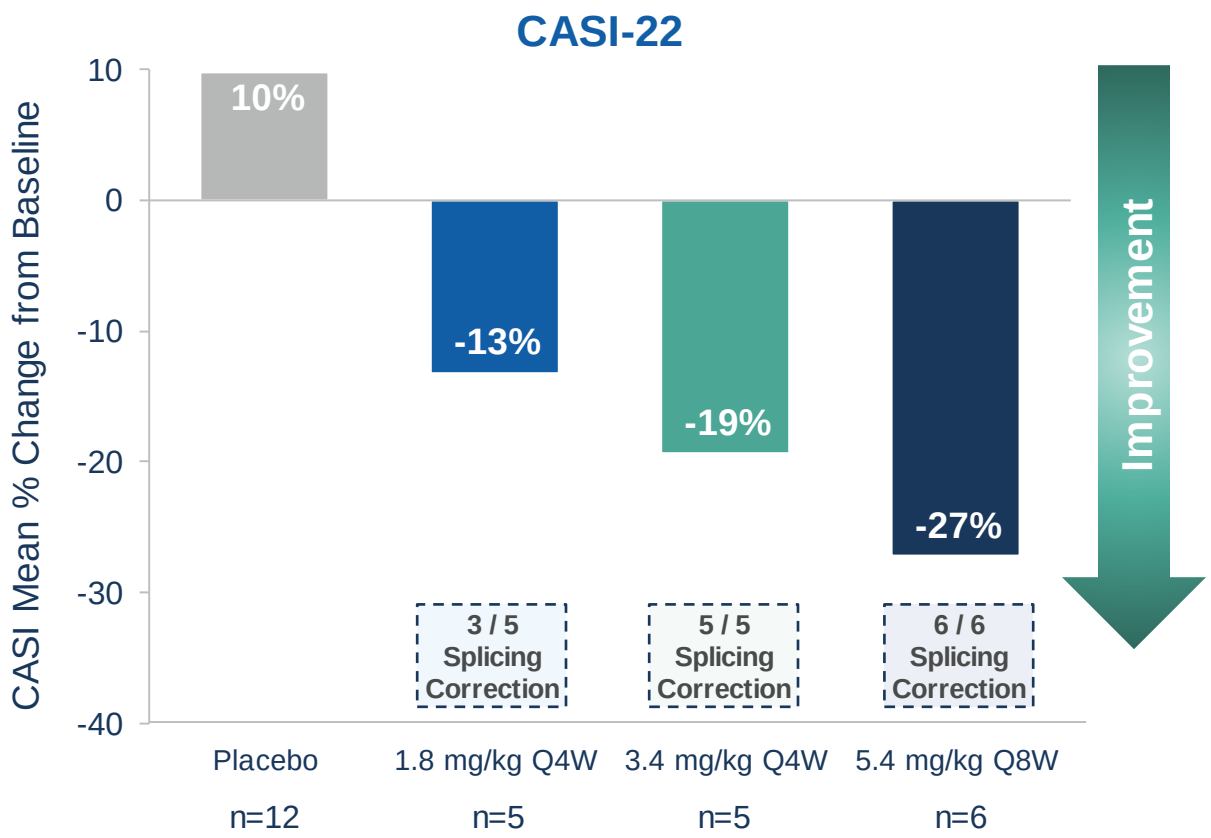
Compute the mean of normalized PSI from a panel of 22 genes.
0 representing median score of healthy subjects; 1 representing 95th percentile severity of DM1 patients

1. Reference PSI described within Thornton CA et al., *Lancet Neurol*, 2023; 22: 218–228; DMCRN NHS: Myotonic Dystrophy Clinical Research Network natural history study.

Monthly Dosing of DYNE-101 Demonstrated Dose-Dependent Delivery and Consistent Splicing Correction at 3 Months



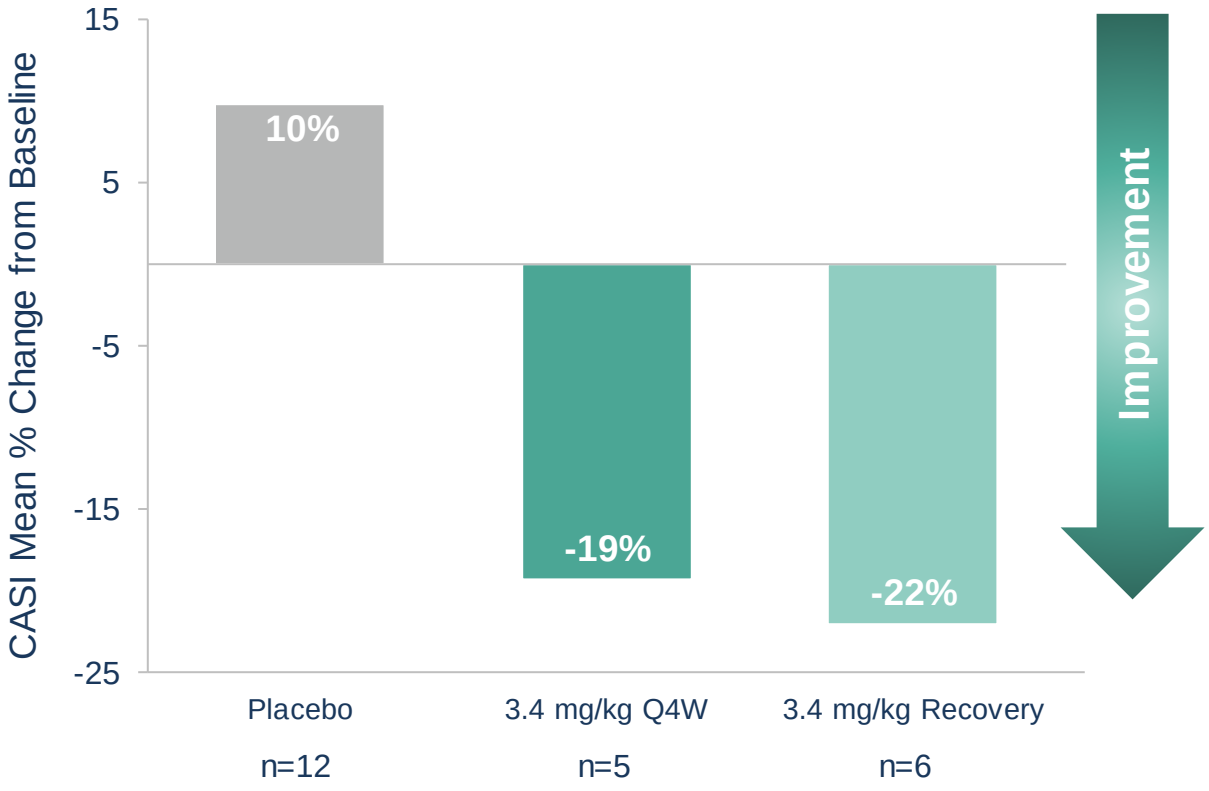




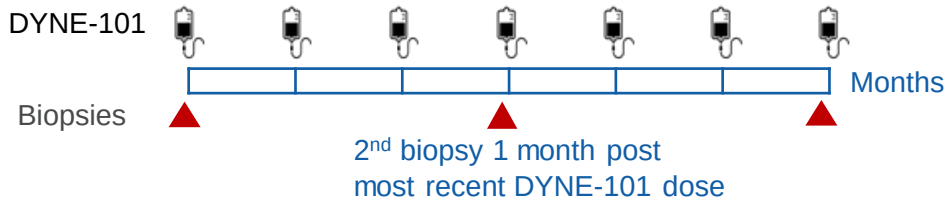
Note: One post-baseline sample in 3.4 mg/kg Q4W treatment group not included within splicing assay as the sample did not meet QCcriteria.

Recovery Data Supports Less Frequent Dosing Regimen

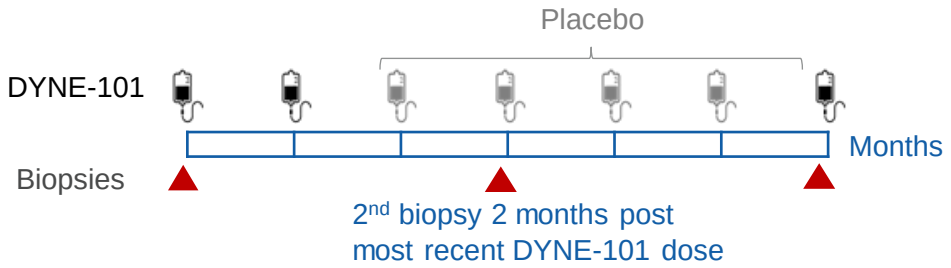
CASI-22 at 3 Months



Q4W Active Arm



Q4W Recovery Arm

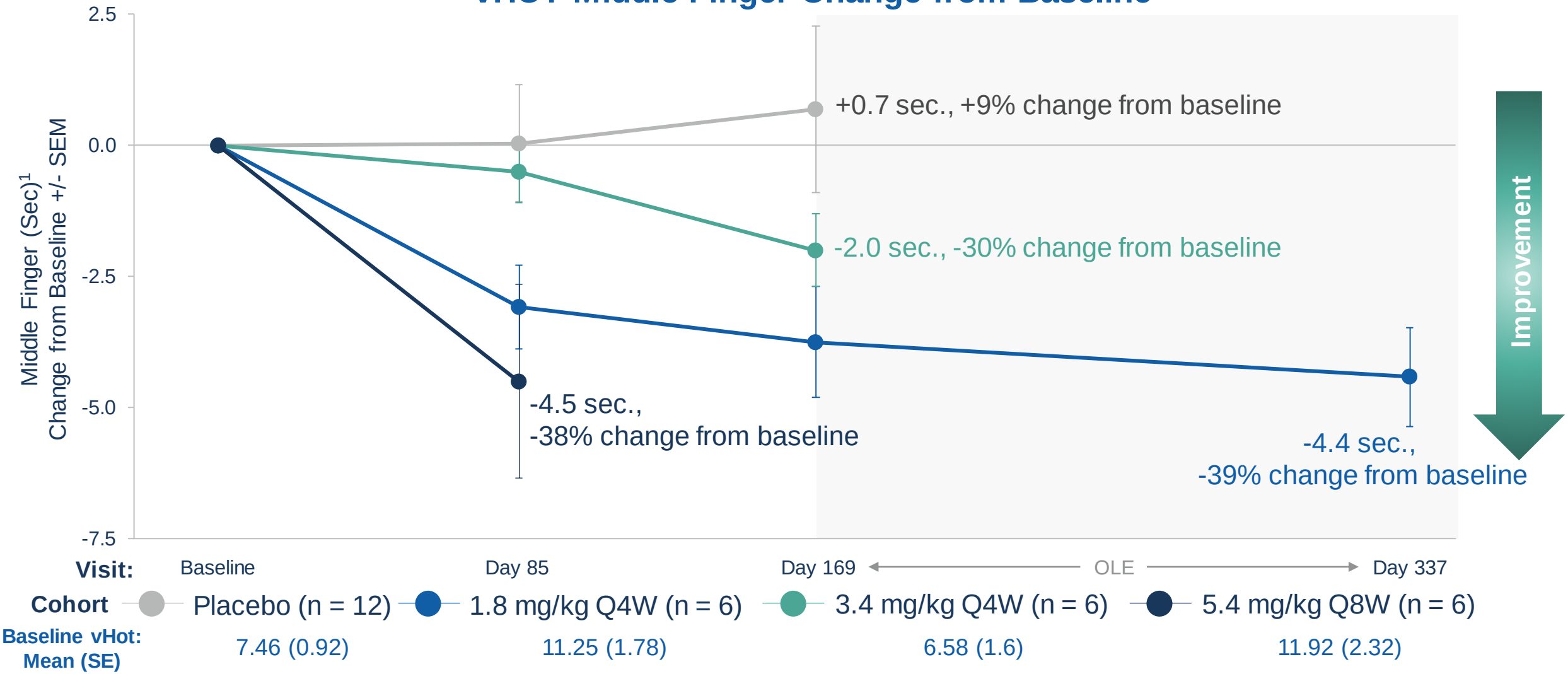


Robust Splicing Correction in Both Q4W and Recovery Arm with 3.4 mg/kg Dose

Continued Improvement in Functional Myotonia at 6 and 12 Months

1.8 mg/kg Q4W myotonia benefit increased from 3.1 seconds at 3 Months to 4.4 seconds at 12 Months

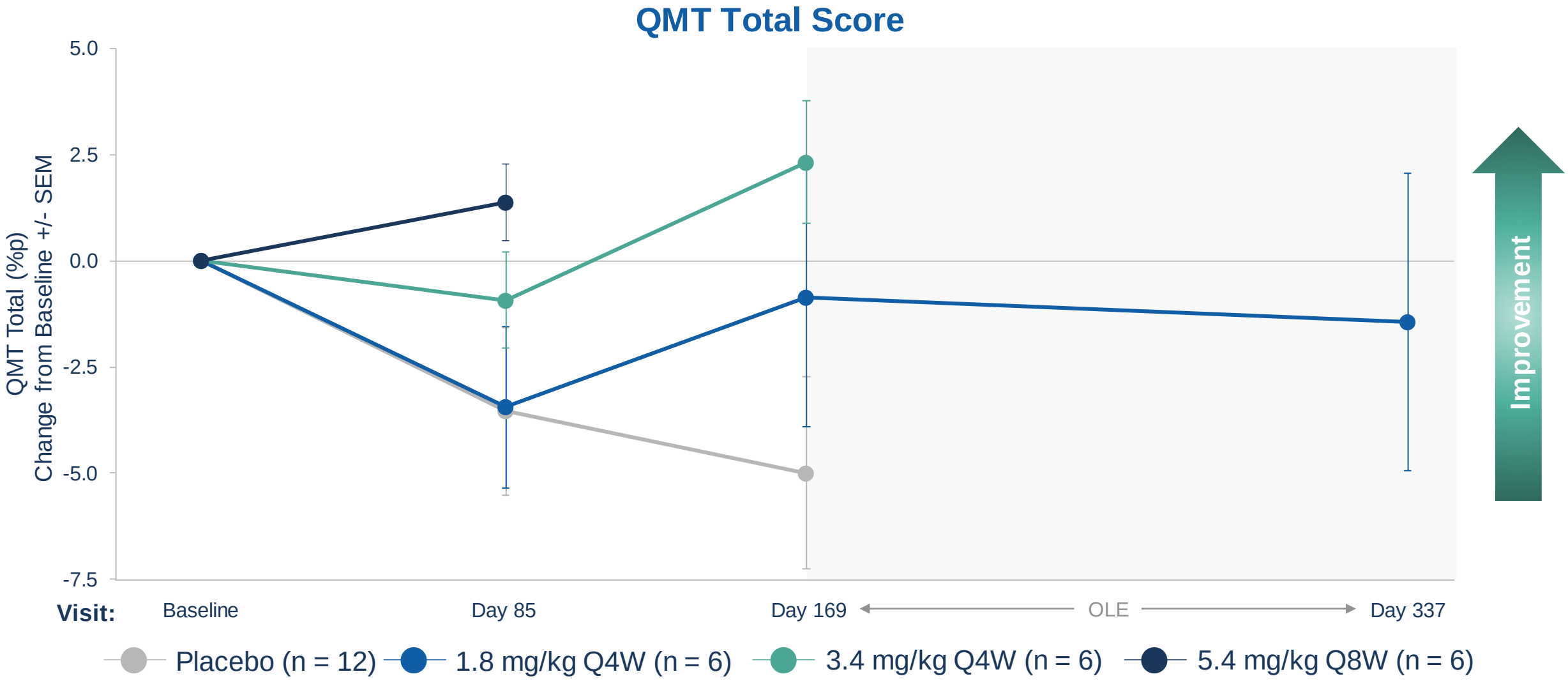
vHOT Middle Finger Change from Baseline



1. Middle Finger (sec) is the average of all myotonia trials for an individual participant in ACHIEVE.
Note: Placebo group includes 12 participants at Day 85 and 8 participants at Day 169. Mean percent change from baseline for placebo group are based on baseline values from 12 patients.

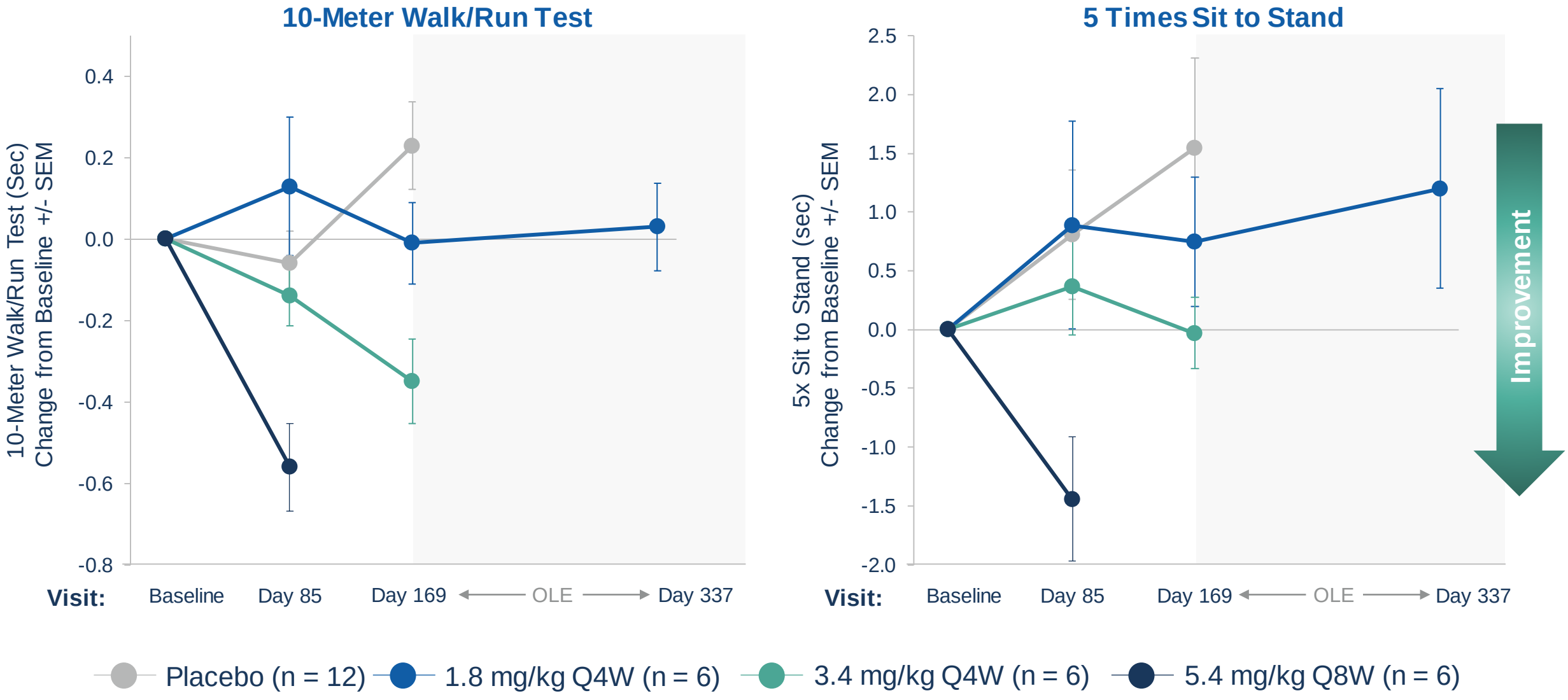
DYNE-101 Demonstrated Improvement in Muscle Strength

Measured by Quantitative Muscle Testing (QMT)



Note: Placebo group includes 12 participants at Day 85 and 8 participants at Day 169.

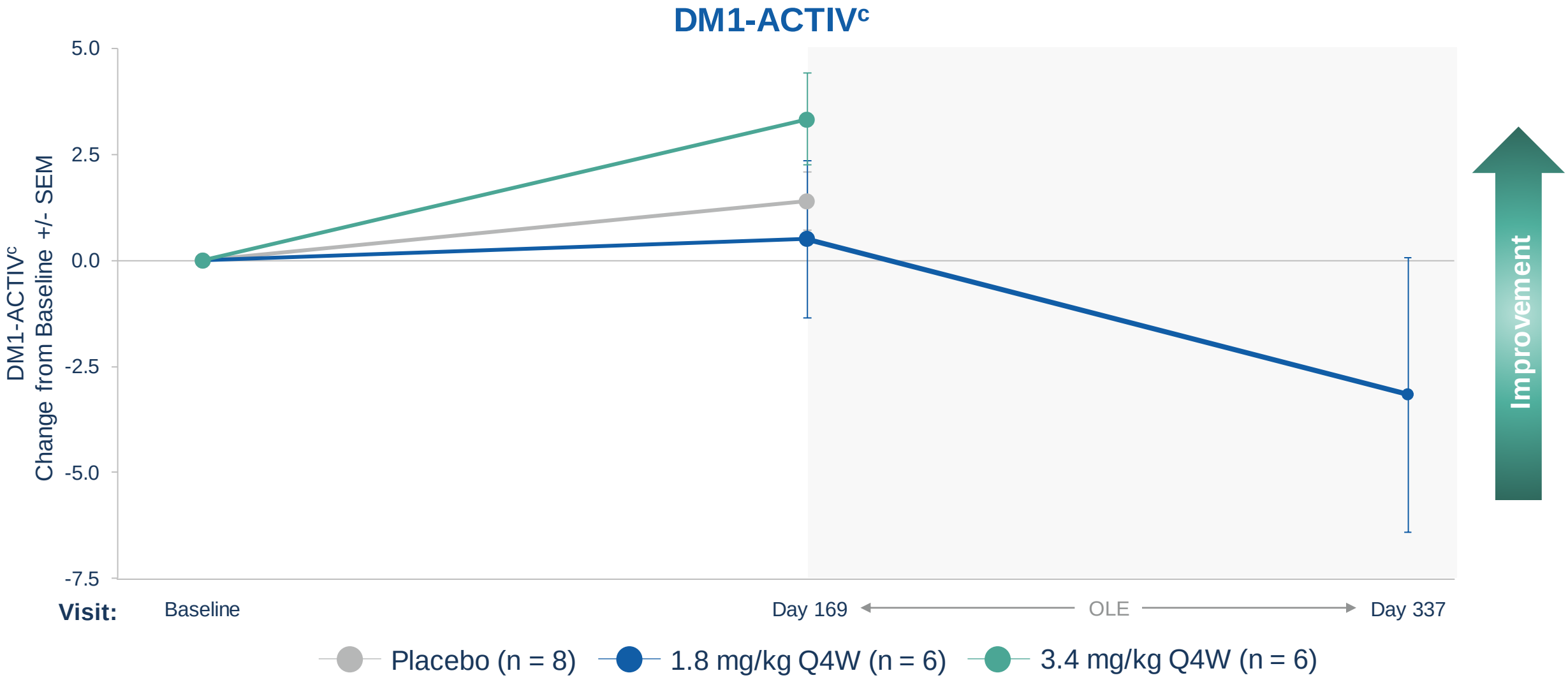
DYNE-101 Demonstrated Early and Sustained Potential Benefit Across Multiple Timed Function Tests



Note: Placebo group includes 12 participants at Day 85 and 8 participants at Day 169.

DYNE-101 Showed Improvement from Baseline in Activities of Daily Living

Measured by DM1-ACTIV^{c} Patient Reported Outcome

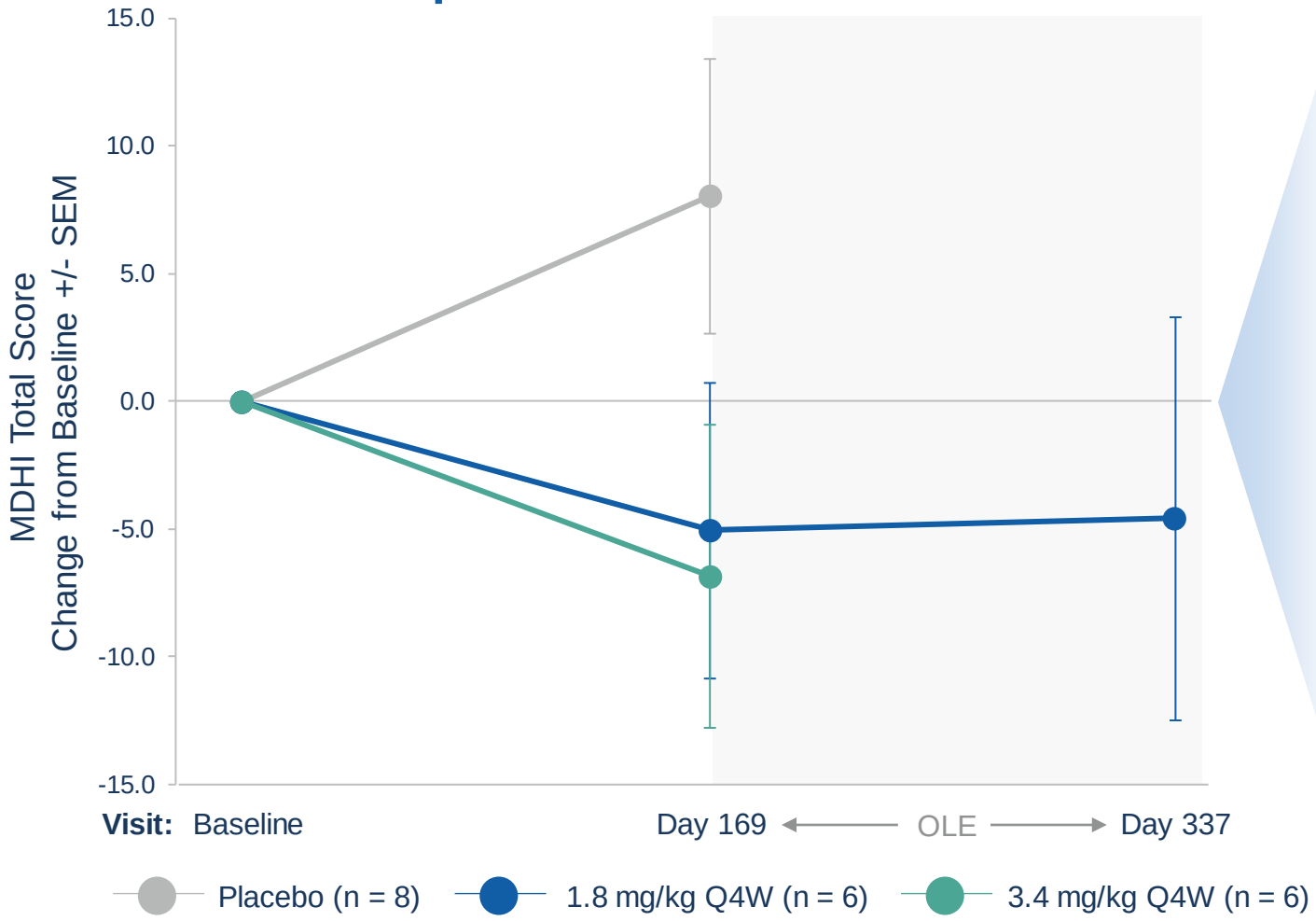


Notes: Patient-reported outcomes (PRO), including DM1-ACTIVc, collected at baseline, Day 169 and Day 337.

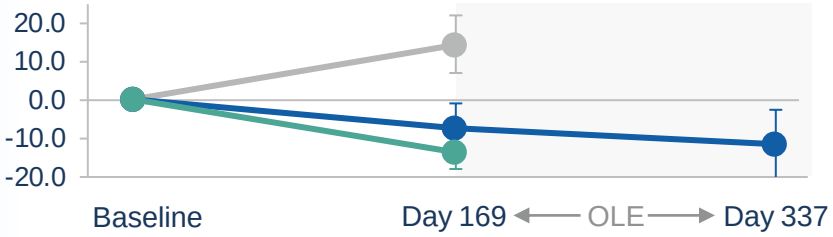
DYNE-101 Demonstrated Clinical Benefit Based on Well-Validated PRO

Showed Benefit in 17 out of 17 MDHI Subscales

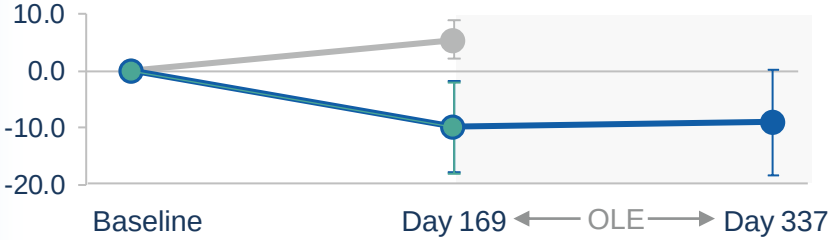
Improved MDHI Total Score



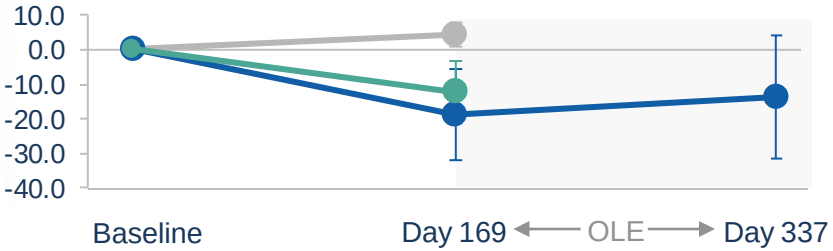
Upper Extremity Function



Gastrointestinal Issues



Fatigue



MDHI Total and Subscale Improvement

Note: Patient-reported outcomes (PRO), including Myotonic Dystrophy Health Index (MDHI) collected at baseline, Day 169 and Day 337.

ACHIEVE Data Demonstrated DYNE-101 Best-in-Class Potential

ACHIEVE

- ✓ Dose-dependent muscle delivery and compelling splicing correction consistent across patients
- ✓ Meaningful improvement in multiple clinical endpoints, including myotonia, muscle strength, timed functional assessments, and patient reported outcomes
- ✓ Early indication of durable effect beyond monthly dosing supports exploration of Q8W dosing
- ✓ Deepening of response with longer time on therapy
- ✓ Favorable safety profile to date[1]; 6.8 mg/kg Q8W cohort fully enrolled

Pursuing expedited approval based on regulatory interactions and strength of results
Additional data from ACHIEVE expected in early January 2025

1. Data as of August 20, 2024.

Building a Global DMD Franchise of Transformative Therapies

Overview

- Mutation in the *DMD* gene that encodes for dystrophin
- Onset in first few years of life
- Life expectancy ~30 years

Clinical Presentation

- Muscle weakness
- Progressive loss of function
- Loss of ambulation
- Respiratory/cardiac failure

Population

- ~12,000 - 15,000 (US)
- ~ 25,000 (Europe)

Current Approved Exon 51 Therapies Only Increased Dystrophin Production <1%

OUR APPROACH

Potential Best-in-class Targeted Exon Skipping

Increase dystrophin expression and enable less frequent dosing to potentially **stop or reverse disease progression**

Phase 1/2 Clinical Trial to Evaluate DYNE-251 in Patients with DMD

Population

- Male patients with DMD with mutations amenable to exon 51 skipping therapy
- Ages 4 to 16 years
- Ambulant and non-ambulant

Primary Endpoints

- Safety and tolerability
- Change from baseline in dystrophin protein levels by Western Blot

Additional Endpoints

- Pharmacokinetics
- Change from baseline of:
  - Exon 51 skipping levels
  - Muscle tissue PDPF
  - Multiple assessments of muscle function, including NSAA score, SV95C and certain timed functional tests

Stages of DELIVER

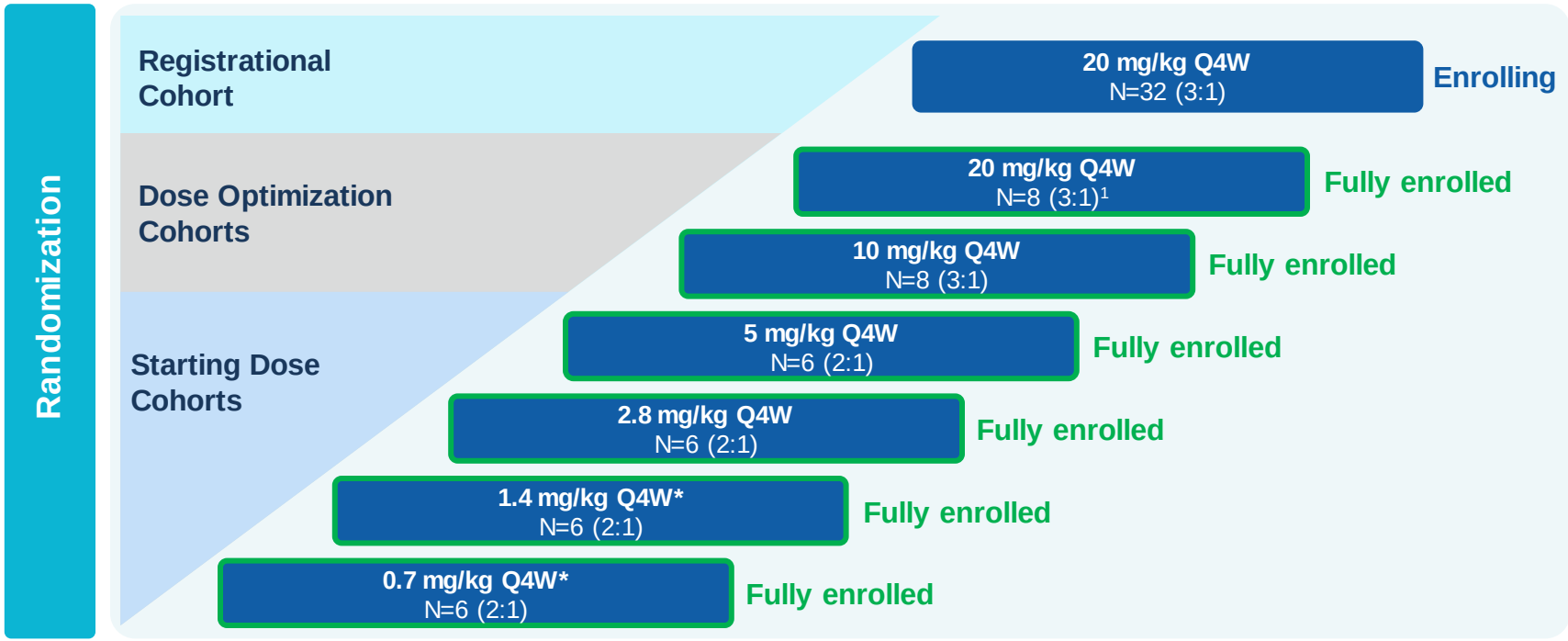
- Multiple Ascending Dose (MAD): 24 weeks
- Open-Label Extension (OLE): 24 weeks
- Long-Term Extension (LTE): 96 weeks

Note: Additional endpoints include select secondary and exploratory endpoints
PDPF: percent dystrophin-positive fibers; NSAA: North Star Ambulatory Assessment; SV95C: Stride Velocity 95th Centile.

DELIVER Trial Design

DELIVER

Global, Randomized, Placebo-Controlled Stage Evaluating Administration of DYNE-251 in Ambulant and Non-Ambulant Male DMD Patients with Mutations Amenable to Exon 51 Skipping Therapy



MAD Study Details

- IV administration of DYNE-251 or placebo every 4 weeks or every 8 weeks
- Muscle biopsies: Baseline and 24 weeks[2]
- Patients in MAD study escalated to highest tolerable dose in OLE and LTE

Global Trial Designed to be Registrational and to Enable Rapid Achievement of Predicted Pharmacologically Active Dose Levels

Doses provided refer to PMO component of DYNE-251. Cohorts randomized to active arm or placebo.
1. All participants in DELIVER starting dose and dose optimization cohorts are currently receiving 20 mg/kg dose, including 32 participants dose escalated following the placebo-controlled period from starting doses lower than 20 mg/kg and 14 participants initiated at 40 mg/kg who are now being dosed at 20 mg/kg following evaluation of the safety profile at 40 mg/kg. 2. Muscle biopsies taken at baseline and 24 weeks in 2.8 mg/kg Q4W cohort to 20 mg/kg Q4W cohort; biopsies not taken in 0.7 mg/kg and 1.4 mg/kg cohorts.

DELIVER Baseline Participant Characteristics: By Cohort

mean (SD) or n(%)	0.7 mg/kg (N=6)	1.4 mg/kg (N=6)	2.8 mg/kg (N=6)	5 mg/kg (N=6)	10 mg/kg (N=8)	20 mg/kg (N=8)
Age (years)	10.8 (2.2)	8.0 (3.5)	10.7 (2.9)	8.3 (2.8)	6.6 (2.2)	8.1 (2.4)
BMI (kg/m^2)	19.5 (3.4)	18.6 (2.2)	22.6 (6.3)	20.9 (1.6)	18.3 (3.2)	18.6 (5.1)
Age of Symptom Onset (years)	3.7 (1.8)	4.5 (2.1)	2.8 (1.8)	3.7 (3.1)	2.8 (1.6)	2.9 (2.0)
Corticosteroid dosing regimen (n (%))[1] Daily Other	 4 (66.7%) 2 (33.3%)	 4 (66.7%) 3 (50.0%)	 5 (83.3%) 2 (33.3%)	 6 (100.0%) 0	 8 (100.0%) 0	 8 (100.0%) 2 (25.0%)
Prior DMD Therapy (n (%)) Eteplirsen Other	 4 (66.7%) 2 (33.3%)	 2 (33.3%) 1 (16.7%)	 5 (83.3%) 0	 1 (16.7%) 0	 1 (12.5%) 1 (12.5%)	 0 2 (25.0%)
NSAA Total Score	22.2 (7.2)	22.8 (10.5)	20.3 (9.0)	21.0 (7.0)	25.3 (6.4)	15.6 (5.1)
10 Meter Run/Walk (sec)	6.1 (1.5)	6.3 (5.2)	6.9 (3.6)	5.1 (1.5)	4.6 (1.9)	7.7 (3.8)
Time Rise From Floor (sec)	8.5 (4.0)	3.1 (0.3)	6.9 (4.9)	5.0 (2.6)	6.3 (5.6)	5.1 (2.3)
Stride Velocity 95th Percentile (m/sec)	N/A	N/A	N/A	N/A	1.9 (0.5)	1.4 (0.5)

Note: Q4W and placebo arms are reported together for baseline characteristics. N/A: not applicable as data not collected.
1. Historical corticosteroid regimen based on medical history; a participant can be counted in multiple categories.

DYNE-251 Safety Profile Is Favorable to Date

Summary of Treatment Emergent Adverse Events (TEAEs)[1]

TEAE Category	Participants with ≥1 TEAE – n (%)								
	0.7mg/kg Q4W N=6	1.4 mg/kg Q4W N=6	2.8 mg/kg Q4W N=6	5 mg/kg Q4W N=6	10 mg/kg Q4W N=8	20 mg/kg Q4W N=8	40 mg/kg Q8W [7] N=8	40 mg/kg Q4W [7] N=6	Overall[1] N=54
Any TEAE	6 (100%)	6 (100%)	4 (67%)	6 (100%)	7 (88%)	8 (100%)	6 (75%)	4 (67%)	47 (87%)
Any related TEAE	3 (50%)	3 (50%)	0	6 (100%)	3 (38%)	4 (50%)	1 (13%)	2 (33%)	22 (41%)
Any serious TEAE	0	0	1 (17%)	0	0	1 (13%)	2 (25%)	2 (33%)	6 (11%)
Any serious related TEAE	0	0	0	0	0	0	0	2 (33%)	2 (4%)
Any TEAE leading to withdrawal	0	0	0	0	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0	0	0	0	0

Most TEAEs Were Mild or Moderate in Intensity

- 3 serious TEAEs potentially related to study drug in two participants
  - Acute kidney injury (1); thrombocytopenia (1) [2]
  - Pancytopenia (1) [3]
- 6 serious TEAEs unrelated to study drug
  - Dehydration due to gastroenteritis (1)
  - Femoral neck fracture (1); gastric volvulus (1) [4]
  - Tibia fracture (1)
  - Febrile convulsion (1); pyrexia (1) [5]
- Most common TEAEs (>20% participant incidence)[6]
  - Pyrexia (32%)
  - Nasopharyngitis, headache, vomiting (each 26%)
  - Fall (26%)
  - Infusion-related reaction (20%)

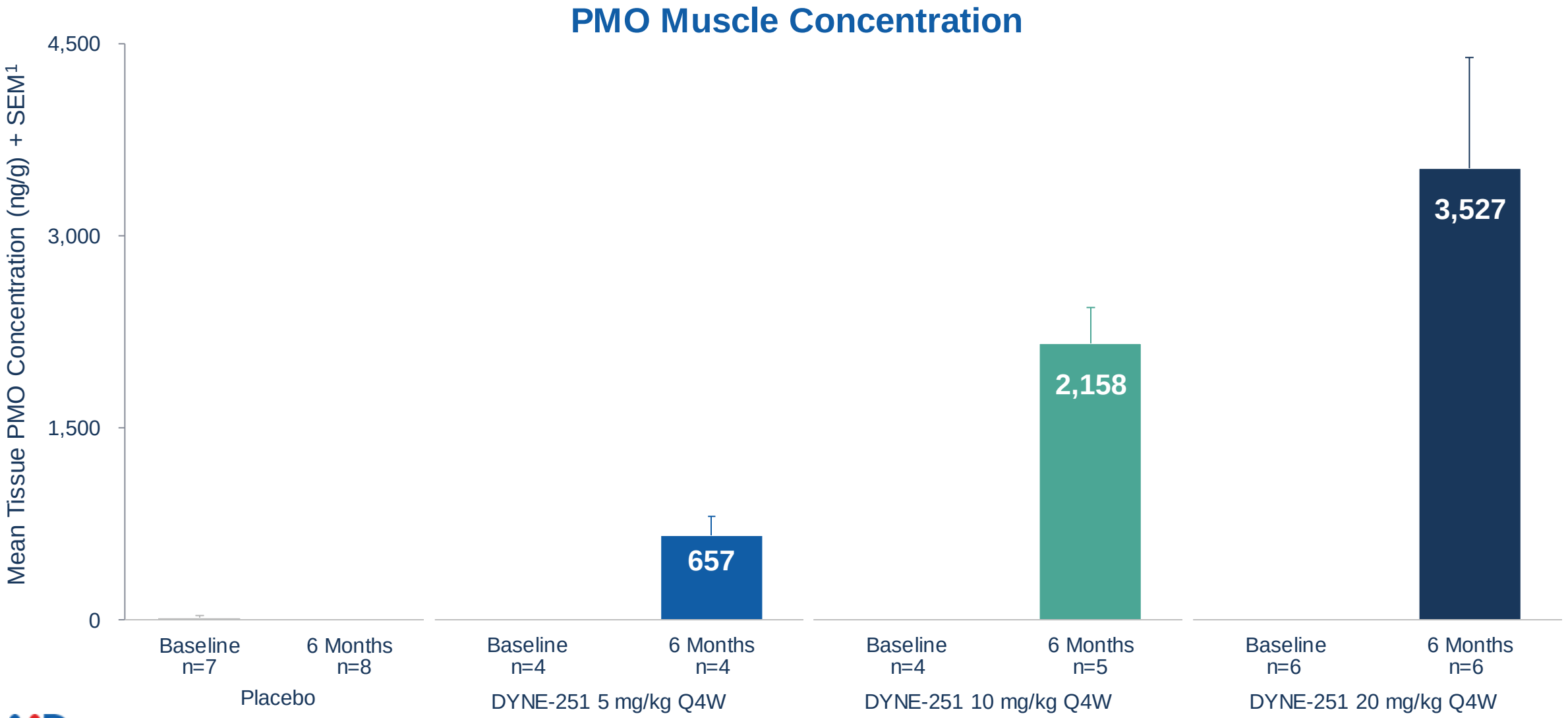
Additional Safety Data

- Other than two participants with serious TEAEs in 40 mg/kg Q4W cohort:
  - No participants have demonstrated persistent related anemia or thrombocytopenia
  - No participants have demonstrated kidney injury
- No participants have demonstrated clinically meaningful changes in electrolytes, including magnesium

~675 Doses Administered to Date Representing Over 50 Patient-Years of Follow-Up[1]

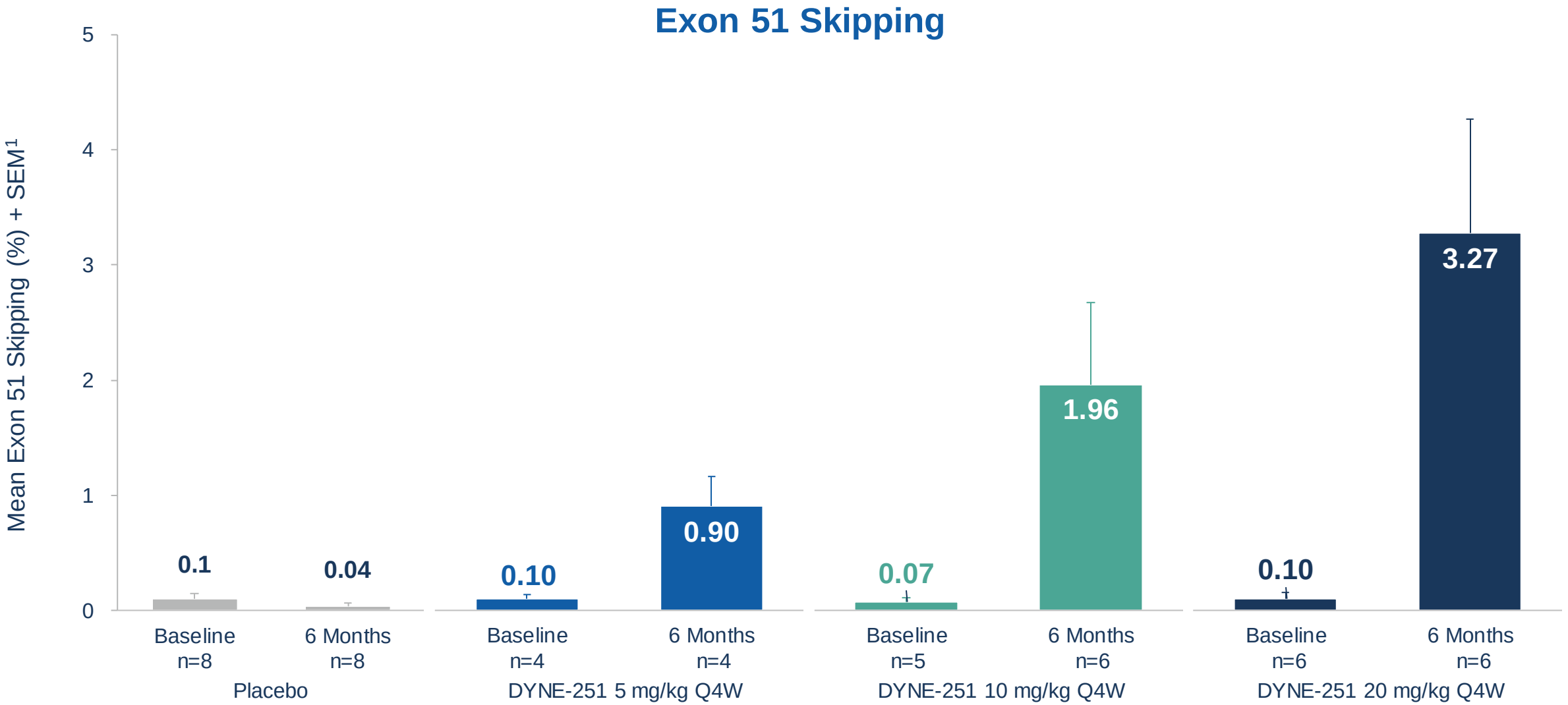
1. Data as of August 21, 2024; 2. Events have same day of onset in a single participant in the context of fever, hemolysis, diarrhea and positive blood in stool; together, these events are potentially consistent with hemolytic uremic syndrome (HUS) with a potential infectious etiology. 3. Participant had a history of hemolytic anemia of unidentified etiology prior to enrolling in DELIVER. Presented with fever and tonsilitis; all symptoms resolved without therapeutic intervention 4. Events occurred in same participant at different times; 5. Events occurred in same participant at different times; 6. All cohorts combined; preferred terms are reported; 7. 14 participants initiated at 40 mg/kg who are now being dosed at 20 mg/kg following evaluation of the safety profile at 40 mg/kg.

DYNE-251 Drove Dose Dependent Delivery of PMO to Muscle



1. DELIVER biopsy taken approximately 28 days after most recent dose; 6 months = Week 25 for DELIVER.

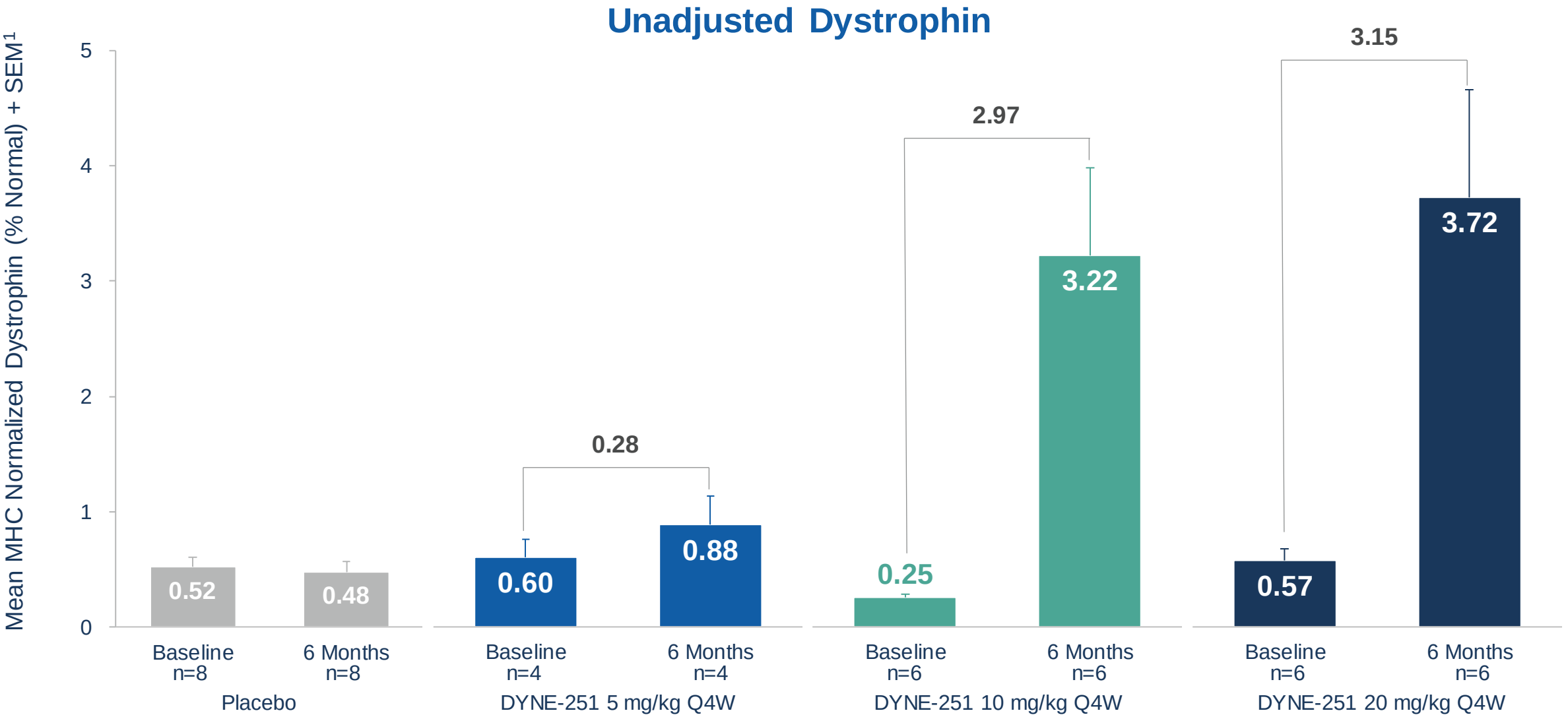
DYNE-251 Demonstrated Dose-Dependent Exon Skipping



1. DELIVER biopsy taken approximately 28 days after most recent dose; 6 months = Week 25 for DELIVER.

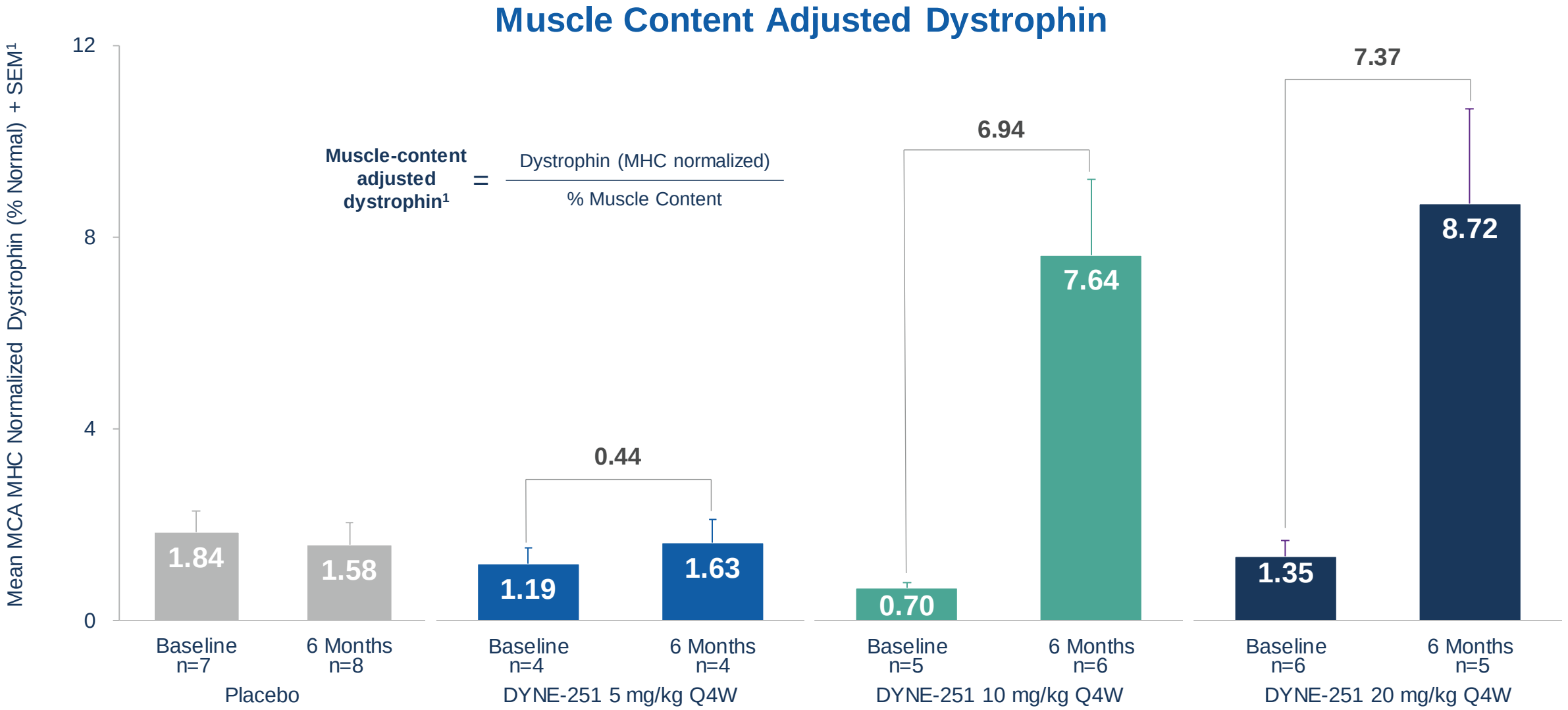
Higher Doses of DYNE-251 Continued to Drive Robust Dystrophin Expression

DYNE-251 Showed 3.7% Unadjusted Dystrophin at 6 Months



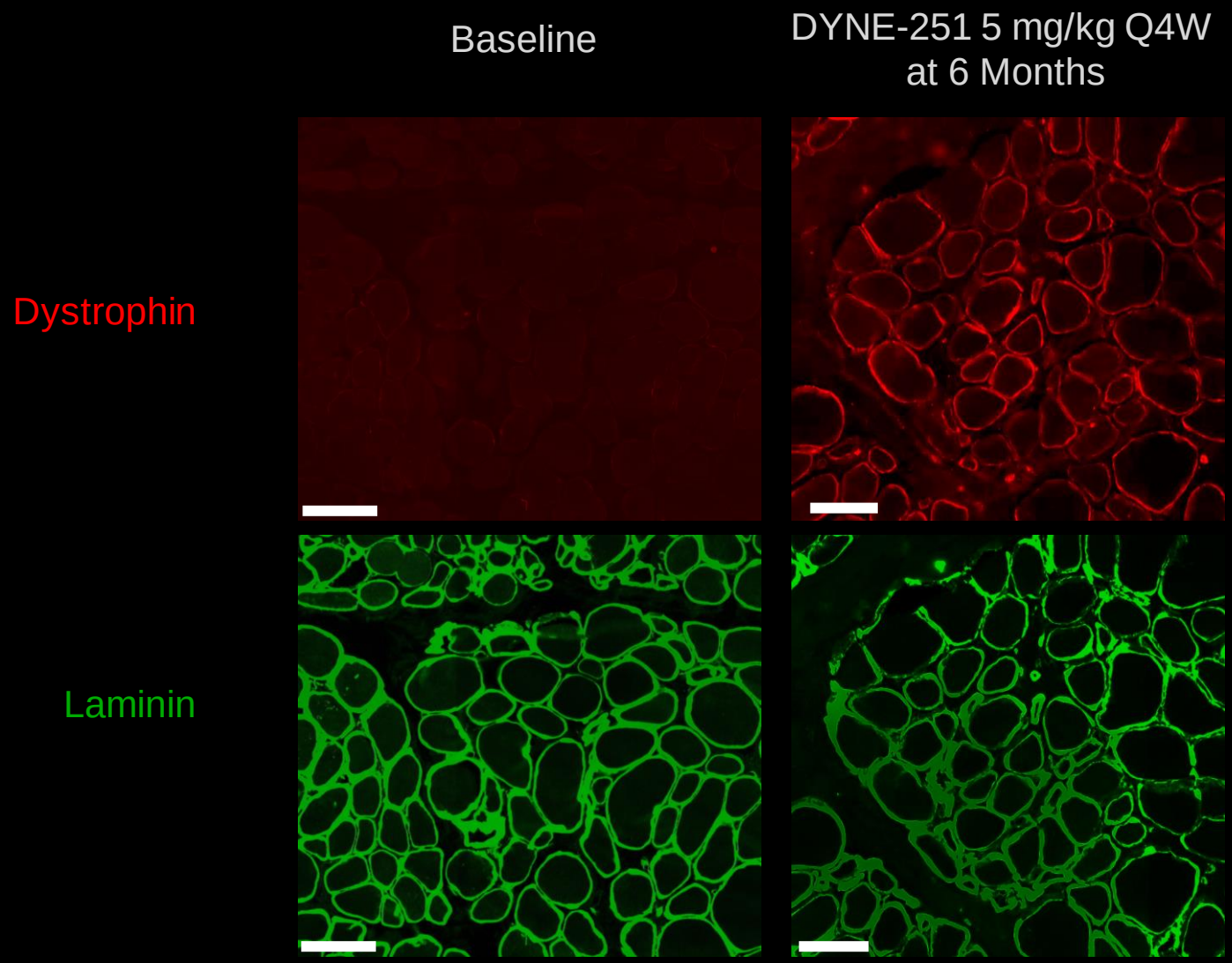
1. DELIVER biopsy taken approximately 28 days after most recent dose; 6 months = Week 25 for DELIVER.

DYNE-251 Positioned as a Potentially Best-in-Class Next Generation Exon Skipper, Achieving 8.7% Muscle Content Adjusted Dystrophin at 6 Months



1. DELIVER biopsy taken approximately 28 days after most recent dose; 6 months = Week 25 for DELIVER.

PDPF: Clear Improvement in Dystrophin Localization to Sarcolemma

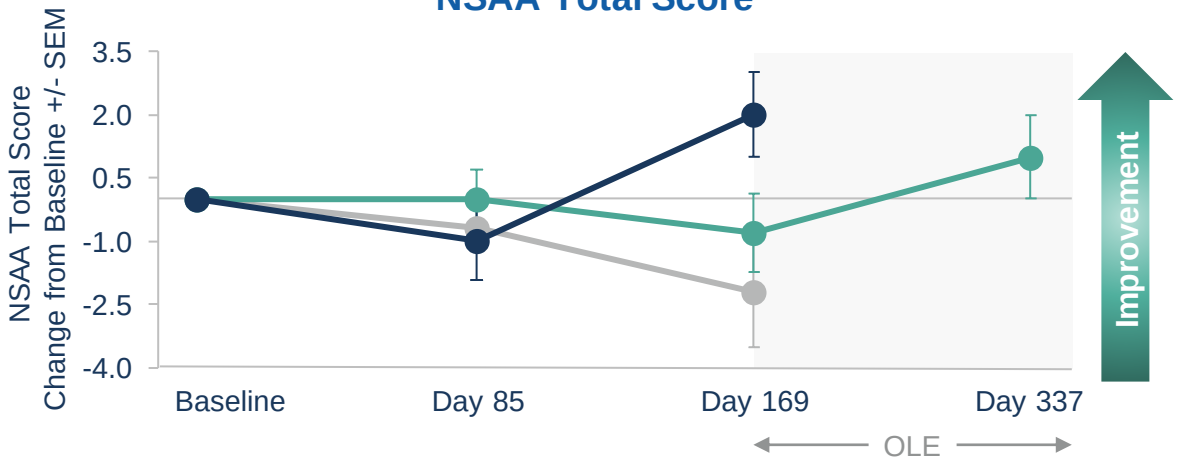


Notes: DELIVER biopsy taken approximately 28 days after most recent dose. Notes: scale bar is 100 µm.

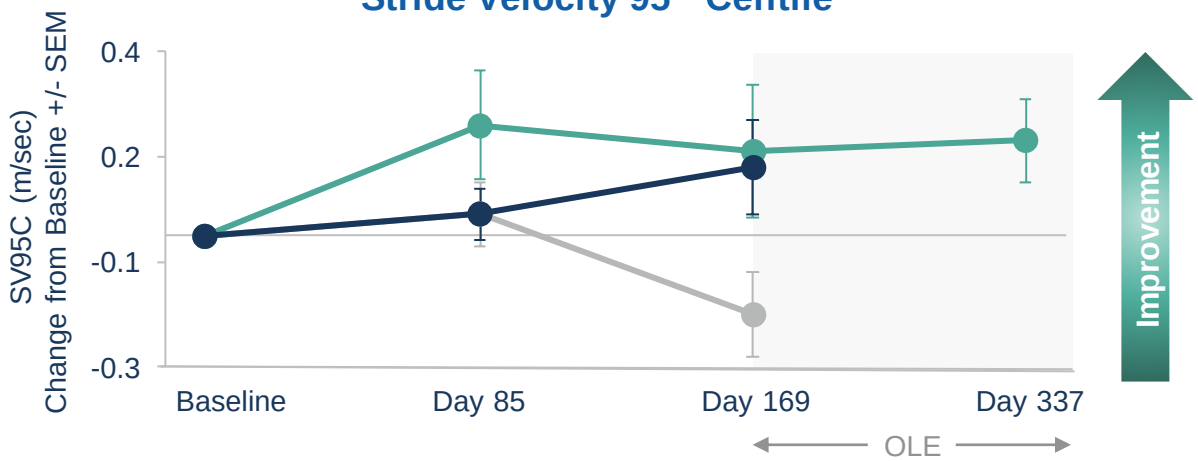
Improvements Across Multiple Functional Endpoints in Multiple Cohorts

Baseline Values Inform Interpretation of Data; Ongoing Exploration of Longer Timepoints

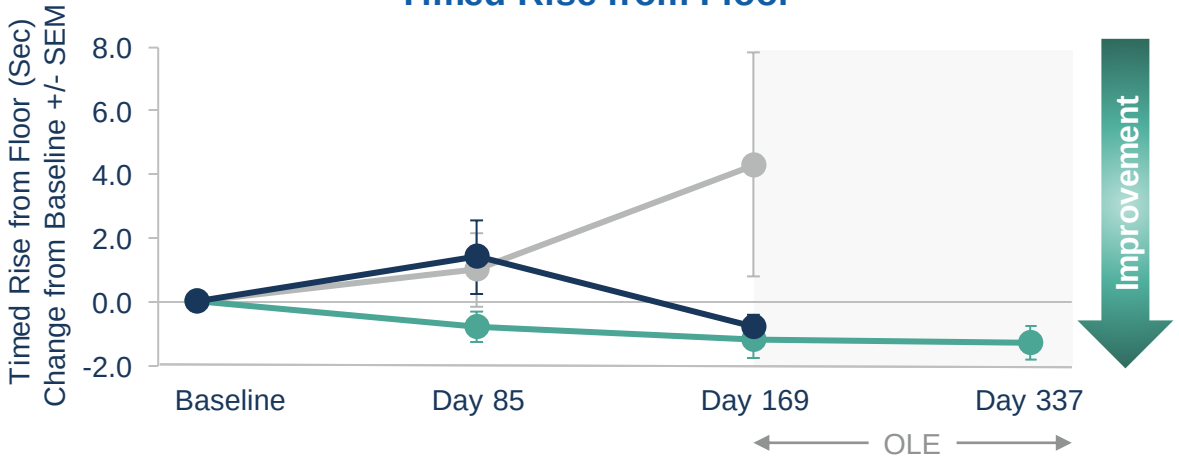
NSAA Total Score



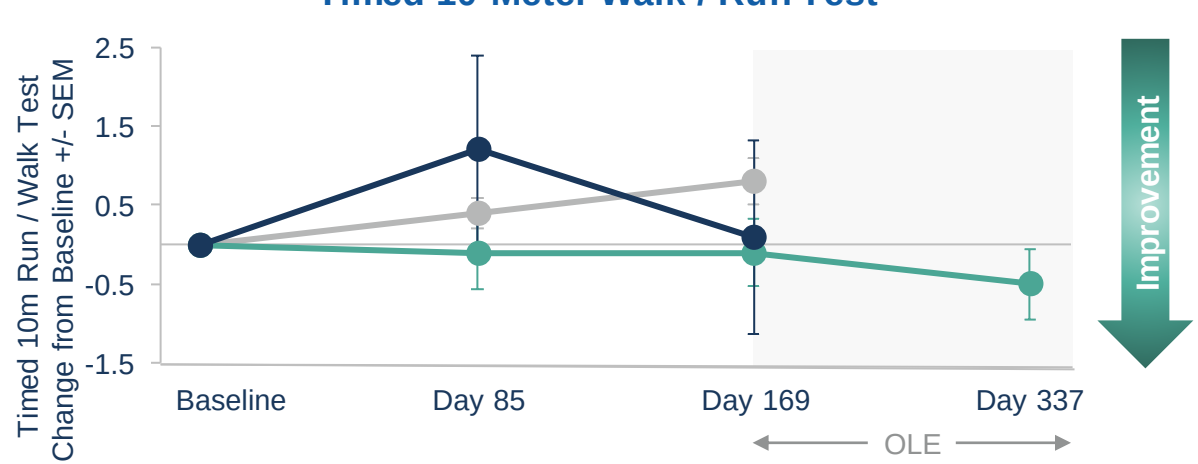
Stride Velocity 95th Centile



Timed Rise from Floor



Timed 10-Meter Walk / Run Test



Placebo (n=6 for SV95C and n=14 for other endpoints)

DYNE-251 10 mg/kg Q4W (n = 6 for all endpoints) [1]

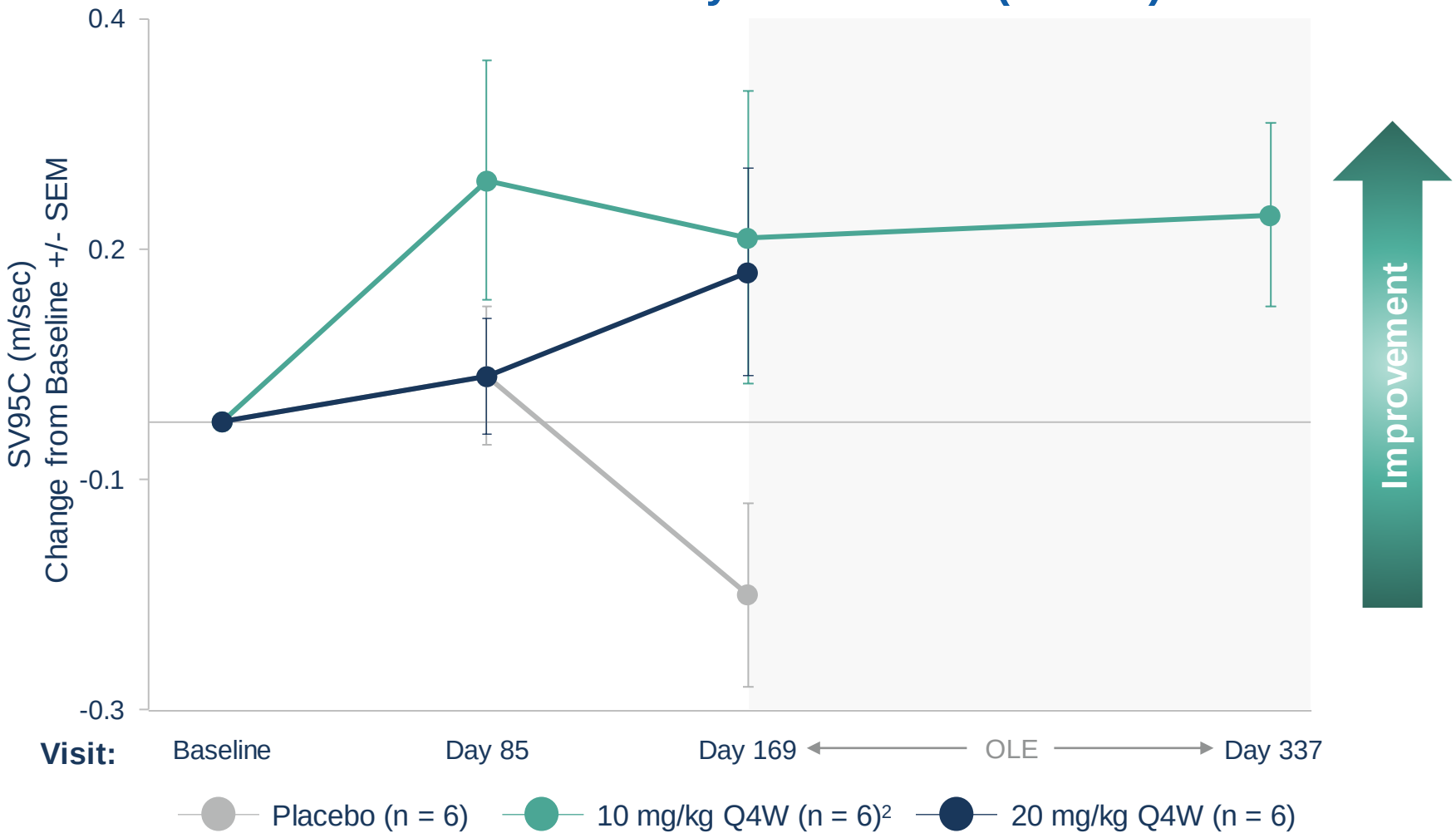
DYNE-251 20 mg/kg Q4W (n = 6 for all endpoints)

1. During the OLE, all participants in 10 mg/kg cohort were dose escalated to 20 mg/kg Q4W regimen.

DYNE-251 Drove Clinically Meaningful Improvements in Stride Velocity 95th Centile

SV95C is a Qualified Primary Endpoint for Duchenne Trials in Europe and Leveraged Across Global Trials

Stride Velocity 95th Centile (SV95C)



- SV95C is a digital objective endpoint of ambulatory performance in patients' normal daily environment
- Patients in DELIVER wore the device on each ankle for 3 weeks prior to the clinic visits
- The change from baseline met the published MCID by the EMA[1]

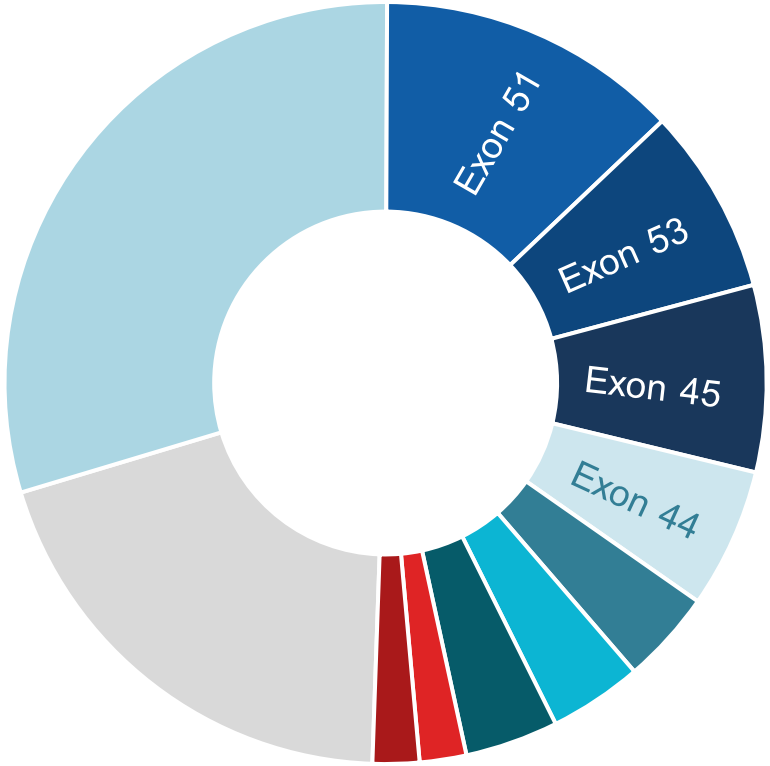
1. Minimal clinically important difference (MCID) as defined by EMA in its qualification opinion for SV95C as primary endpoint in studies in ambulatory DMD studies. 2. During the OLE, all participants in 10 mg/kg cohort were dose escalated to 20 mg/kg Q4W regimen.

Opportunity to Build a Global DMD Franchise: Leading with DYNE-251, Payloads Identified for Exons 53, 45, 44

Approximately

80% of patients

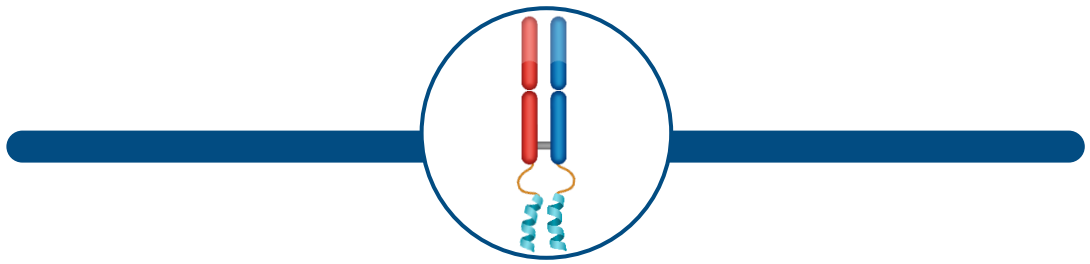
have genotypes amenable to exon skipping



- Exon 51 – **13%**
- Exon 53 – **8%**
- Exon 45 – **8%**
- Exon 44 – **6%**
- Exon 50 – **4%**
- Exon 52 – **4%**
- Exon 43 – **4%**
- Exon 55 – **2%**
- Exon 8 – **2%**
- Other exon skips – **~30%**
- May not be amenable to exon skipping – **~20%**

FORCE Positions Dyne With Potential Leading Role in Evolving DMD Therapeutic Landscape

FORCE



Potency	✓ Targeted muscle delivery, near full-length dystrophin
Durability	✓ Durable target engagement
Dosing	✓ Re-dosable, titratable
Tolerability	✓ Favorable safety profile
Manufacturing	✓ Well-established, scalable

- Muscle delivery is the challenge
- Clinical data to date validates FORCE's targeted delivery to muscle
- Non-targeted delivery modalities face significant challenges, including an acceptable therapeutic index
- SMA landscape strong analogue to DMD with ZOLGENSMA (gene therapy) and SPINRAZA (oligo) playing an important role in evolving standard of care

Advancing DYNE-251 Towards Potentially Registrational Data Set

- ✓ Unprecedented level of dystrophin generated, with 3.7% unadjusted and 8.7% muscle content adjusted dystrophin
- ✓ Improvements in multiple functional outcomes, including SV95C, an approvable endpoint in Europe, in multiple cohorts
- ✓ Favorable safety profile to date[1]; enrolling registrational cohort at 20 mg/kg Q4W
- ✓ Supports further development of DMD global franchise

Enrolling registrational cohort based on regulatory interactions and strength of data

1. Data as of August 21, 2024.

Driving Towards Potentially Transformative DM1 and DMD Therapies

ACHIEVE | DELIVER

Delivered on the Promise of FORCE: Enhanced Delivery of Therapeutics to Muscle

Compelling Impact on Key Disease Biomarkers and Improvements in Multiple Functional Endpoints in Both DM1 and DMD

Favorable Safety & Tolerability Profile

Fully Enrolled Through 6.8 mg/kg Cohort Additional Data Expected in Early January 2025

Enrolling Registrational Cohort at 20 mg/kg

Pursuing Expedited Approvals, including Accelerated Approval in the U.S., for Both Programs

FSHD Program

Overview

- Aberrant expression of DUX4
- Onset in teen years or young adulthood
- Normal life expectancy

Clinical Presentation

- Progressive wasting and skeletal muscle loss
- Significant physical limitations

Population

- ~16,000 - 38,000 (US)
- ~35,000 (Europe)

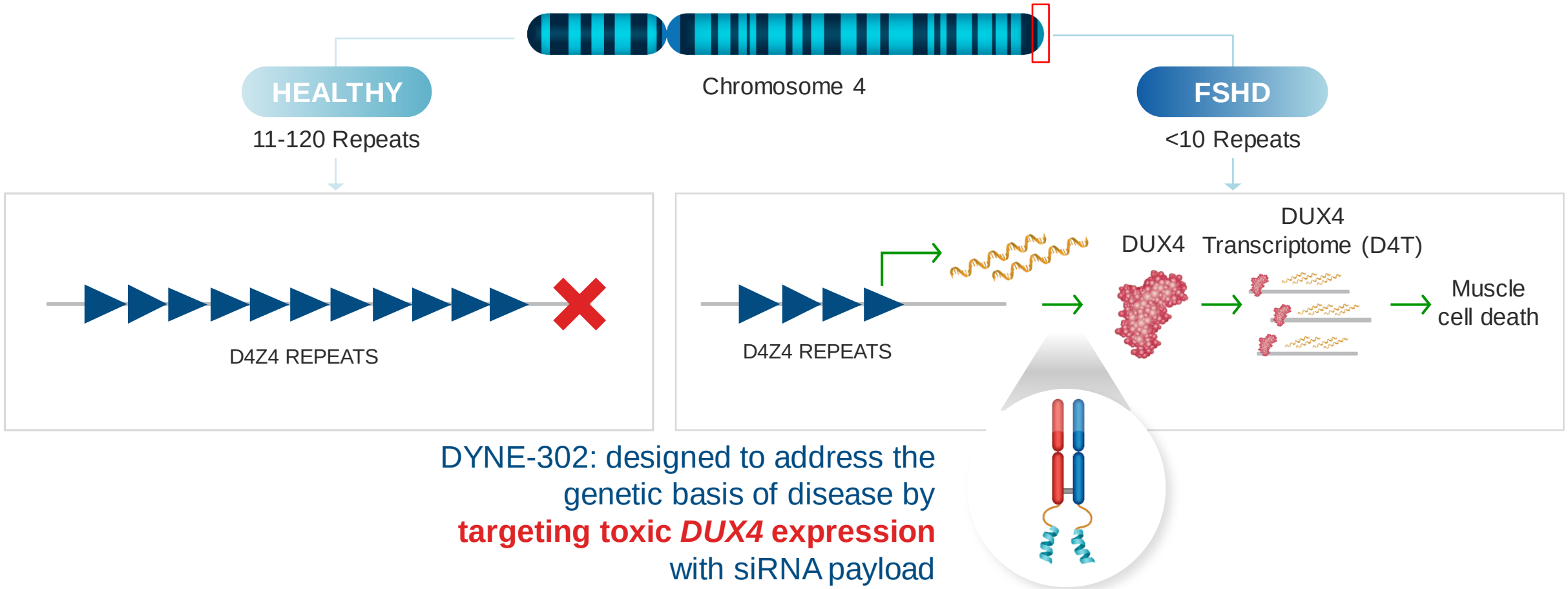
NO approved therapies

OUR APPROACH

Disease-Modifying DUX4 Knockdown

Targeting toxic *DUX4* mRNA expression to potentially **stop or reverse disease progression**

DYNE-302 Targets the Genetic Basis of FSHD

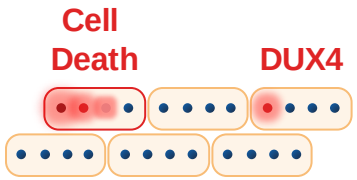


DYNE-302: designed to address the genetic basis of disease by **targeting toxic *DUX4* expression** with siRNA payload

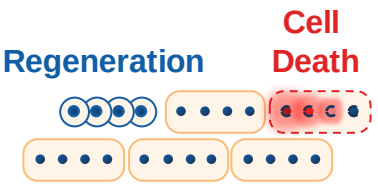
The hTfR1/iFLExD Mouse Model Recapitulates Multiple Aspects of Human FSHD

FSHD

Sporadic DUX4 activation



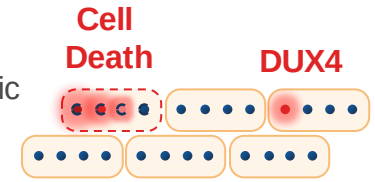
Years



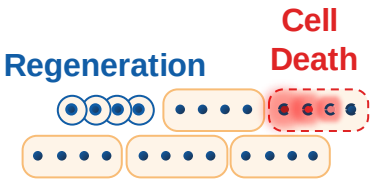
Slowly progressing myopathy and functional decline

hTfR1/iFLExD (Uninduced)

Chronic, sporadic DUX4 activation



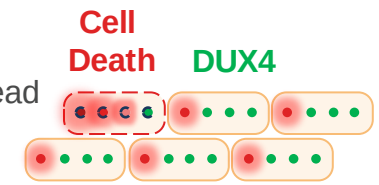
Weeks



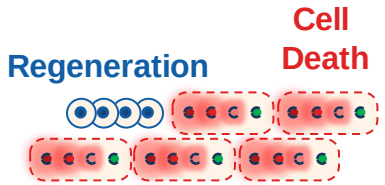
Slowly progressing myopathy without functional decline

hTfR1/iFLExD (Induced)

Acute, widespread DUX4 activation



Days

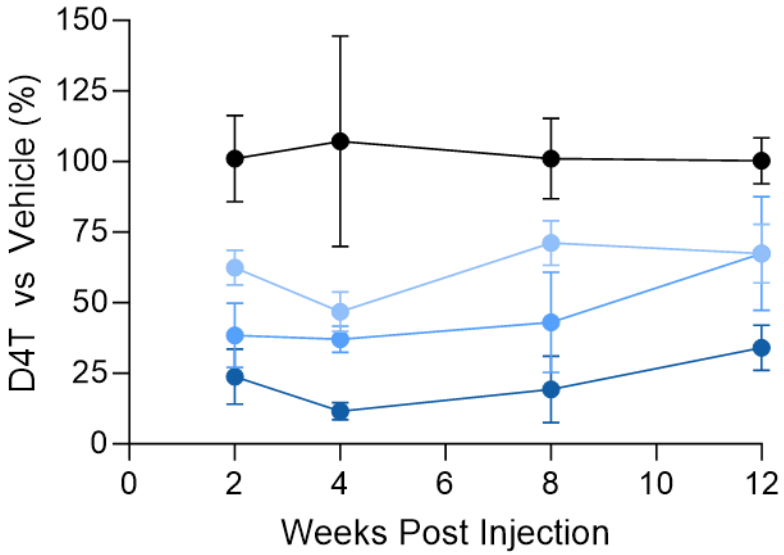


Rapidly progressing myopathy with functional decline

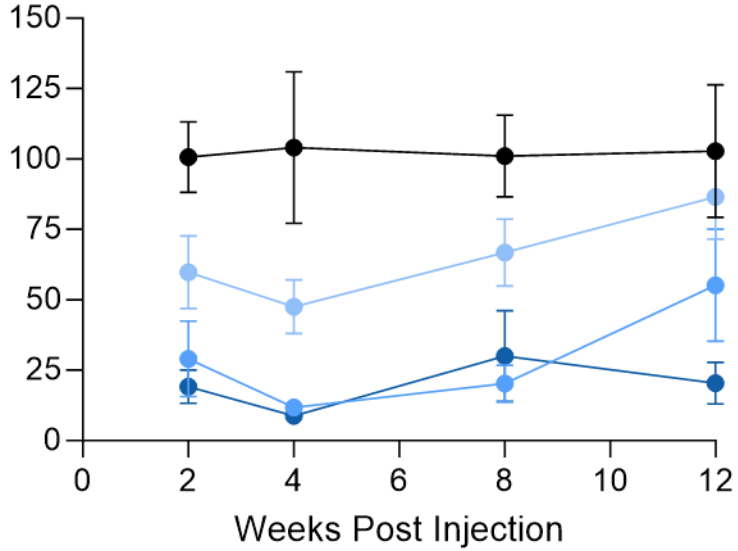
Notes: Jones et al. (2020) DOI: 1186/s13395-020-00227-4

Single Dose of DYNE-302 Achieved Robust, Durable, and Dose-Dependent D4T Knockdown in Skeletal Muscle of hTfR1/iFLExD FSHD Mice

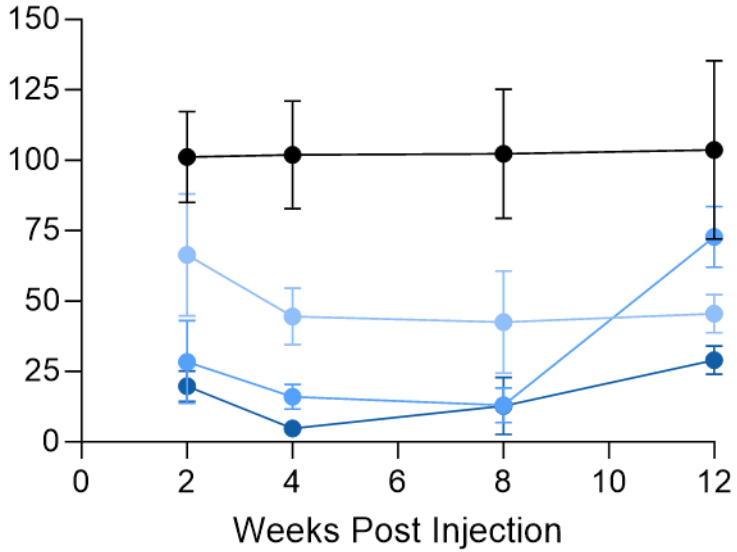
Quadriceps



Gastrocnemius



Tibialis Anterior



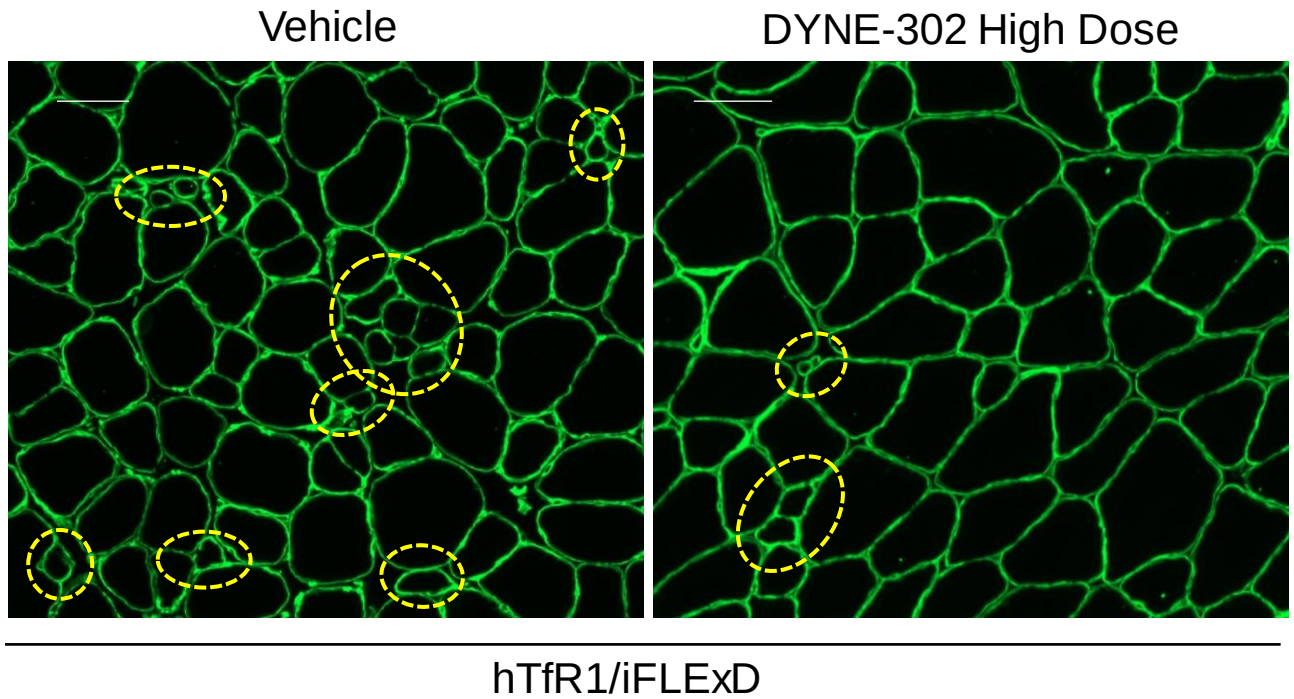
Vehicle | DYNE-302 Low Dose | DYNE-302 Medium Dose | DYNE-302 High Dose

DYNE-302 demonstrates potential for infrequent dosing, out to Q12W

Notes: Uninduced hTfR1/iFLExD mice dosed with vehicle or DYNE-302 on day 0, analyzed at indicated weeks. Data are means ± SD; n = 4 - 12. D4T is an average of mouse *Wfdc3*, *Sord*, and *Serpinb6c* mRNA markers.

Single Dose of DYNE-302 Corrected Muscle Pathology in Quadriceps of the Uninduced hTfR1/iFLExD FSHD Model at 12 Weeks

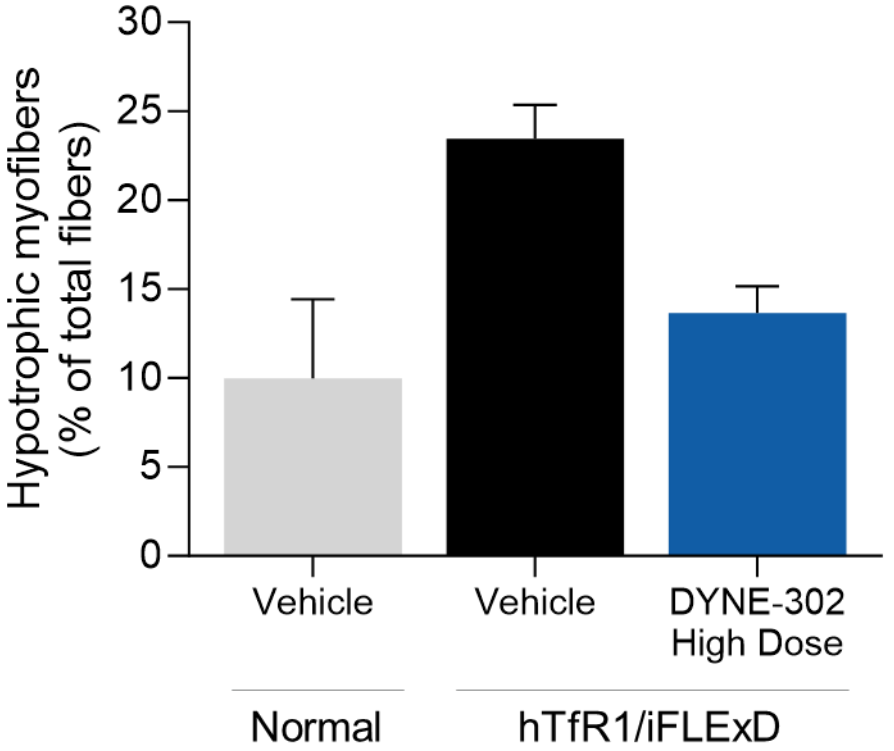
DYNE-302 reduces hypotrophic myofibers



Laminin

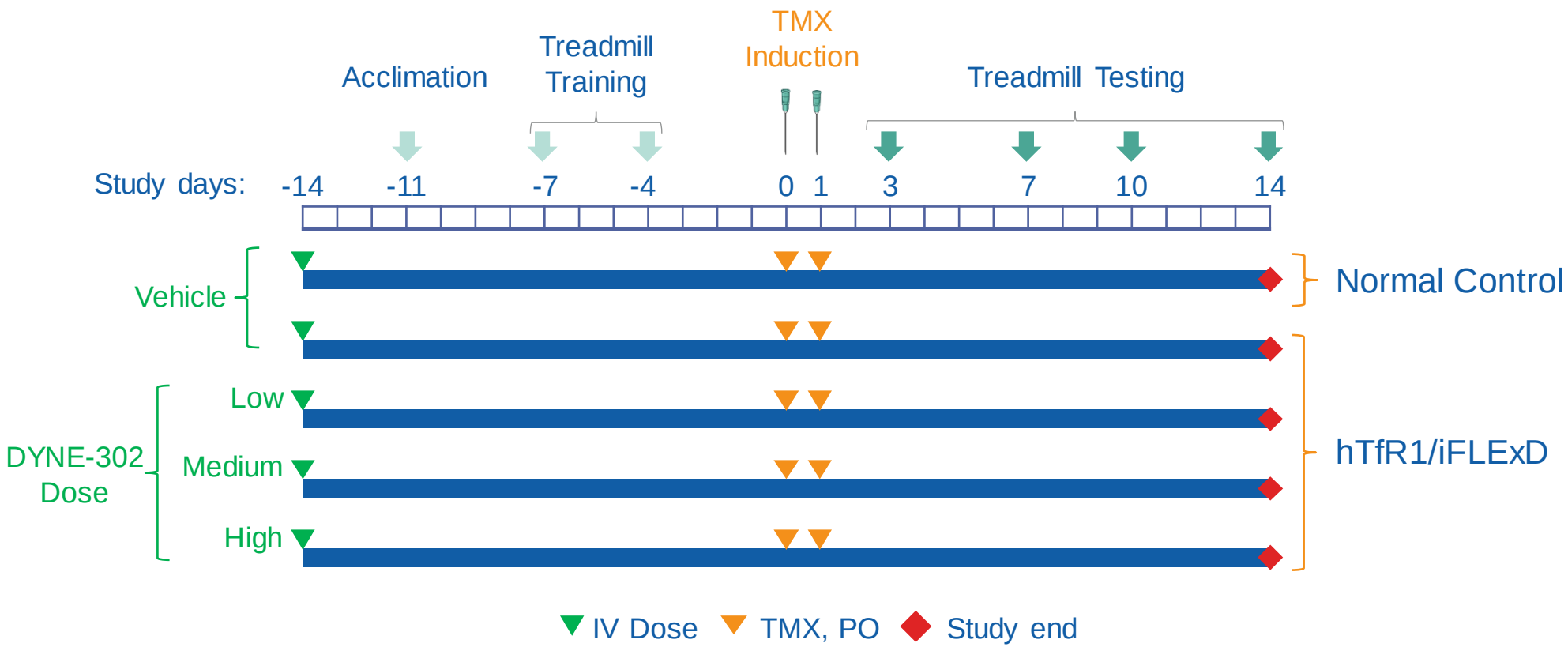
Fiber splitting (hypotrophic myofibers)

Quantification of hypotrophic myofiber reduction



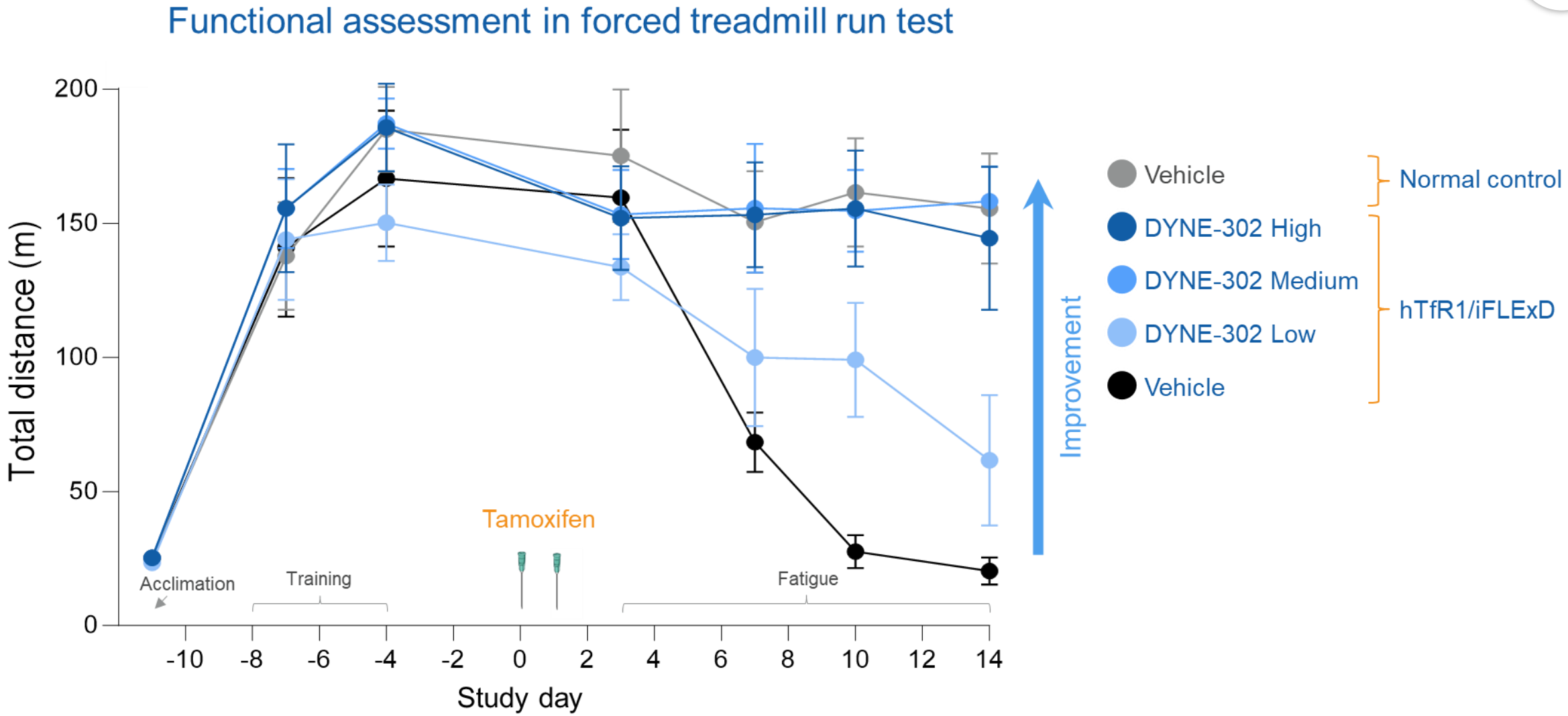
Notes: Uninduced hTfR1/iFLExD mice dosed with vehicle or DYNE-302 on day 0, analyzed on week 12. Data are means + SD; n = 4 – 9.

Study to Establish DYNE-302 Functional Benefit in the Induced hTfR1/iFLExD FSHD Mouse Model



Notes: IV = intravenous; PO = oral gavage; TMX = tamoxifen; hTfR1/iFLExD mice lacking ACTA-CRE-ER transgene were used as controls for TMX effect on function (normal control). hTfR1/iFLExD mice that were not induced with tamoxifen were also included as uninduced control (not shown).

Single Dose of DYNE-302 Demonstrated Functional Benefit in the Induced hTfR1/iFLExD FSHD Mouse Model



Notes: Mice dosed with vehicle or DYNE-302 on Day -14. Data are means ± SEM; n = 5 - 6.

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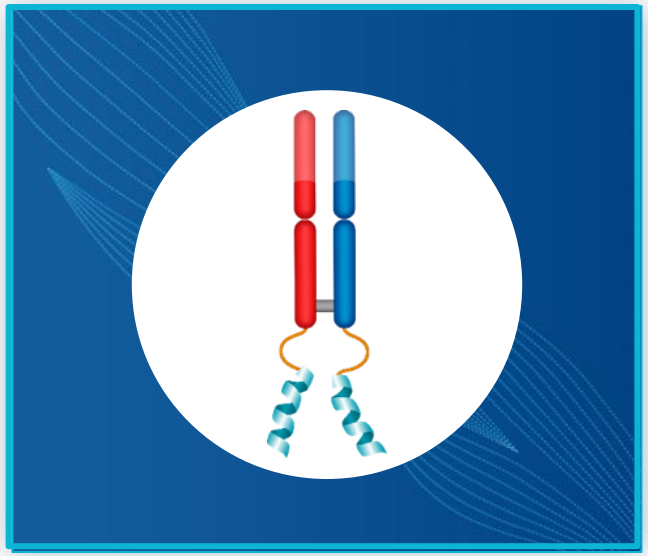

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