ACHIEVE

Dyne® THERAPEUTICS

DELIVER

Achieving the Promise of

FORCE

to Deliver for Patients

FORCE

DELIVER CLINICAL UPDATE | SEPTEMBER 3, 2024

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Program

Opening remarks
John Cox, President & CEO

DYNE-251 DELIVER Trial in DMD Data
Wildon Farwell, M.D., MPH, Chief Medical Officer

Closing Remarks
John Cox, President & CEO

Q&A

OUR MISSION

Life-transforming therapies

for patients with serious muscle diseases

Committed to Building the World's Leading Muscle Disease Company

DELIVER CLINICAL UPDATE

- Potential to transform the treatment paradigm for people living with DMD
- Best-in-class dystrophin resulting in unprecedented improvements in multiple functional outcomes, including NSAA and SV95C, in multiple cohorts[1]
- Favorable safety profile to date[2]

LEADERSHIP UPDATE

- Proven team of biopharma executives to deliver on Dyne's next chapter
  - Doug Kerr (CMO), Johanna Friedl-Naderer (CCO), and Lucia Celona (CHRO) bring decades of global experience across rare disease clinical development, commercial execution, and organizational builds
- Accelerating commercial preparedness across key functions

NEXT STEPS

- Continue to pursue expedited approval pathways globally
- Initiating registrational cohorts in DELIVER trial of DYNE-251 in DMD
- Provide update on the path to registration for DYNE-101 and DYNE-251 by the end of 2024

1. NSAA: North Star Ambulatory Assessment; SV95C: Stride Velocity 95th Centile. 2. Data as of August 21, 2024.

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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

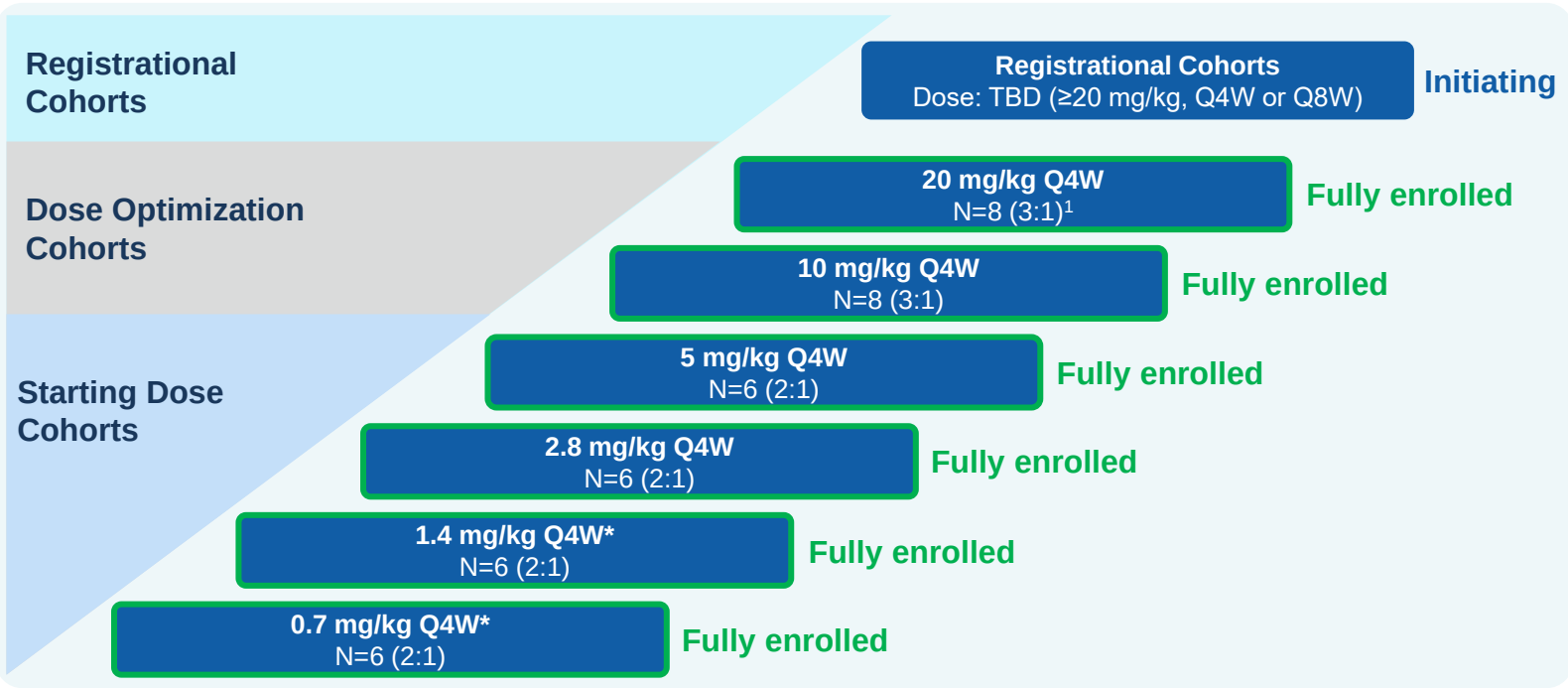
Note: Additional endpoints include select secondary and exploratory endpoints
PDPF: percent dystrophin-positive fibers; NSAA: North Star Ambulatory Assessment; SV95C: Stride Velocity 95th Centile.

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

Randomization



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

Dyne THERAPEUTICS

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)	7.8 (3.3)	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 (2.3)	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%)

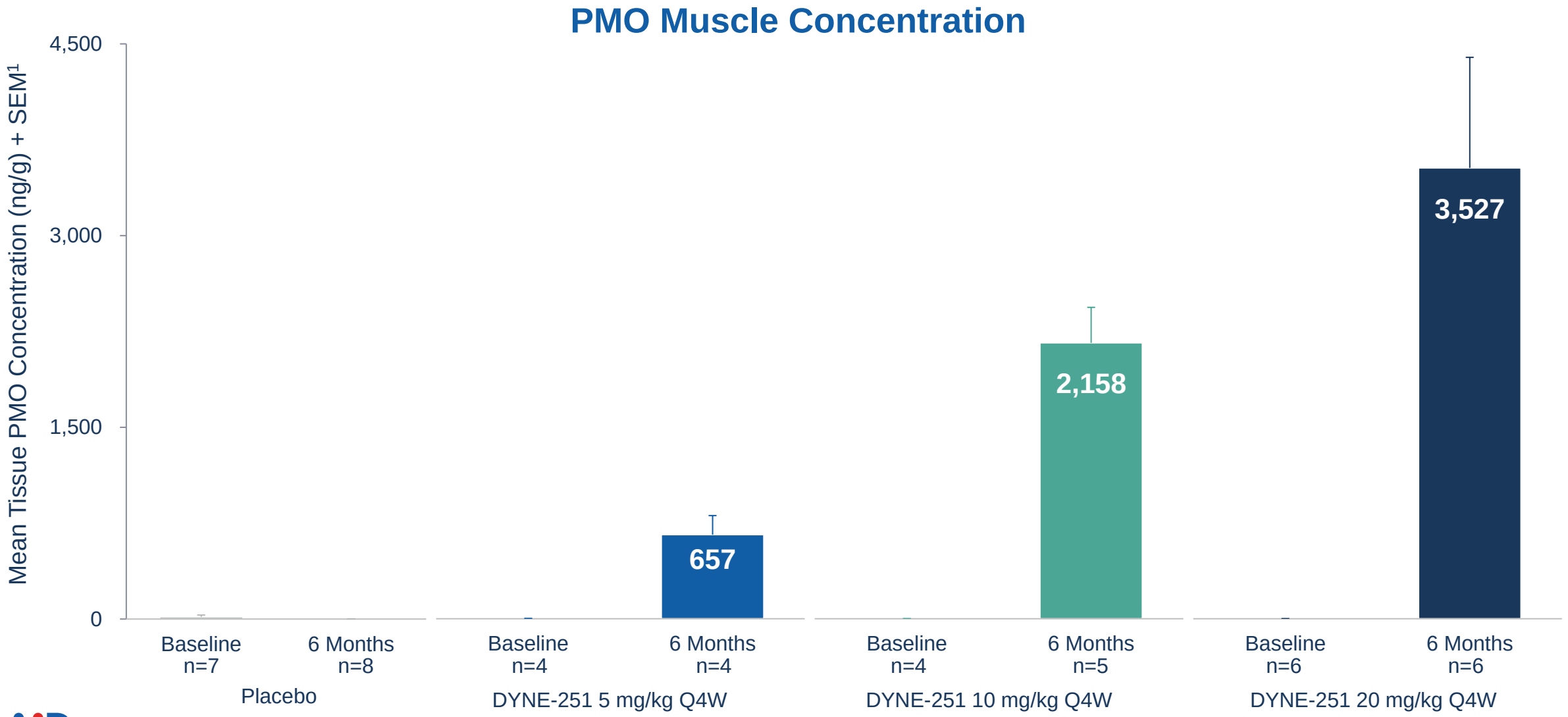
Additional Safety Data

- 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]

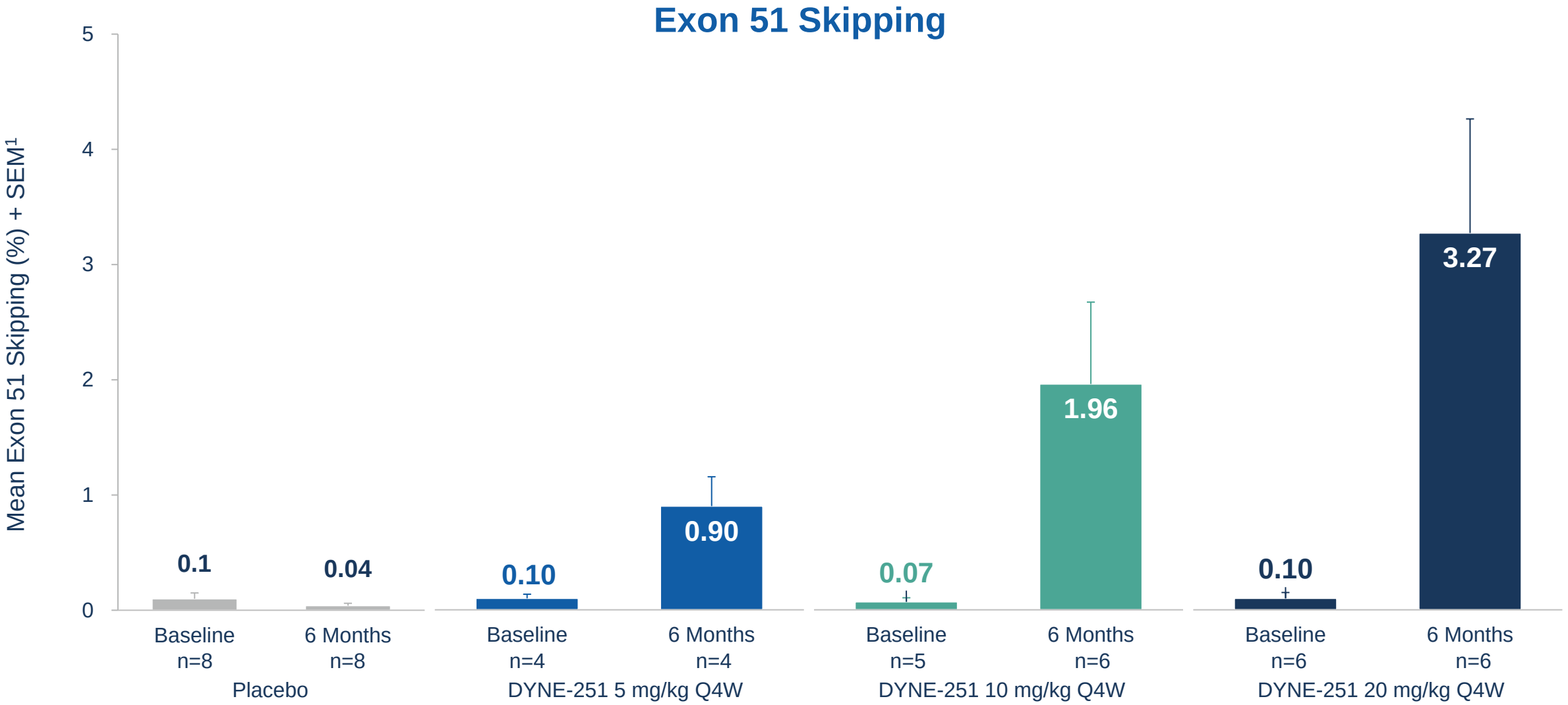
1. Data as of August 21, 2024; 2. Events have same day of onset in a single participant in the context of fever, hemolysis, diarrhea and positive blood in stool; together, these events are potentially consistent with hemolytic uremic syndrome (HUS) with a potential infectious etiology. 3. Participant 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.

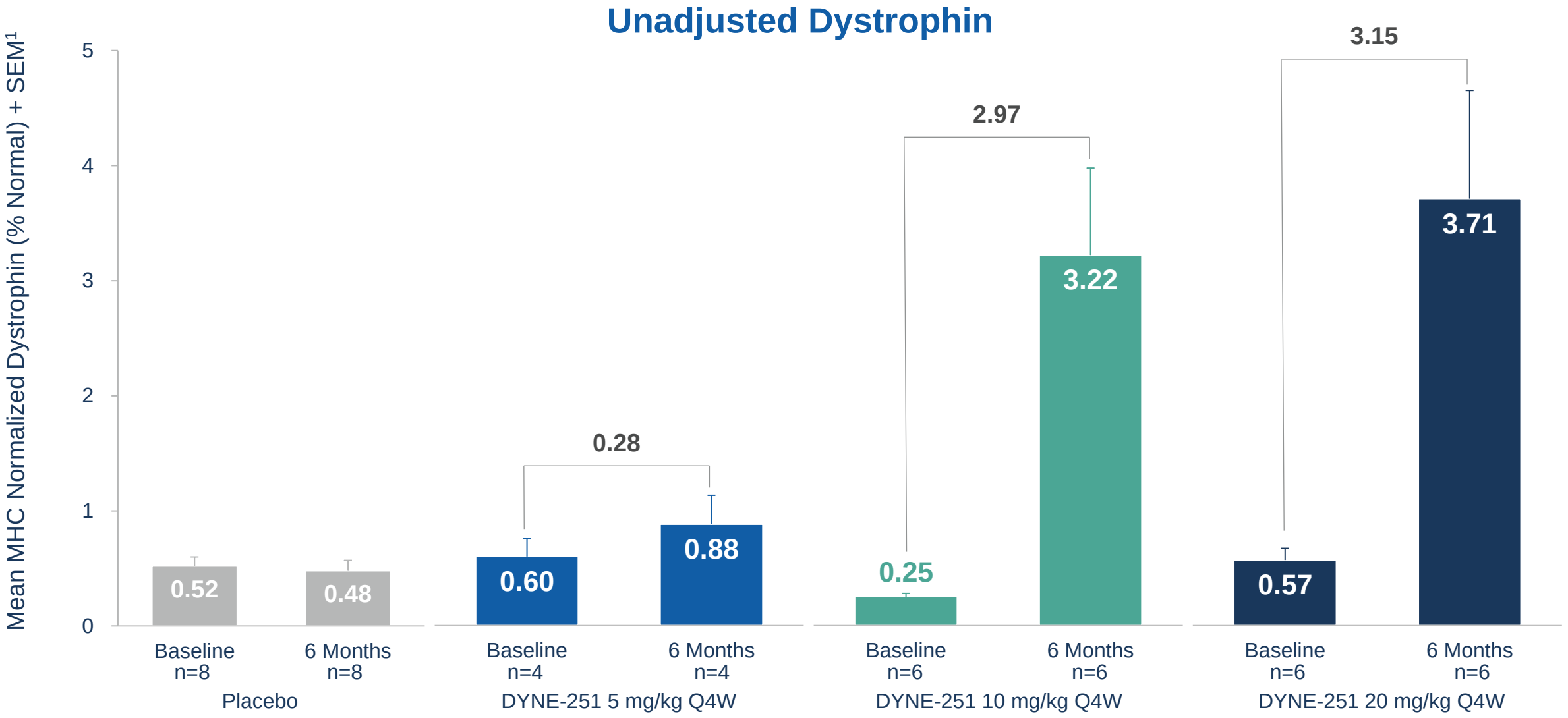
DYNE-251 Demonstrated Dose-Dependent Exon Skipping



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

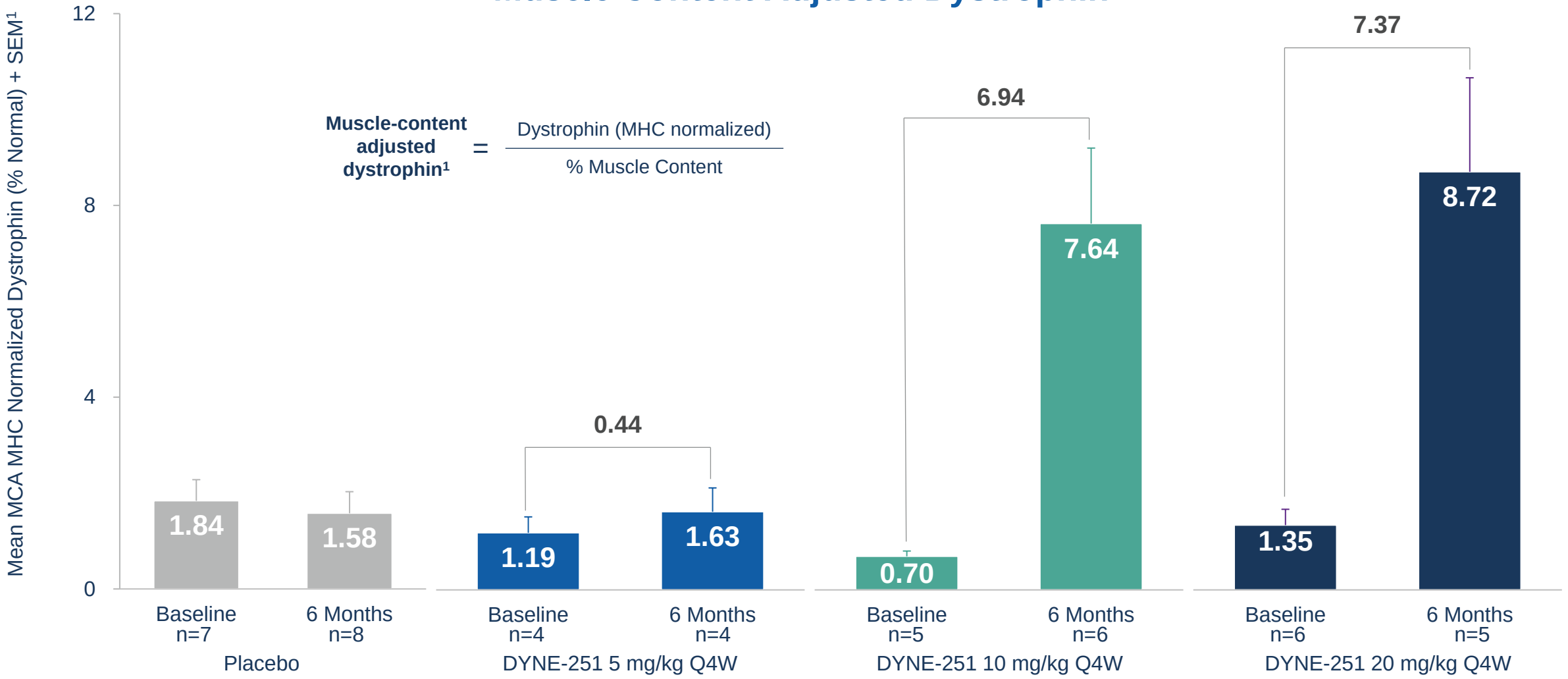
DYNE-251 Showed 3.7% Unadjusted Dystrophin at 6 Months



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

Muscle Content Adjusted Dystrophin

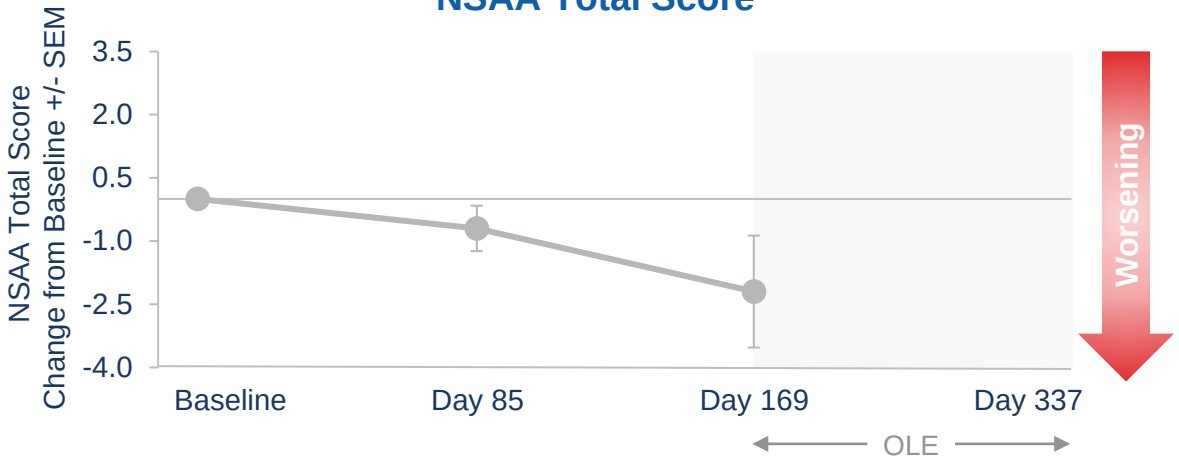


1. DELIVER biopsy taken approximately 28 days after most recent dose; 6 months = Week 25 for DELIVER.

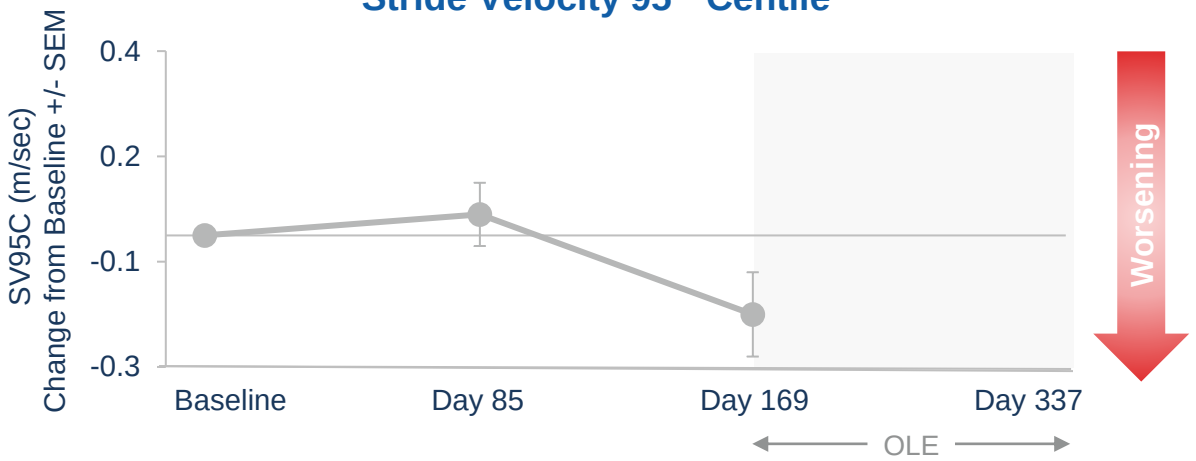
Placebo Response is Consistent with Duchenne Natural History [1]

DMD Patients Worsen Across a Number of Functional Measurements Over Time

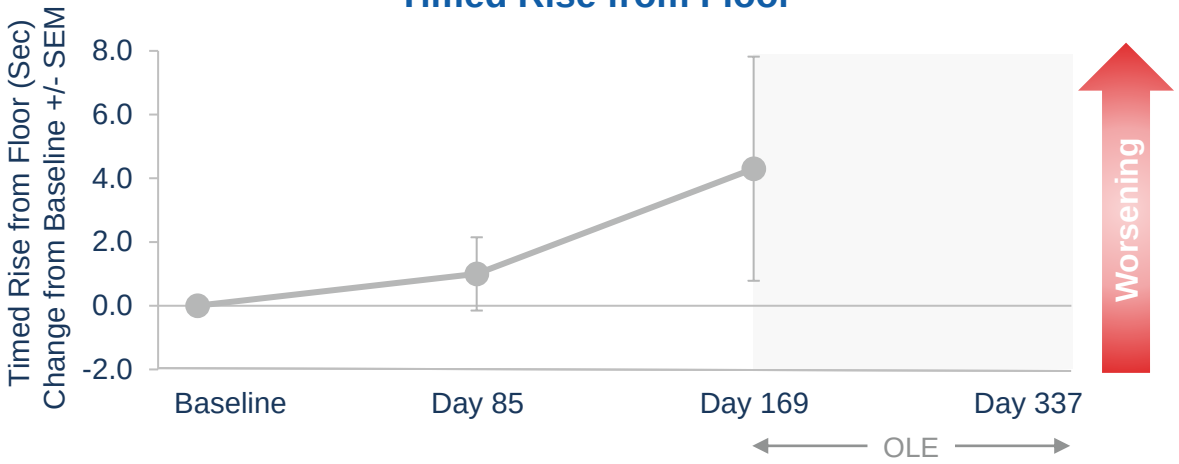
NSAA Total Score



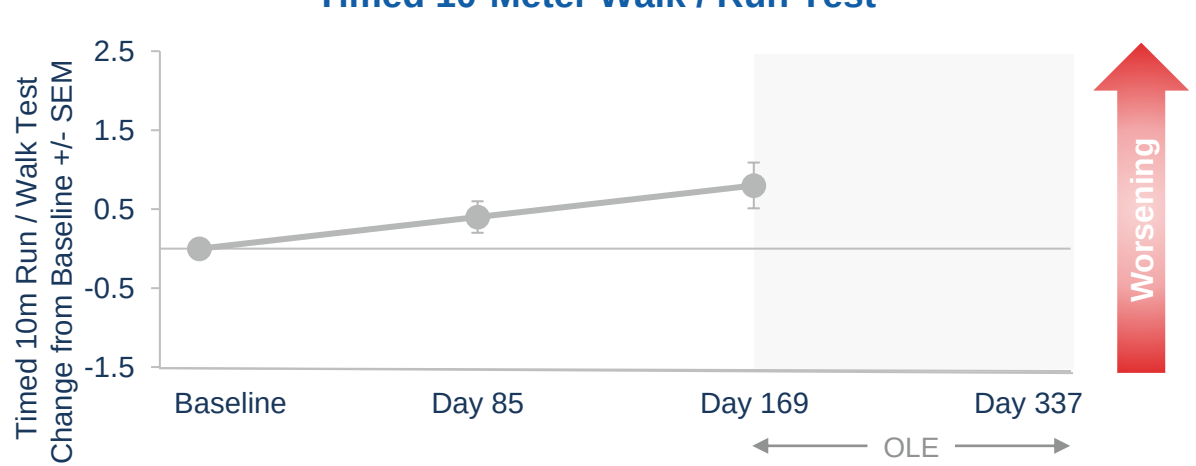
Stride Velocity 95th Centile



Timed Rise from Floor



Timed 10-Meter Walk / Run Test

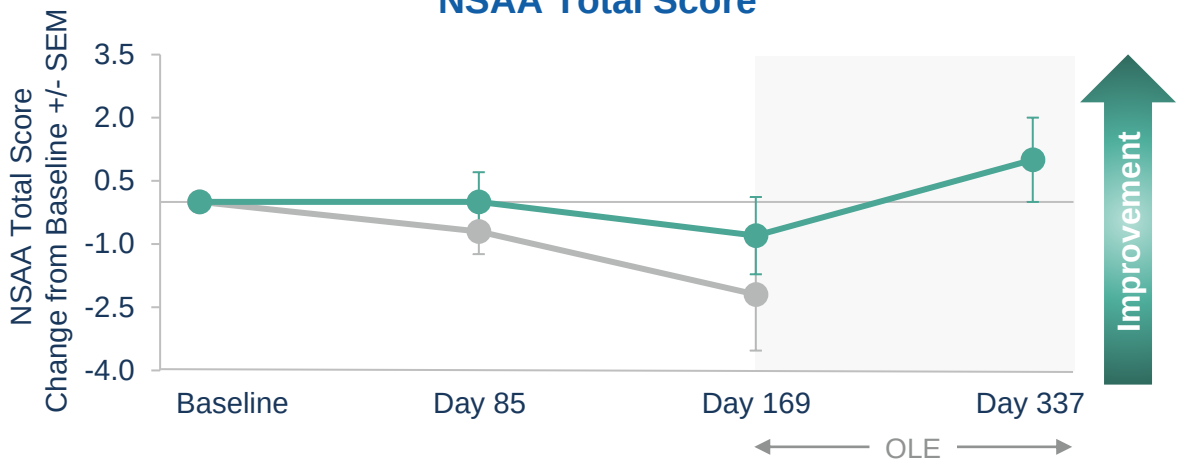


Placebo (n=6 for SV95C and n=14 for other endpoints)

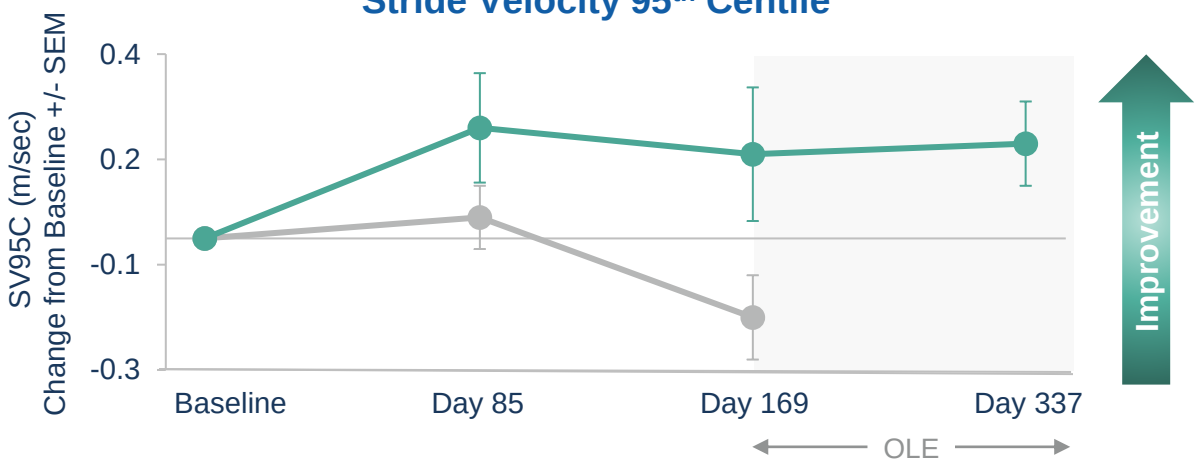
1. J Neuromuscul Dis 2024;11(3):701-714; Neuromuscul Disord 2010 Nov;20(11):712-6.; PLoS One 2014 Oct 1;9(10):e108205.

Data from 10 mg/kg Cohort Highlights Extension of Effect from 6 Months to 1 Year

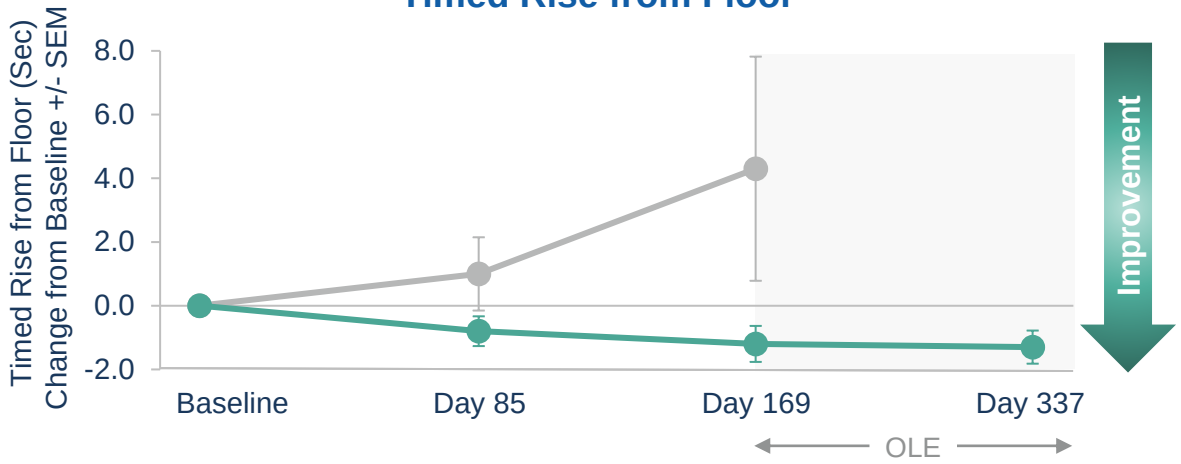
NSAA Total Score



Stride Velocity 95th Centile



Timed Rise from Floor



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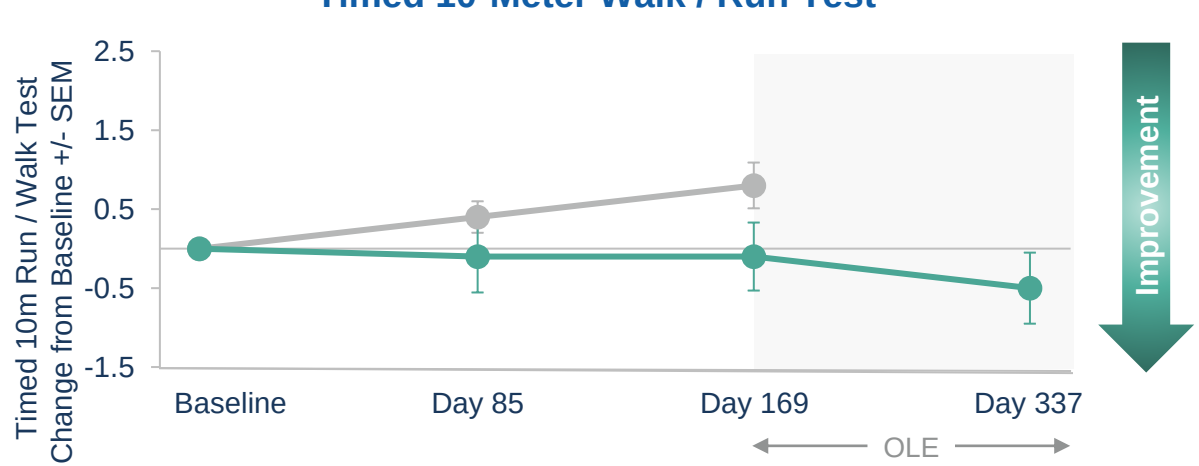


Placebo (n=6 for SV95C and n=14 for other endpoints)

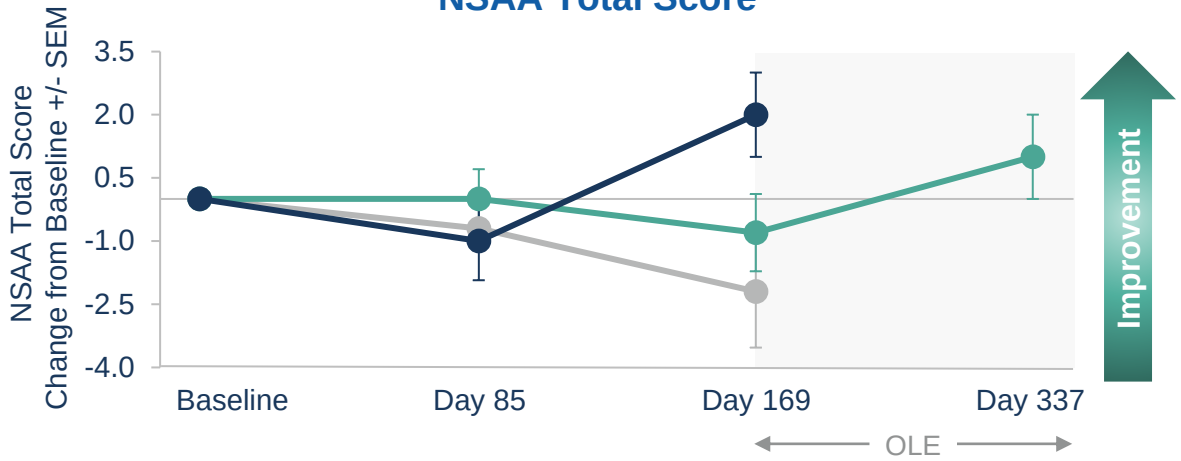
DYNE-251 10 mg/kg Q4W (n = 6 for all endpoints) [1]

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

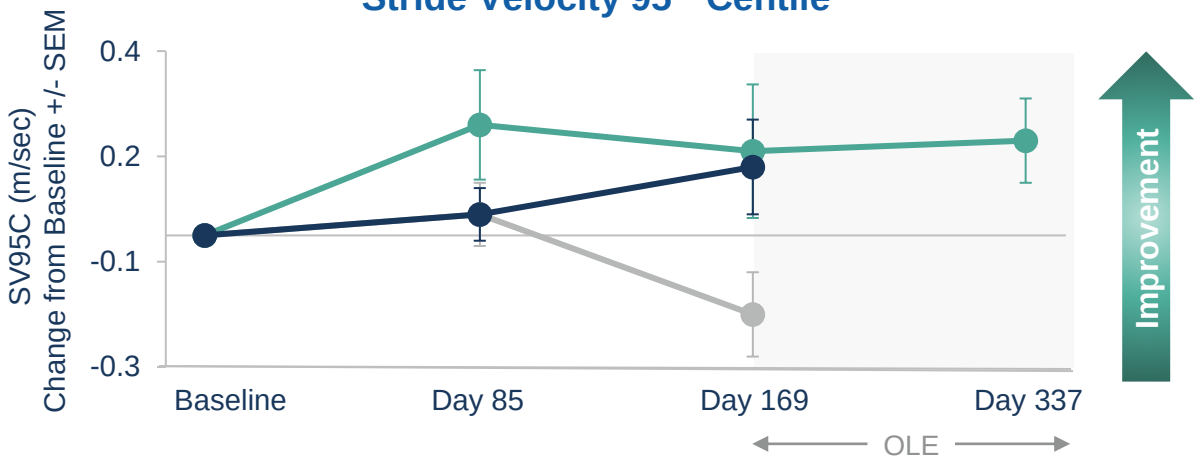
Improvements Across Multiple Functional Endpoints in Multiple Cohorts

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

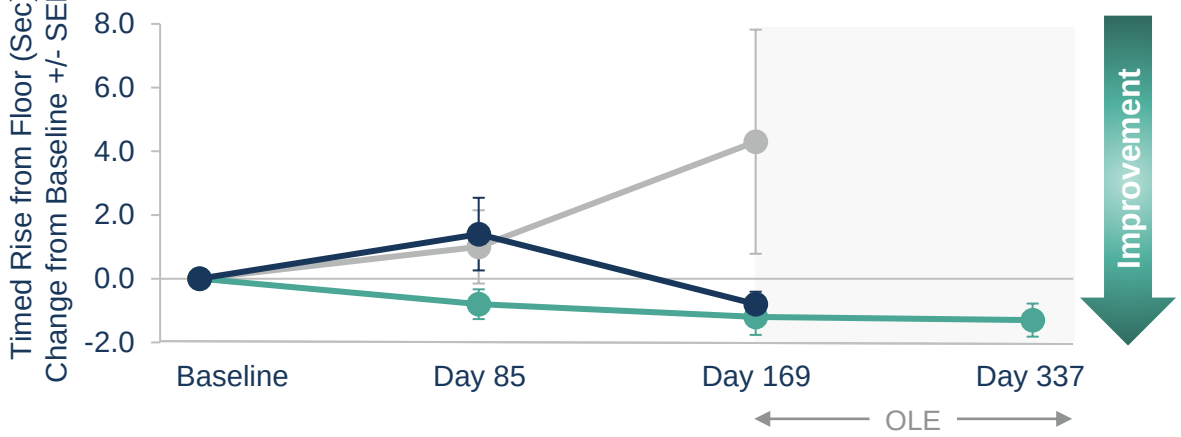
NSAA Total Score



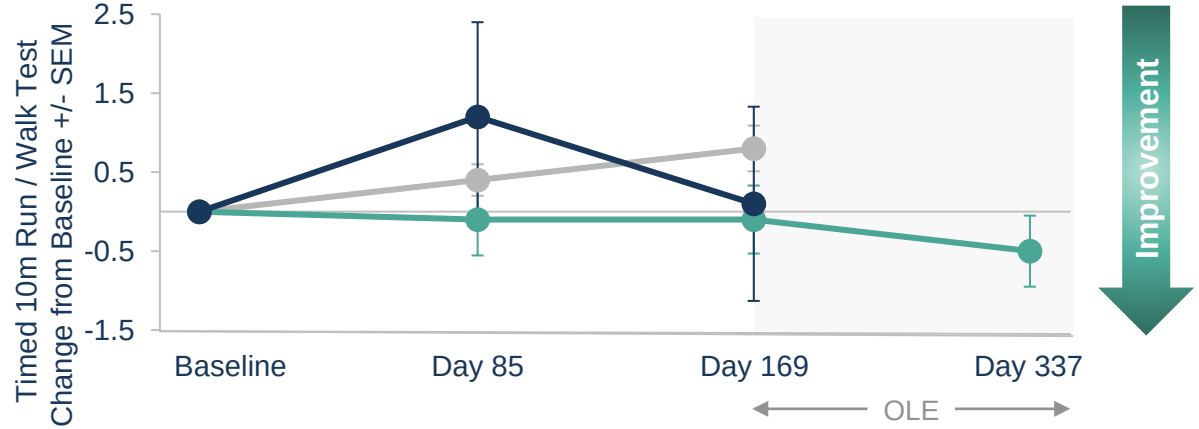
Stride Velocity 95th Centile



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]

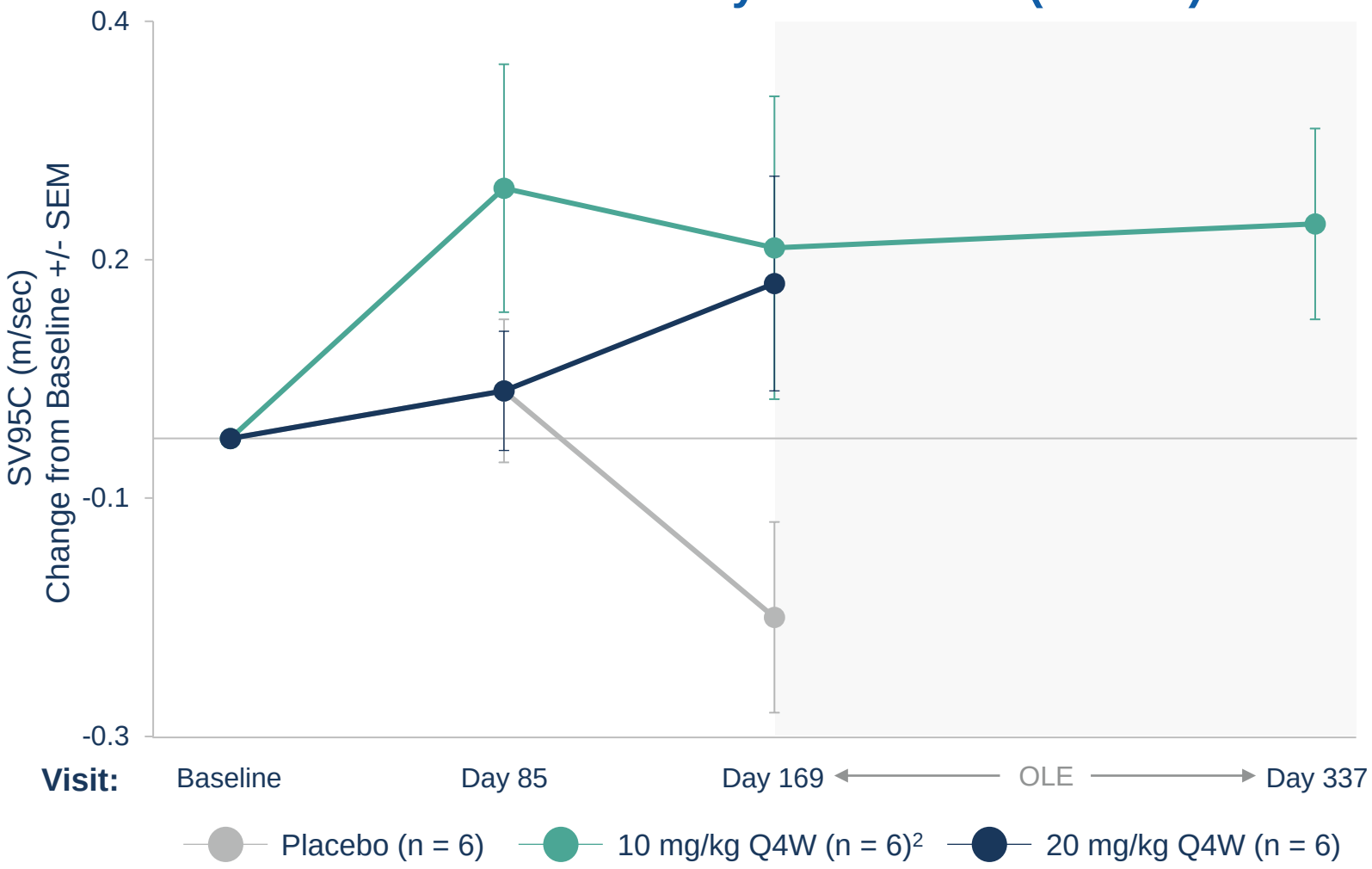
DYNE-251 20 mg/kg Q4W (n = 6 for all endpoints)

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]

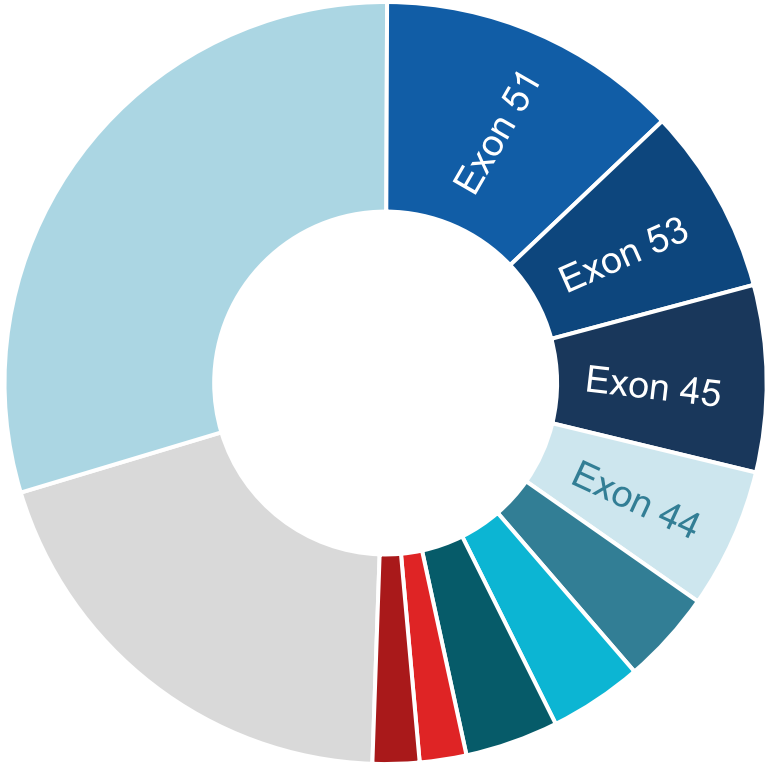
1. Minimal clinically important difference (MCID) as defined by EMA in its qualification opinion for SV95C as primary endpoint in studies in ambulatory DMD studies. 2. During the OLE, all participants in 10 mg/kg cohort were dose escalated to 20 mg/kg Q4W regimen.

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%**

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 with ~675 doses administered representing over 50 patient-years of follow up to date[1]
- Supports further development of DMD global franchise

Initiating registrational cohorts based on regulatory interactions and strength of data

Update on path to registration for DYNE-251 expected by YE 2024

1. Data as of August 21, 2024.

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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

Initiating Registrational Cohorts

Pursuing Expedited Approvals for Both Programs with Update on Registrational Pathway by YE 2024

Strengthening the Team to Deliver on Dyne's Next Chapter

Doug Kerr
Chief Medical Officer

Biogen · Shire · generation bio

Johanna Friedl-Naderer
Chief Commercial Officer

Biogen · VIR

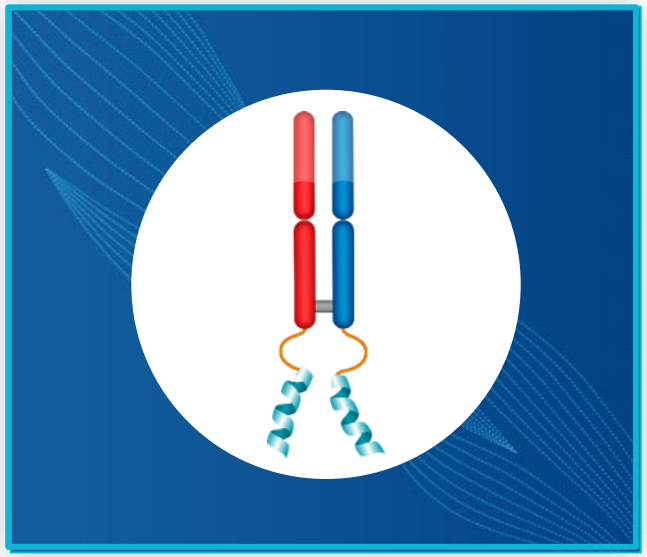
Lucia Celona
Chief Human Resources Officer

Bioverativ · Biogen · Apellis · REPERTOIRE immune medicines

Proven Team of Biopharma Executives Prepared to Advance Multiple Programs to Market

Building the World's Leading Muscle Disease Company

Win in DM1, DMD, FSHD



Own Muscle Delivery & Leverage FORCE

Dynamo Culture

ACHIEVE

Dyne® THERAPEUTICS

DELIVER

Achieving the Promise of

FORCE

to Deliver for Patients

FORCE

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