Building the World's Leading Neuromuscular Disease Company

43RD ANNUAL J.P. MORGAN HEALTHCARE CONFERENCE | JANUARY 15, 2025

Dyne® THERAPEUTICS

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This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding Dyne's strategy, future operations, prospects and plans, objectives of management, the potential of the FORCE platform, the therapeutic potential of DYNE-101 and DYNE-251, the anticipated timelines for reporting additional data from the ACHIEVE and DELIVER clinical trials and initiating and enrolling registrational cohorts, expectations regarding the timing and outcome of interactions with global regulatory authorities and the availability of accelerated approval pathways for DYNE-101 and DYNE-251, the occurrence and timing of potential additional clinical trials, and expectations regarding the timing of filing applications for U.S. Accelerated Approval, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," or "would," or the negative of these terms, or other comparable terminology are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Dyne may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including: uncertainties inherent in the identification and development of product candidates, including the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical studies and clinical trials; the timing of and Dyne's ability to enroll patients in clinical trials; whether results from preclinical studies and initial data from early clinical trials will be predictive of the final results of the clinical trials or future trials; uncertainties as to the FDA's and other regulatory authorities' interpretation of the data from Dyne's clinical trials and acceptance of Dyne's clinical programs and the regulatory approval process; whether Dyne's cash resources will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; as well as the risks and uncertainties identified in Dyne's filings with the Securities and Exchange Commission (SEC), including the Company's most recent Form 10-Q and in subsequent filings Dyne may make with the SEC. In addition, the forward-looking statements included in this presentation represent Dyne's views as of the date of this presentation. Dyne anticipates that subsequent events and developments will cause its views to change. However, while Dyne may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Dyne's views as of any date subsequent to the date of this presentation.

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Aiming to Deliver Transformative Therapies for Neuromuscular Diseases

LATE-STAGE PIPELINE	Two clinical programs moving to registrational expansion cohorts for DM1 and DMD following positive proof-of-concept data
NEAR-TERM VALUE DRIVERS	Key data readouts in 2025 & 2026 potentially enabling two submissions for U.S. Accelerated Approval in 2026
DIFFERENTIATED PLATFORM	FORCE™ platform enables targeted delivery to muscle and CNS; broader pipeline includes FSHD and Pompe
STRONG FINANCIAL POSITION	Cash position of ~ $642 million (as of 12/31/24)* with expected runway into H2 2026; all assets fully owned

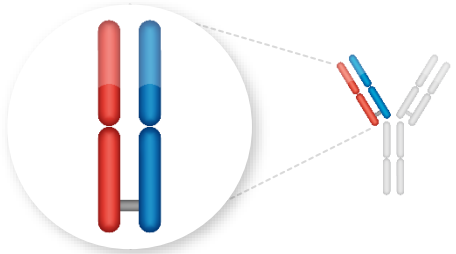
Dyne THERAPEUTICS

Note: DM1 = myotonic dystrophy type 1; DMD = Duchenne muscular dystrophy; FSHD = facioscapulohumeral muscular dystrophy
* Preliminary and unaudited

Leveraging Our FORCE™ Platform for Targeted Delivery

ANTIBODY

Proprietary Fab against TfR1 to enable targeted delivery

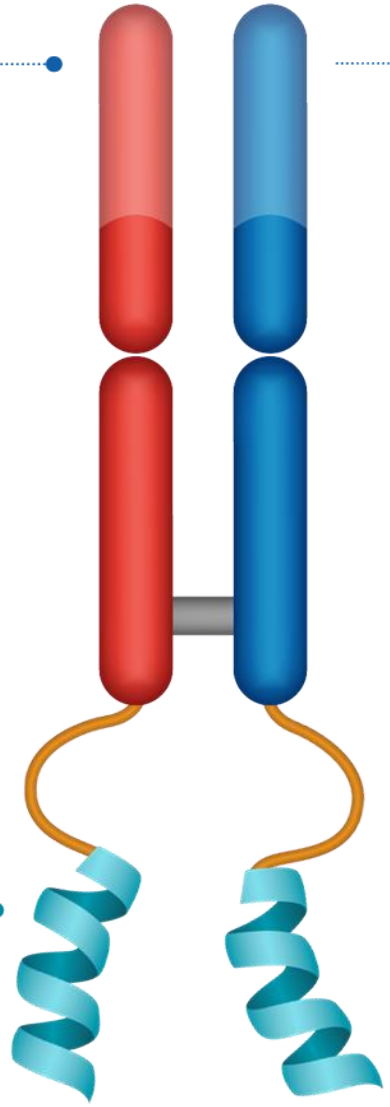


LINKER

Enables precise conjugation of payloads to Fab

PAYLOAD

ASO or siRNA, modularity enables rational selection of payload to target the genetic basis of disease

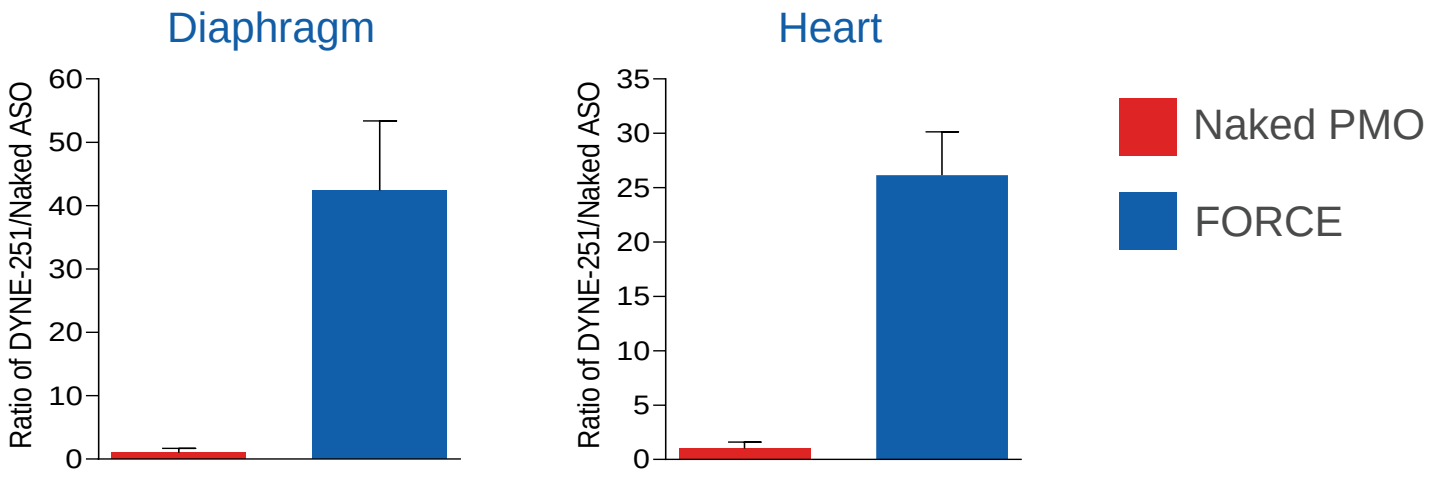


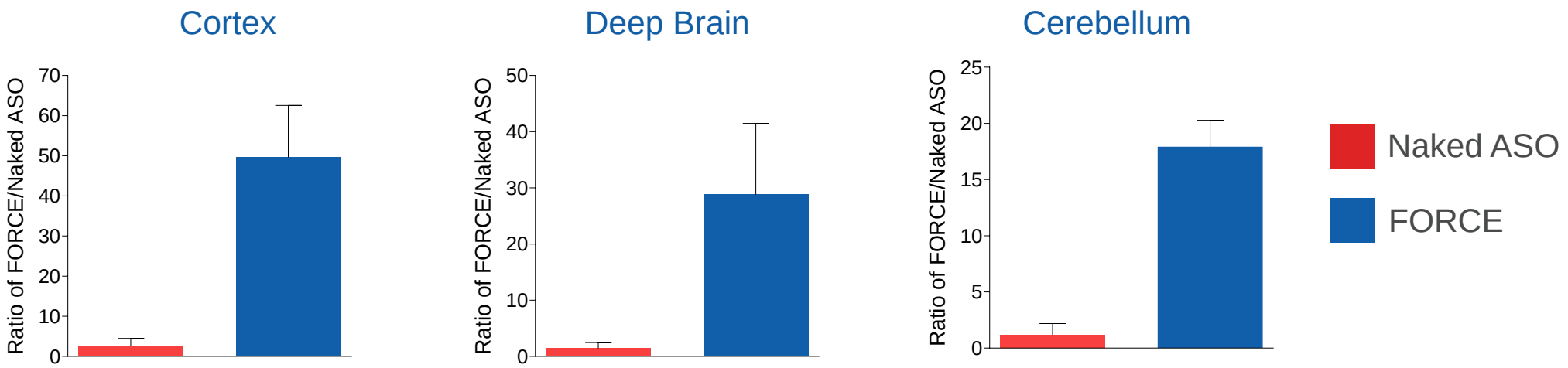
Skeletal and smooth muscle

Cardiac muscle

CNS

FORCE Enabled Oligonucleotide Delivery to Muscle and CNS





Notes for PMO: Results after repeat IV dose of naked ASO or DYNE-251 in male cynomolgus monkeys, 2 x 30 mg/kg on day 0 and day 7, analyzed day 28; n = 4 – 5.
Notes for ASO: Results after a single IV dose of naked ASO or FORCE in male cynomolgus monkeys, 1 x 10 mg/kg on day 0, analyzed day 3; n = 2. FORCE conjugate consists of lead Fab and surrogate *DMPK*-targeting payload.
The FORCE platform and DYNE-251 are investigational or otherwise in development and have not been approved as safe or effective by the FDA or any other regulatory authority.

Myotonic Dystrophy Type 1 (DM1) Clinical Data Show Broad Functional Impact and Support Potential for Accelerated Approval

- **Initiating Registrational Expansion Cohort: primary endpoint of splicing correction at 3 months, supported by functional endpoints and PROs; full enrollment expected mid-2025**
- **6.8 mg/kg Q8W dose showed robust splicing correction at 3 months and broad functional improvement, starting at 3 months and continuing at 6 months**
- **Continued favorable safety profile[1]; no serious related TEAEs**

1. DYNE-101 safety data as of December 6, 2024

Developing Transformative Therapeutics 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

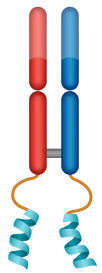
Disease-Modifying Nuclear *DMPK* Knockdown

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

Note: CNS = central nervous system

DYNE-101 Addressing the Central Pathobiology of DM1 to Enable Broad Functional Improvement[1]

Robust and widespread delivery → ***DMPK* degradation in the nucleus** → **MBNL release and splicing correction** → **Correction of myotonia and broad functional improvement**



DYNE-101

Differentiated MOA

MBNL released:
Splicing corrected

Early effect on myotonia

Muscle Strength:
Quantitative Muscle Testing

Functional Outcomes:
10-Meter Walk / Run;
5 Times Sit to Stand

Patient Reported Outcomes:
Myotonic Dystrophy Health Index (MDHI)

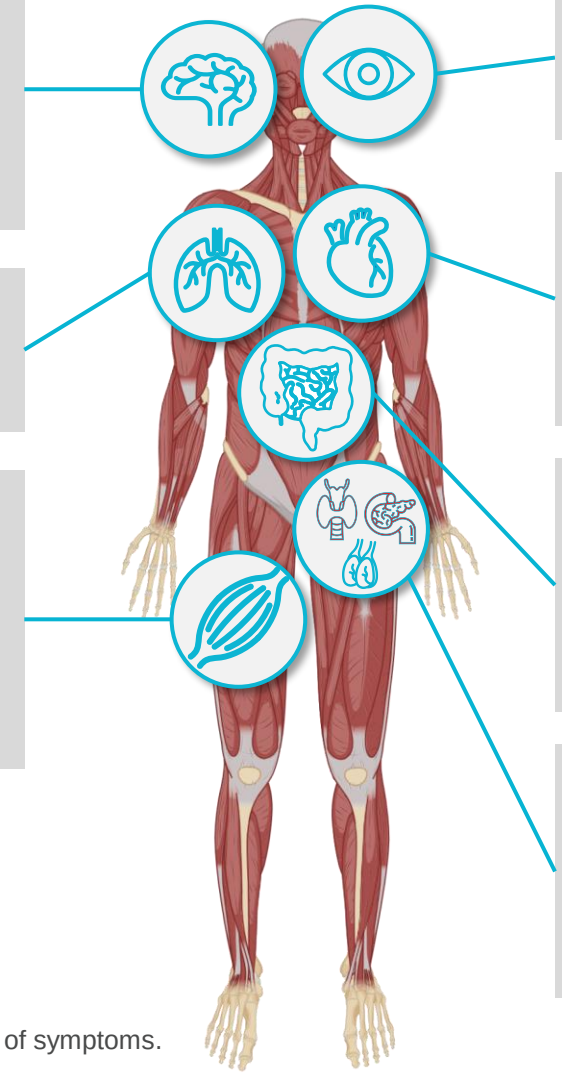
1. Image depicts the intended DYNE-101 mechanism of action.

DM1 is a Heterogeneous Disease with Widespread Muscle and CNS Manifestations

CNS[1–4]
- Fatigue
- Excessive daytime sleepiness
- Difficulty concentrating
- Behavioral/personality changes

Skeletal muscle (respiratory)[1–4]
- Restrictive ventilatory pattern
- Shortness of breath

Skeletal muscle[1–4]
- Muscle weakness
- Myotonia
- Balance issues
- Muscle pain
- Atrophy



Ocular[1–4]
- Cataracts
- Ptosis

Cardiac[1–4]
- Conduction disturbances
- Arrythmia
- Cardiomyopathy
- Sudden death

Smooth muscle[1–4]
- Dysphagia
- Constipation
- Heartburn
- Regurgitation

Endocrine[1–4]
- Thyroid disorders
- Diabetes
- Male hypogonadism
- Vitamin D deficiency

Slide does not represent an exhaustive list of symptoms.

1. Thornton CA. *Neurol Clin.* 2014;32:705-719; 2. Ho G, et al. *World J Clin Pediatr*. 2015;4:66–80.
3. Hagerman KA, et al. *Muscle Nerve.* 2019;59:457–464; 4. Gutierrez Gutierrez G, et al. Neurologia (Engl Ed). 2020;35:185–206.

Multiple Ascending Dose (MAD) Portion of ACHIEVE is Complete

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 ↓ **Registrational Expansion Cohort**

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

DYNE-101: Favorable Safety Profile with No Serious Related TEAEs

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%)	8 (100%)	56 (100%)
Any related TEAE	9 (56%)	9 (56%)	2 (25%)	3 (38%)	6 (75%)	29 (52%)
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 from study	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[1]

- 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 (38%)
  - Procedural pain (30%)
  - Influenza (27%)
  - Infusion-related reaction (25%)
  - Diarrhea; headache (each 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

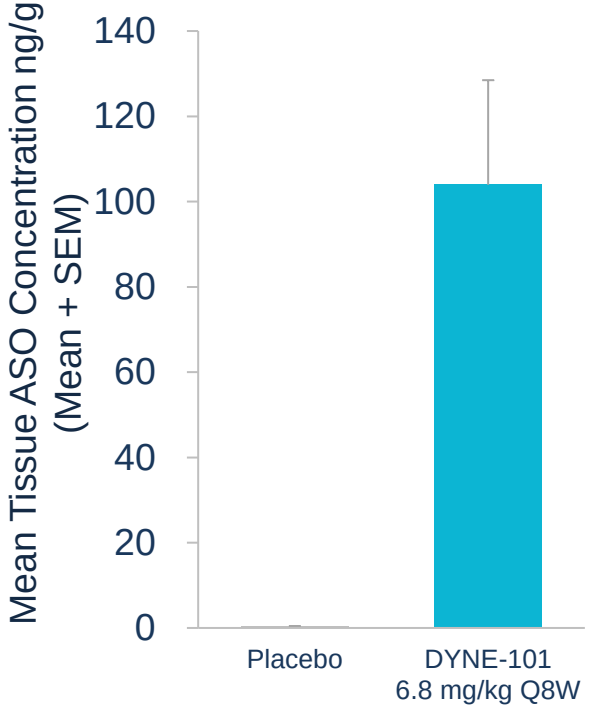
~855 Doses Administered to Date Representing Over 72 Patient-Years of Follow-Up[1]

1. Data as of December 6, 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.

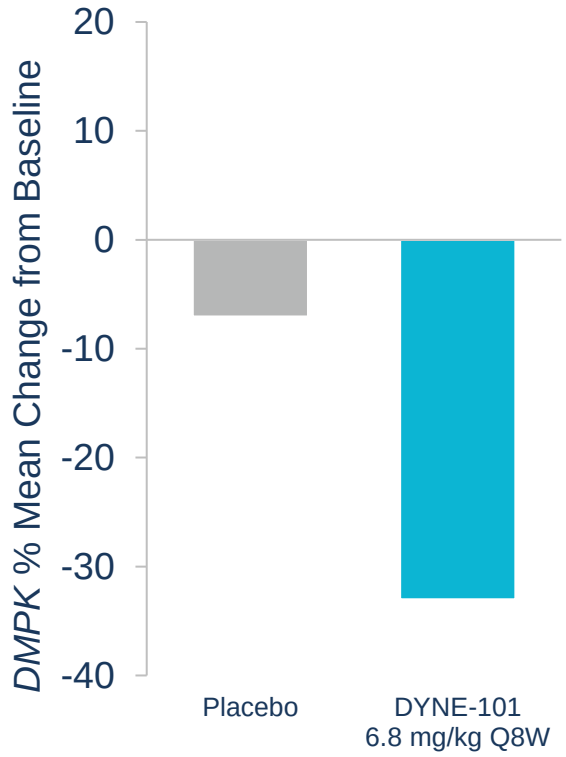
DYNE-101 Addresses Central Pathobiology: Differentiated Pharmacology with Potential to Lead to Broad Functional Benefit

Delivery and exposure → ***DMPK* knockdown** → **Splicing correction** → **Broad functional benefit**

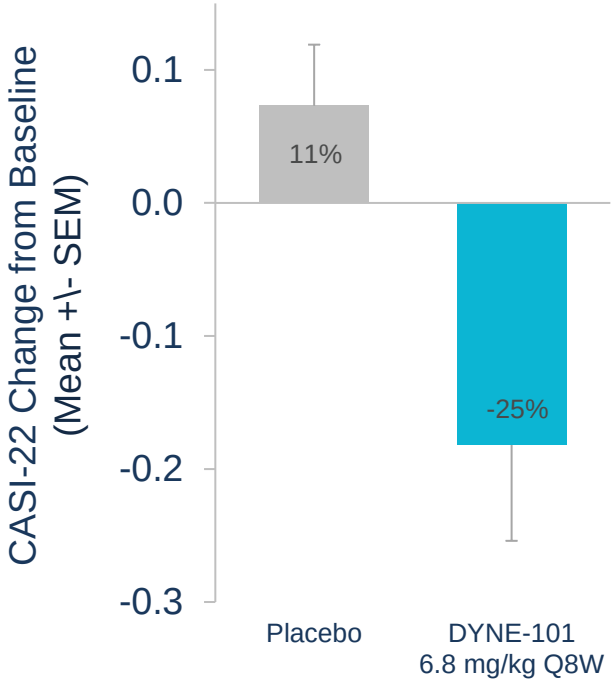
Muscle delivery at 3 mo



Target engagement at 3 mo



Biomarker response at 3 mo



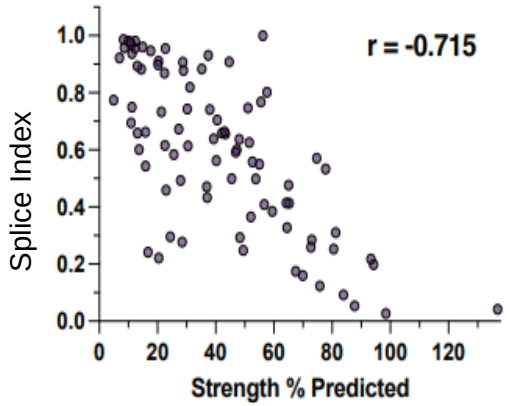
Benefit at 6 mo

Notes: CASI-22 = composite alternative splicing index; vHOT = video hand opening time; QMT = quantitative muscle testing; 10MWR = 10-meter walk/run test; 5xSTS = 5 times sit to stand; 3 months = 85 days, 6 months = 169 days. Values within bars represent % mean change relative to baseline.

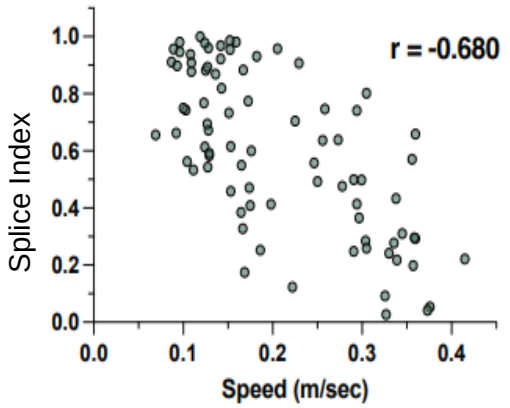
ACHIEVE Shows CASI is a Robust Endpoint to Predict Clinical Benefit

Natural History[1] Correlations (CASI / Muscle Function)

Hand Grip



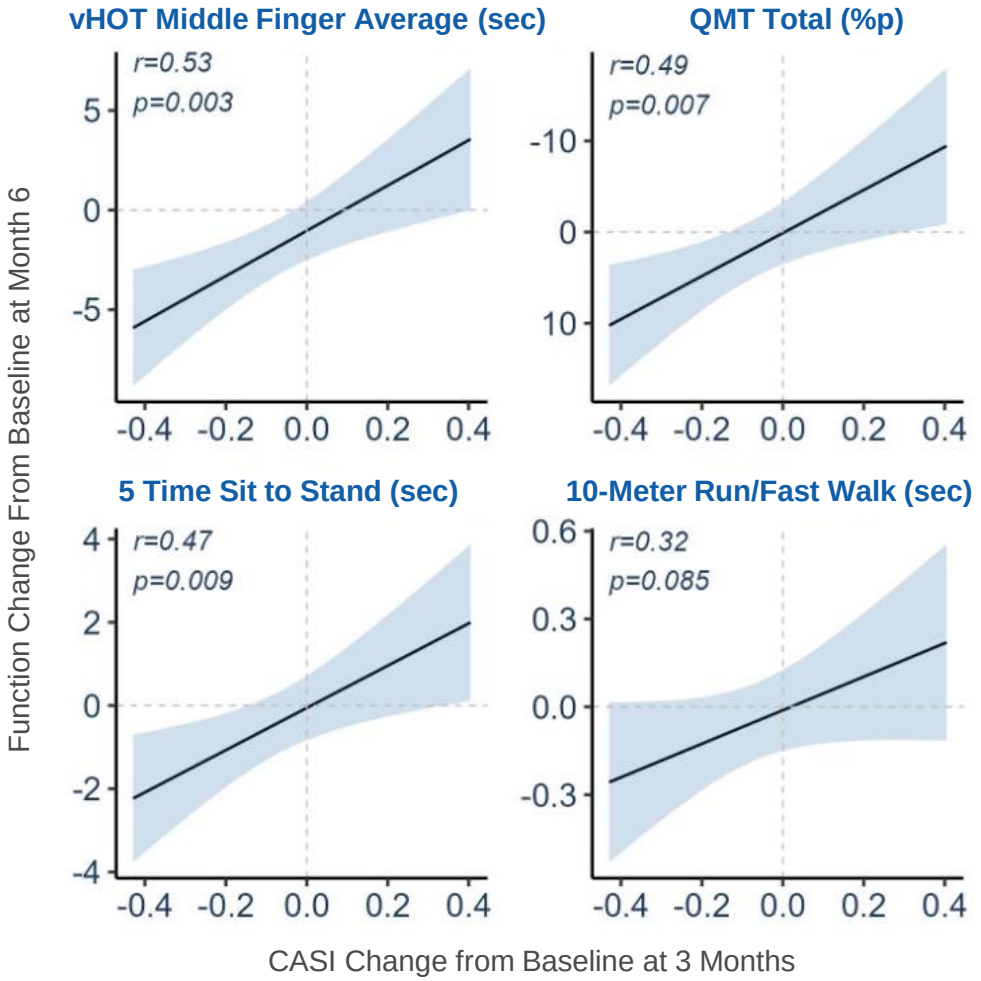
10-Meter Run/Fast Walk



CASI as a Reliable Endpoint

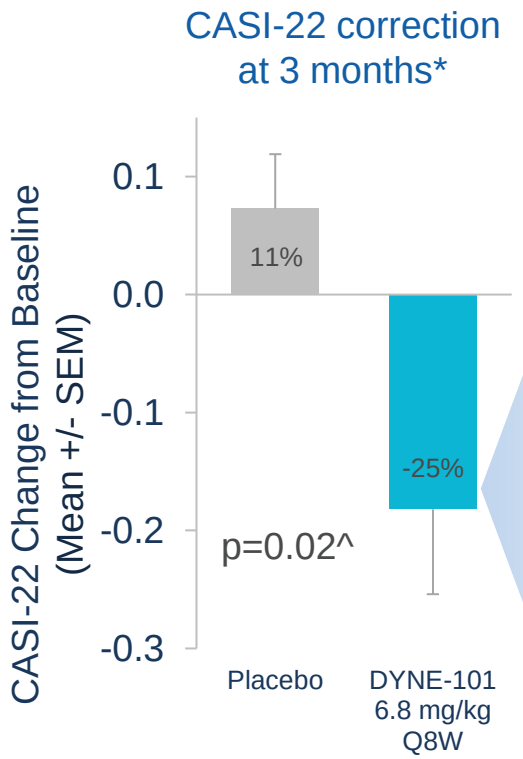
- Fully validated method with very low analytical variability (<5%)
- FDA alignment on analytical validation of splicing assay
- Adequacy of muscle biopsy ensured both visually and by RNA quality assessments
- Statistical QC to exclude results from fat-predominant biopsy (~4% QC rejection rate)
- Dual muscle biopsy samples assessed per timepoint per patient to account for biological variability:
  - High concordance in pairs (R = 0.9)
  - 4% discordance rate

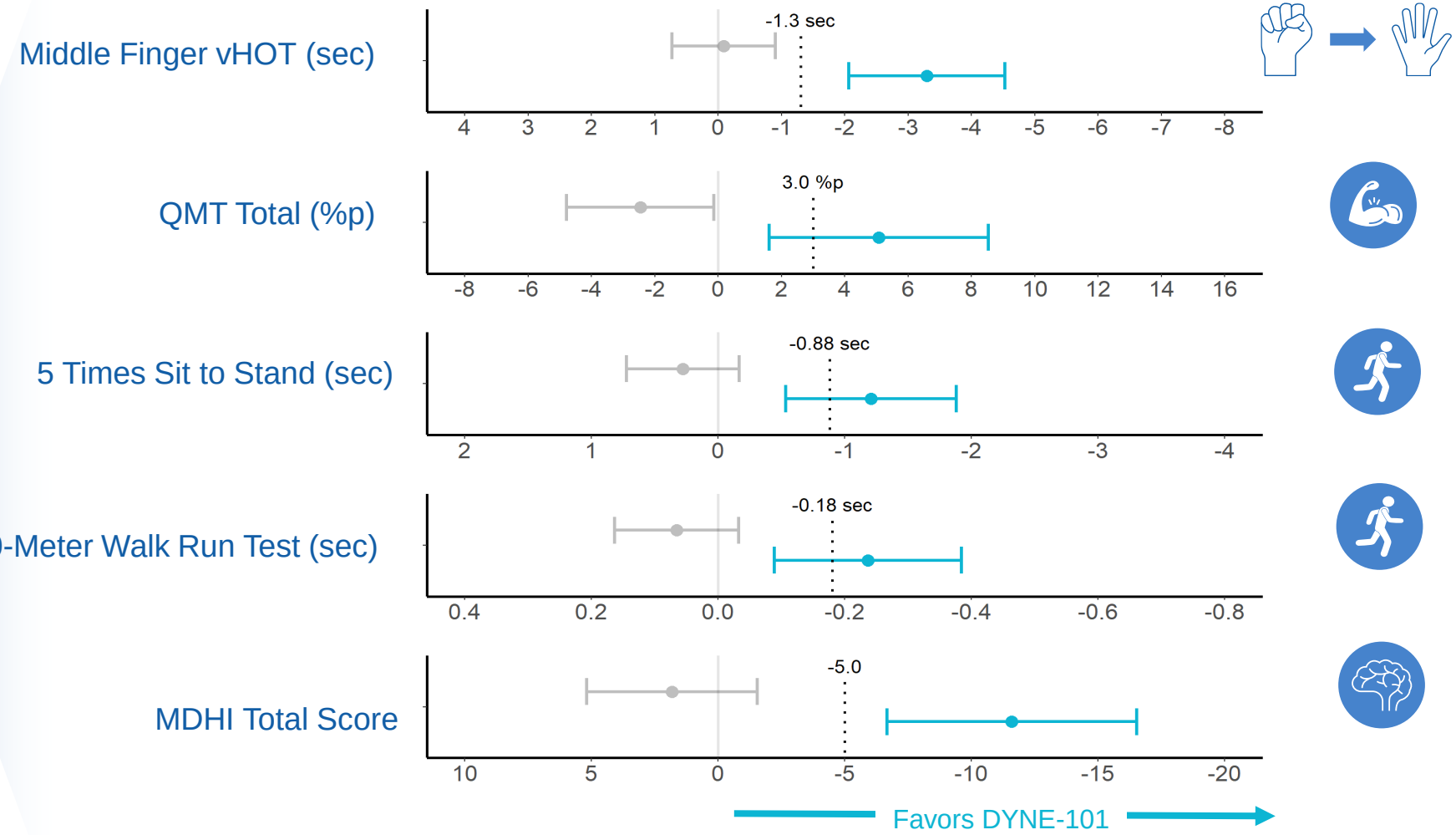
In ACHIEVE, 3 Month CASI Predicted 6 Month Functional Outcomes[2]



1. Provenzano M, et al. bioRxiv. 2024. 2. Shown are linear regression lines and correlation analysis for pooled 3.4 mg/kg Q4W, 5.4 mg/kg Q8W and 6.8 mg/kg Q8W and Placebo. Band for model predicted mean with 95%CI.

Splicing Correction at 3 Months Predicted Broad Functional Benefit

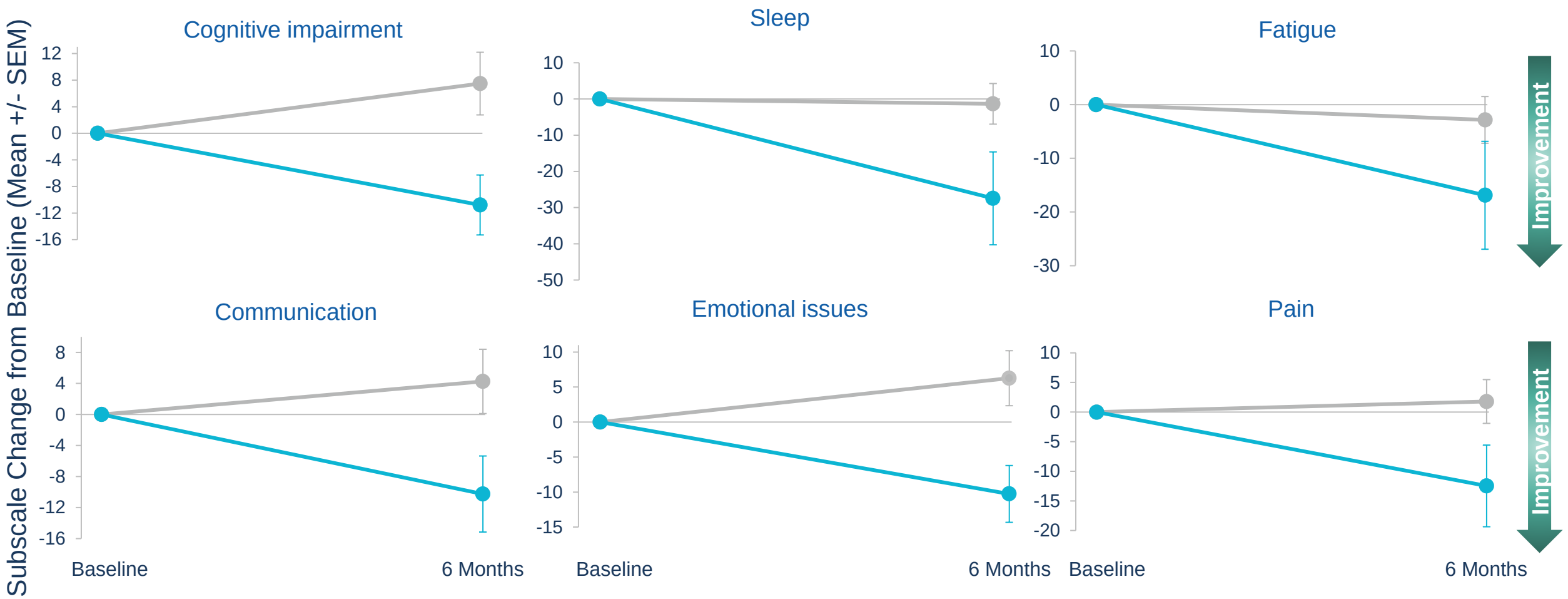




Note: 3 months = 85 days; 6 months = 169 days; MCID = minimal clinically important difference.
* Placebo 11% mean Δ relative to baseline; n=14. DYNE-101 6.8mg/kg Q8W -25% mean Δ relative to baseline; n=5.
^ Nominal p-value (post-hoc 2-sample t-test)

Mixed model for repeated measures (MMRM): fixed effects: dose, visit, baseline, dose by visit interaction, baseline by visit interaction. Data: all dose groups except recovery group; excluding placebo data after 6 months; Data presented are least squares (LS) mean change from baseline ± SE; 3 months = 85 days; 6 months = 169 days. MCID estimate is calculated as the average of 2 distribution-based methods using ACHIEVE data (0.2 SD of baseline (N=56) and 0.5 SD placebo change from baseline at 6 months (n=14)).

CNS-related MDHI Subscales Show Improvement at Registrational DYNE-101 Dose



Cohort: Placebo (N = 14) DYNE-101 6.8 Q8W mg/kg (N = 6)

Note: Patient-reported outcomes (PRO) including Myotonic Dystrophy Health Index (MDHI) collected at baseline and 6 months (169 days).

Accelerated Approval (AA) to be Supported by Robust ACHIEVE Dataset Defined by Biomarker, Myotonia, Strength, Function and PRO Data

AA Path Enables Speed to Filing with Functional Benefit

ACHIEVE Registrational Expansion Cohort
N: 32 - 48, 3:1
6.8 mg/kg Q8W

Placebo Controlled Period | **Extension**

- **Full Enrollment (mid-2025)**
- **Splicing Data (3 months)**
- **Functional Endpoints (6 months)**

→ **(H1 2026) Potential Submission for U.S. Accelerated Approval**

Planned ACHIEVE AA Registration Package

- Registration Expansion Cohort: n = 32 – 48
- Long-Term Extension Cohort: n = 56 patients
- **~ 100** *patients on drug for 6M+ at 6.8 mg/kg Q8W dose*

Potential Profile

Planned Primary Endpoint (3 months)

- Change from baseline in CASI[1]

Planned Secondary Endpoints (6 months)

- Change from baseline in
  - vHOT (middle finger)
  - 10MWR
  - QMT
  - 5xSTS
  - MDHI Total Score

Phase 3 (N ~ 200)

- **Potential Interim Data**

1. N=32 (48): 90% (>95%) power to detect at least 0.12 (17%) change from baseline in CASI at 3 months within DYNE-101 treated group, or to detect at least a 0.23 (33%) difference versus placebo

Advancing Next-Generation Exon 51-Skipping Therapeutic for Duchenne Muscular Dystrophy (DMD)

1. **Ongoing Registrational Expansion Cohort in DYNE-251 DELIVER trial to support potential submission for U.S. Accelerated Approval early 2026, using dystrophin as surrogate endpoint based on recent FDA feedback**

2. **Unprecedented dystrophin expression and functional benefit previously demonstrated at registrational dose of 20 mg/kg Q4W**

3. **DELIVER Registrational Expansion Cohort on-track for full enrollment in Q1 2025**

4. **Continued favorable safety profile[1] since last update**

1. DYNE-251 safety data as of November 21, 2024

Building a Global DMD Franchise of Transformative Therapeutics

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**

Registrational Expansion Cohort of DELIVER Rapidly Enrolling

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): 192 weeks

Registrational Expansion Cohort

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

DYNE-251 Safety Profile Is Favorable

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 N=8	40 mg/kg Q4W N=6	Overall[1] N=54
Any TEAE	6 (100%)	6 (100%)	6 (100%)	6 (100%)	7 (88%)	8 (100%)	7 (88%)	5 (83%)	51 (94%)
Any related TEAE	3 (50%)	3 (50%)	0	6 (100%)	3 (38%)	4 (50%)	2 (25%)	3 (50%)	24 (44%)
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 from study	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[1]

- 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 (44%)
  - Fall; vomiting (each 33%)
  - Headache (32%)
  - Nasopharyngitis (28%)
  - Cough; infusion-related reaction[7] (each 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

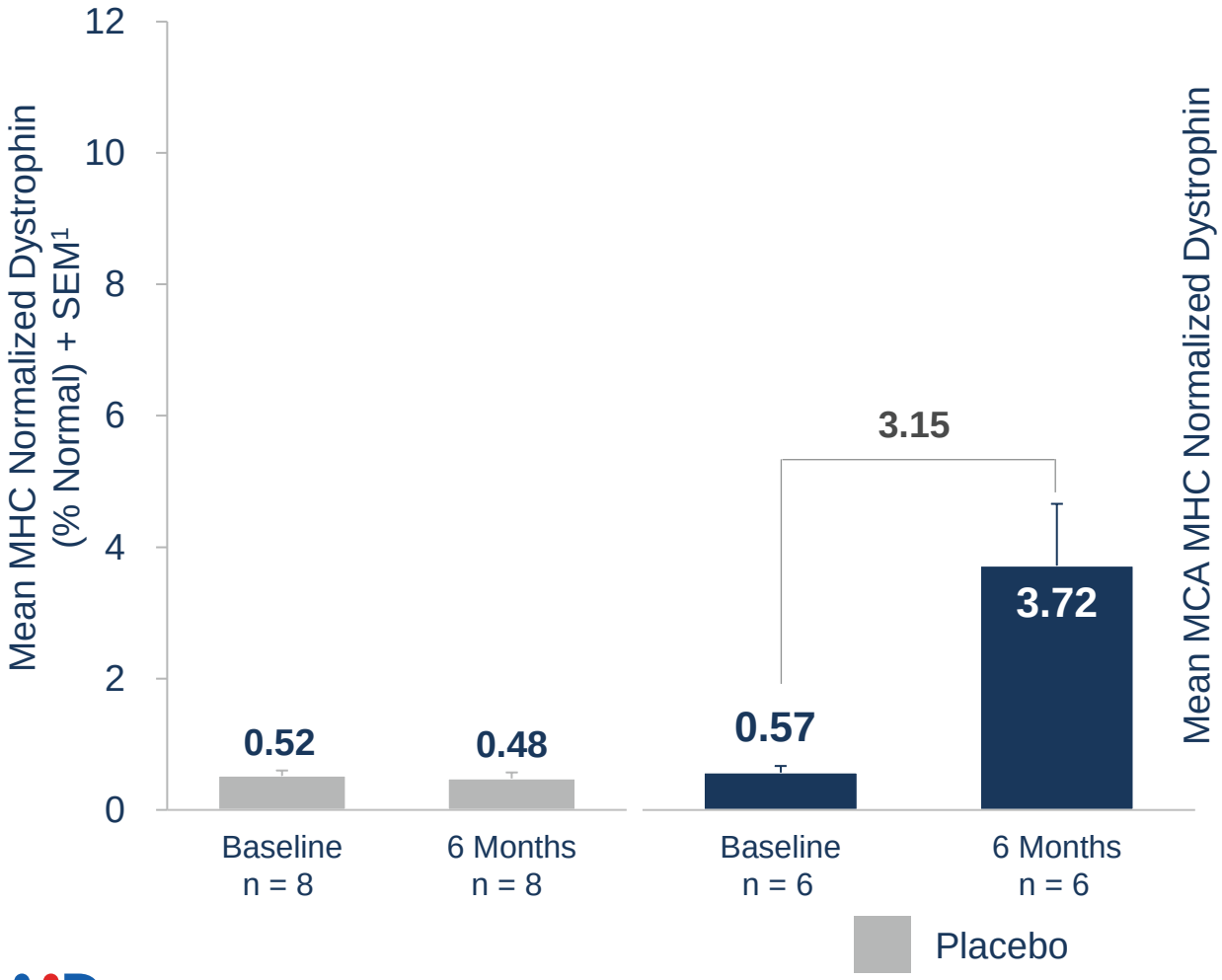
837 Doses Administered to Date Representing Over 65 Patient-Years of Follow-Up[1]

1. Data as of November 21, 2024; 2. Events have same day of onset in a single participant with a nonserious related TEAE of anemia in the context of fever, hemolysis, diarrhea and positive blood in stool; together these events are consistent with hemolytic uremic syndrome (HUS) with a possible infectious etiology; 3. Participant has a history of hemolytic anemia of unidentified etiology; presented with fever and tonsilitis; 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. All infusion-related reactions have been mild or moderate in intensity; dosing has continued in all participants who experienced infusion-related reactions.

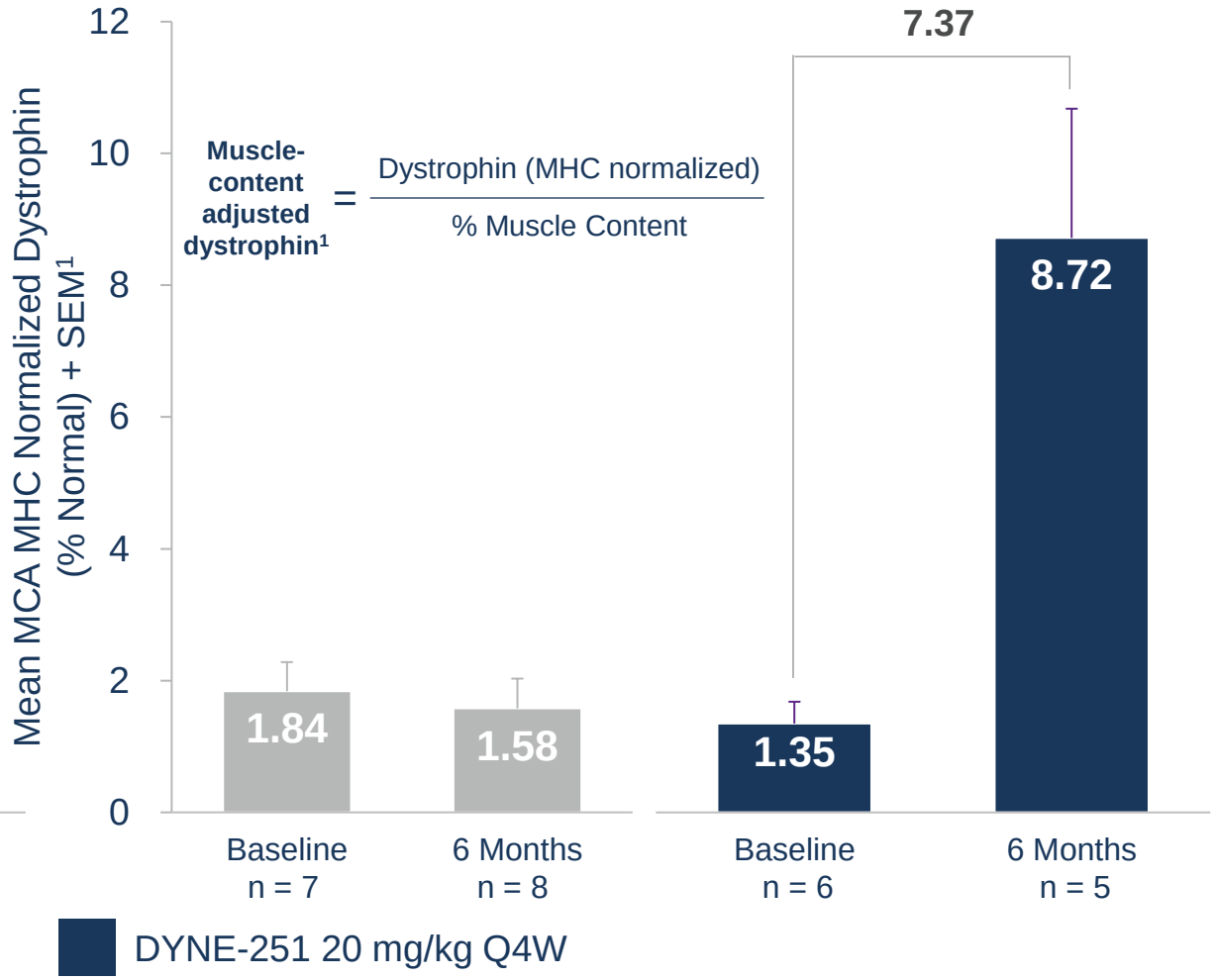
DYNE-251 Achieved Robust Dystrophin Expression

DYNE-251 Showed 3.7% Unadjusted and 8.7% Adjusted Dystrophin at 6 Months

Unadjusted Dystrophin



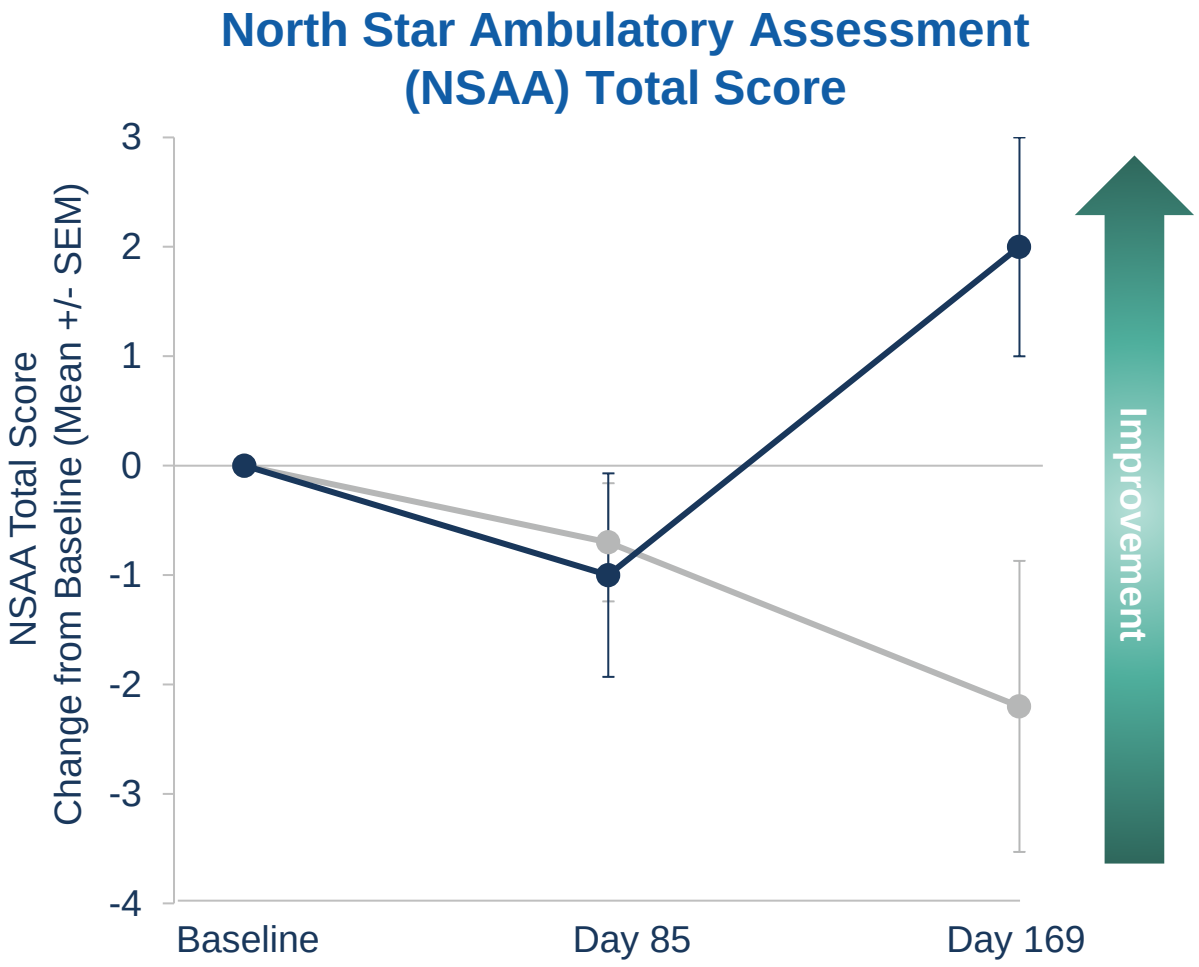
Muscle Content Adjusted Dystrophin

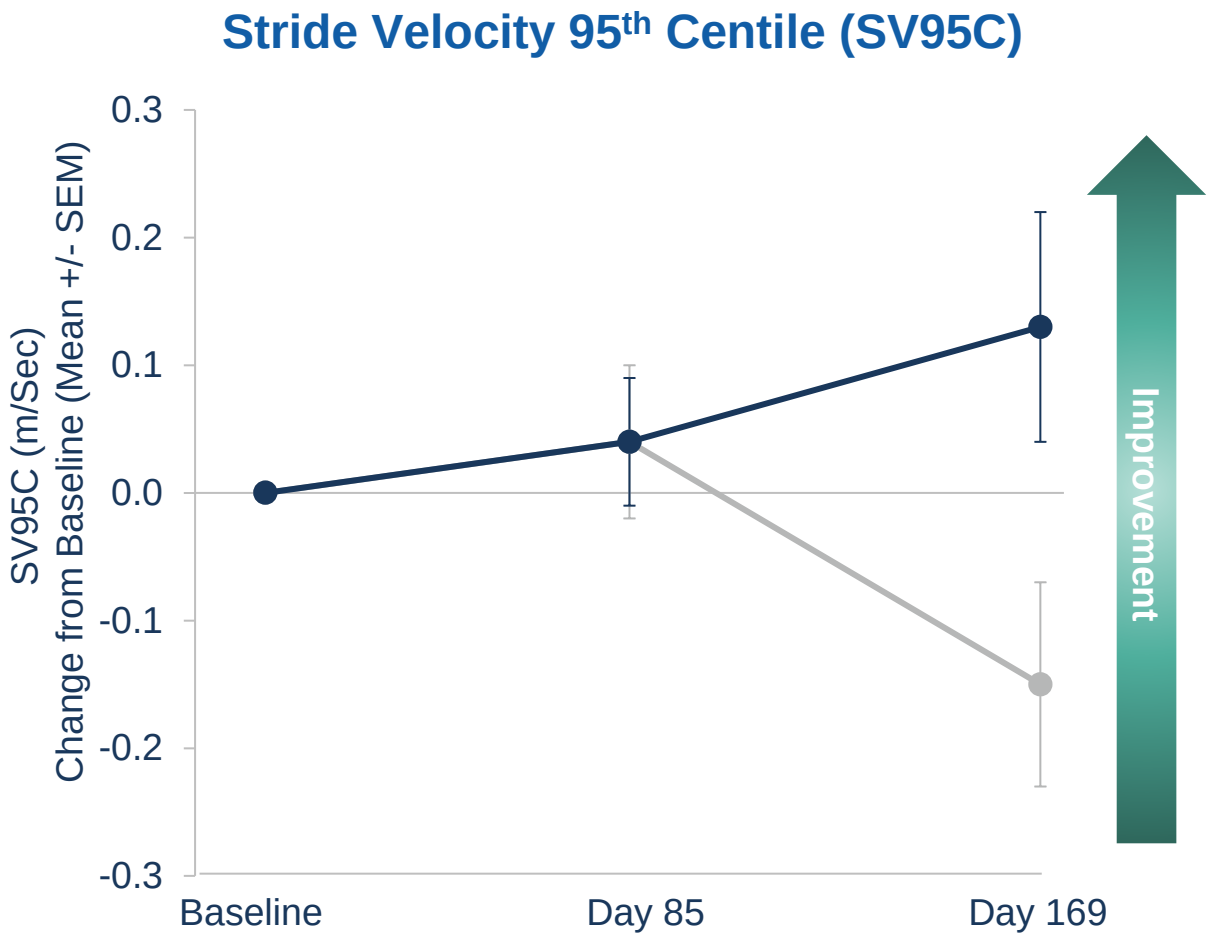


Note: MHC = myosin heavy chain

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

Unprecedented Clinically Meaningful Benefits Observed at Registrational Dose





Placebo (n = 6) for SV95C and (n = 14) for NSAA

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

Registrational Expansion Cohort Timeline Enables Potential Submission for U.S. Accelerated Approval in Early 2026

Accelerated Approval Path Enables Speed to Filing

DELIVER Registrational Expansion Cohort
N ~ 32, 3:1
20 mg/kg Q4W

Full Enrollment (Q1 2025)

Primary Endpoint (6 months)

Potential Submission for U.S. Accelerated Approval (Early 2026)

Potential Profile

Primary Endpoint (6 months)

- Change from baseline in dystrophin protein levels by Western Blot

Additional Endpoints

- Change from baseline of:
  - Exon 51 skipping levels
  - Muscle tissue PDPF
- NSAA
- SV95C

Robust Portfolio Focused on Neuromuscular Diseases with Opportunities to Expand by Leveraging FORCE Delivery

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**
Pompe disease	GAA	DYNE-401	US: **~3,800** Europe: **~7,000**

Pipeline expansion opportunities in CNS, rare skeletal, cardiac and metabolic

Building Momentum Toward Potential Launches in 2027

	2024	2025	2026
DYNE-101 for DM1	✓ MAD Complete ✓ Registrational dose selected	Fully enroll Registrational Expansion Cohort (mid-2025)	Registrational Expansion Cohort readout (H1 2026) Submission for U.S. Accelerated Approval (H1 2026)
DYNE-251 for Exon 51 DMD	✓ Registrational Expansion Cohort initiated	Registrational Expansion Cohort readout (late 2025)	Submission for U.S. Accelerated Approval (early 2026)

Q&A