







FORCE

to Deliver for Patients





ACHIEVE & DELIVER CLINICAL UPDATE | MAY 20, 2024

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Program



Opening remarks
John Cox, President & CEO



DYNE-101 ACHIEVE Trial in DM1 Data DYNE-251 DELIVER Trial in DMD Data

Wildon Farwell, M.D., MPH, Chief Medical Officer

Q&A



Closing Remarks
John Cox, President & CEO



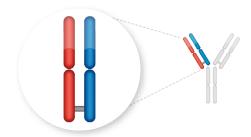




Dyne FORCE™ Platform: Modern Oligo Therapeutics for Muscle Diseases

ANTIBODY

Proprietary Fab targets TfR1 to enable muscle delivery

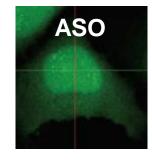


LINKER

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



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



Nuclear localization



Cytoplasmic localization



Compelling Clinical Profiles for DYNE-101 and DYNE-251 Reinforce Opportunity to Transform the Treatment of DM1 and DMD



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

- 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 date¹; 6.8 mg/kg Q8W cohort fully enrolled



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

- Dose-dependent increase in muscle delivery and dystrophin expression
- ✓ At 10.0 mg/kg Q4W dose, DYNE-251 showed compelling profile at 6 months
 - 3.2% unadjusted and 7.6% muscle content adjusted dystrophin
 - Trends in improvement in functional outcomes, including NSAA and SV95C³
- ✓ Favorable safety profile to date²; 40 mg/kg Q8W cohort fully enrolled

Based on Recent Regulatory Interactions, Pursuing Expedited Approvals for Both Programs with Update on Registrational Pathway Expected by Year-End 2024



Program



Opening remarks
John Cox, President & CEO



DYNE-101 ACHIEVE Trial in DM1 Data DYNE-251 DELIVER Trial in DMD Data

Wildon Farwell, M.D., MPH, Chief Medical Officer

Q&A



Closing Remarks
John Cox, President & CEO



Developing Transformative Therapies for People Living with DM1



approved

therapies

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)



OUR APPROACH

Disease-Modifying Nuclear *DMPK* Knockdown

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



DM1 Community Urgently Needs Treatment Options



"In a nutshell, it's a huge, complex disease. It not only affects every muscle in your body, but also your brain, cognition, your stamina, your endurance. And also, I think myotonic dystrophy is not just a physical disability, it also involves mental health."

Sarah, living with DM1



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



Population

- Adult patients living with DM1
- Ages 18 to 49 years

Primary Endpoints

Safety and tolerability

Additional Endpoints

- 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

Stages of ACHIEVE

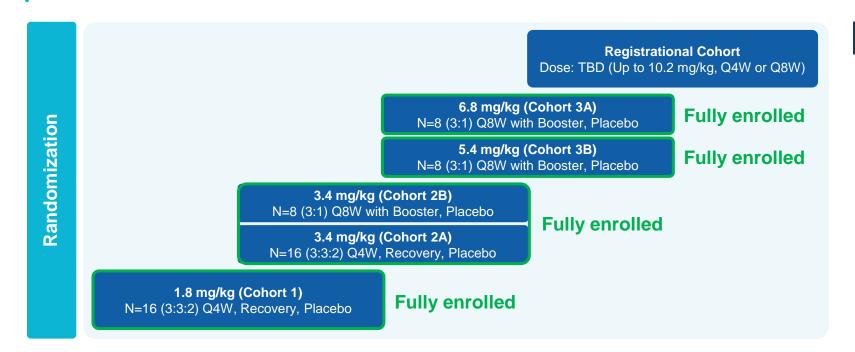
- Multiple Ascending Dose (MAD): 24 weeks
- Open-Label Extension (OLE): 24 weeks
- Long-Term Extension (LTE): 96 weeks



ACHIEVE Trial Design



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



MAD Study Details

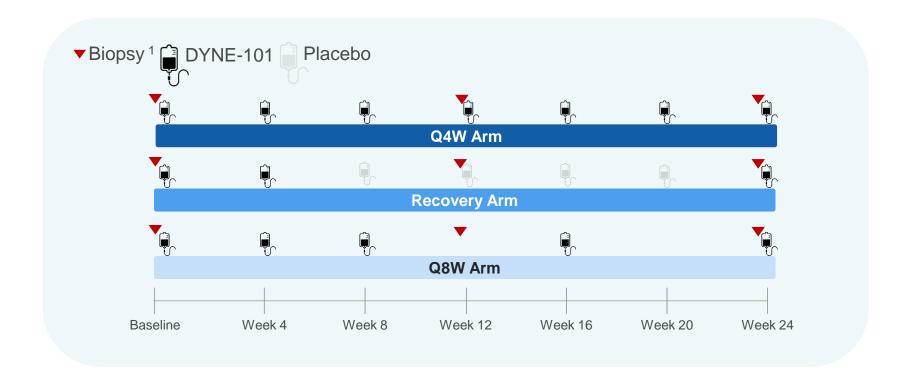
- IV administration of DYNE-101 or placebo every 4 weeks or every 8 weeks
- Muscle biopsies: Baseline, 12 weeks, 24 weeks
- Patients in MAD study escalated to highest tolerable dose in OLE and LTE

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



Dosing Schedules for Treatment Arms







ACHIEVE Baseline Participant Characteristics: By Cohort

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)



Safety Muscle Delivery Splicing Function PRO

DYNE-101 Safety Profile Is Favorable to Date

Summary of Treatment Emergent Adverse Events (TEAEs)¹

	Participants with ≥1 TEAE – n (%)							
TEAE Category	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%)	7 (88%)	8 (100%)	6 (75%)	53 (95%)		
Any related TEAE	7 (44%)	6 (38%)	1 (13%)	3 (38%)	5 (63%)	22 (39%)		
Any serious TEAE	4 (25%)	0	0	0	0	4 (7%)		
Any serious related TEAE	0	0	0	0	0	0		
Any TEAE leading to withdrawal	1 (6%)²	0	0	0	0	1 (2%)²		
Any TEAE leading to death	0	0	0	0	0	0		

Most TEAEs Were Mild or Moderate in Intensity

- 4 serious TEAEs unrelated to study drug
 - Atrioventricular block first degree (1)³
 - Pneumonia (1)
 - Pulmonary embolism (2)⁴
- Most common TEAEs (≥10% participant incidence)⁵
 - Nasopharyngitis (20%)
 - Procedural pain (18%)
 - Influenza; pyrexia (each 16%)
 - Diarrhea; headache (each 14%)
 - Back pain (13%)

Additional Safety Data

- Liver enzyme elevations have been observed in ~19% 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

~500 Doses Administered to Date Representing Over 40-patient Years of Follow-Up



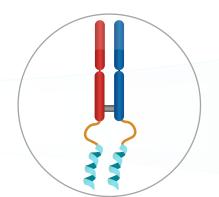
DYNE-101 Designed to Address the Foundational Spliceopathy of DM1 to Enable Comprehensive Functional Improvement

Robust Delivery

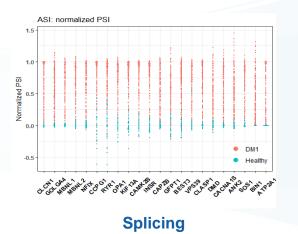
Validated Biomarker

Early Indicator of Functional Improvement

Broad Functional Improvement



FORCE Platform





Myotonia

Muscle Strength:

Quantitative Muscle Testing



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

Patient Reported Outcomes:

Myotonic Dystrophy Health Index (MDHI); DM1-ACTIV^c





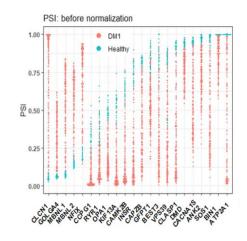
Safety Muscle Delivery Splicing Function PRO

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

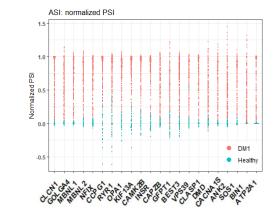
PSI = Percent Spliced In

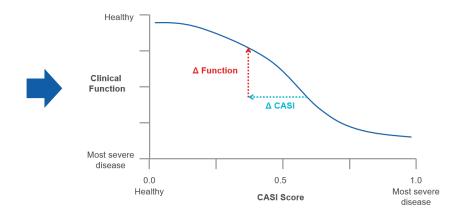
ASI: Alternative Splicing Index

CASI: Composite Alternative Splicing Index









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

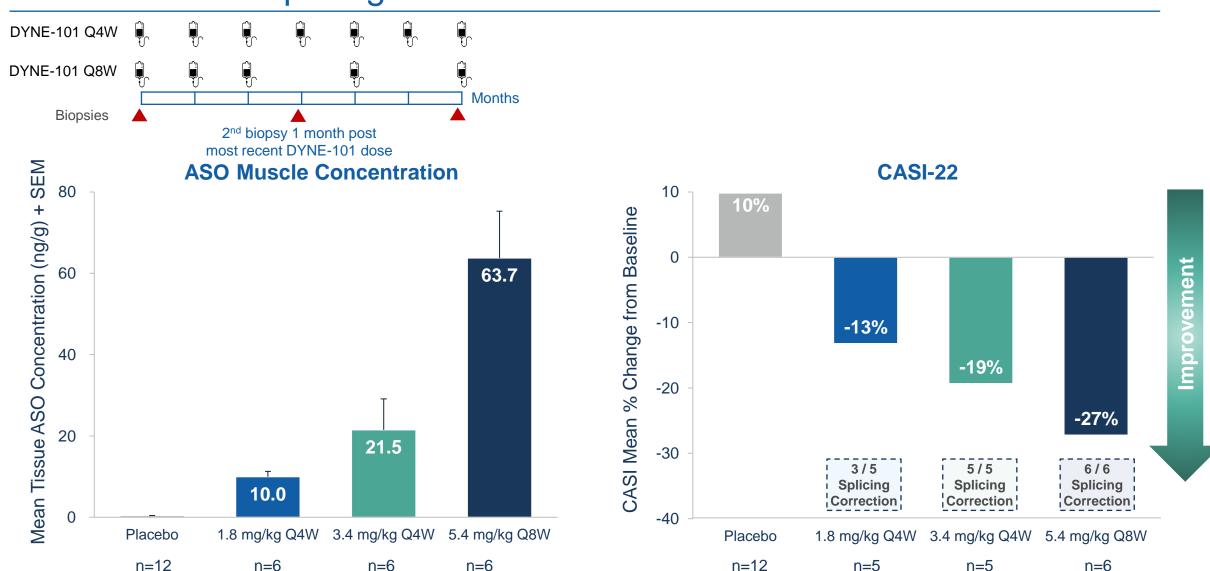
Normalize to reference PSI from healthy controls and patients from DM1 natural history studies ¹ Compute the mean of normalized PSI from a panel of 22 genes.

0 representing median score of healthy subjects; 1 representing 95th percentile severity of DM1 patients



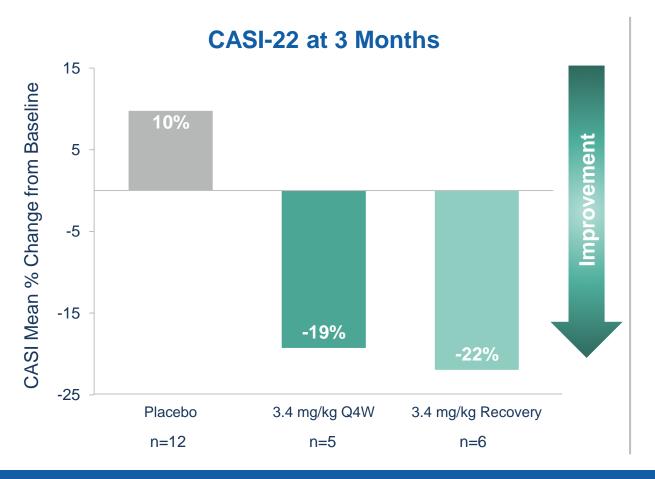
Safety Muscle Delivery Splicing Function PRO

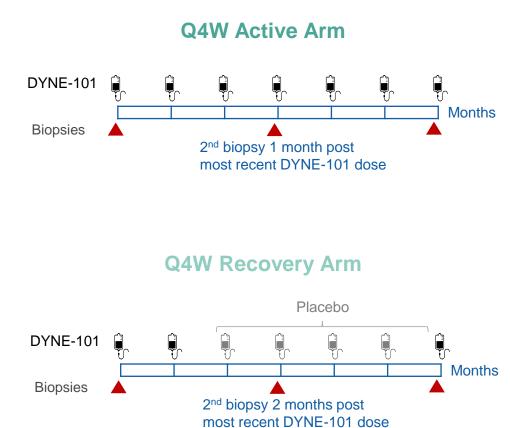
Monthly Dosing of DYNE-101 Demonstrated Dose-Dependent Delivery and Consistent Splicing Correction at 3 Months





Recovery Data Supports Less Frequent Dosing Regimen





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



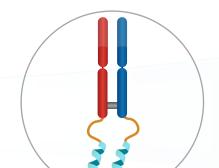
DYNE-101 Designed to Address the Foundational Spliceopathy of DM1 to Enable Comprehensive Functional Improvement

Robust Delivery

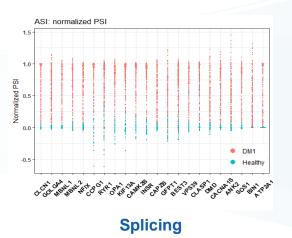
Validated Biomarker

Early Indicator of Functional Improvement

Broad Functional Improvement



FORCE Platform



Myotonia

Muscle Strength:

Quantitative Muscle Testing



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



Patient Reported Outcomes:

Myotonic Dystrophy Health Index (MDHI); DM1-ACTIV^c

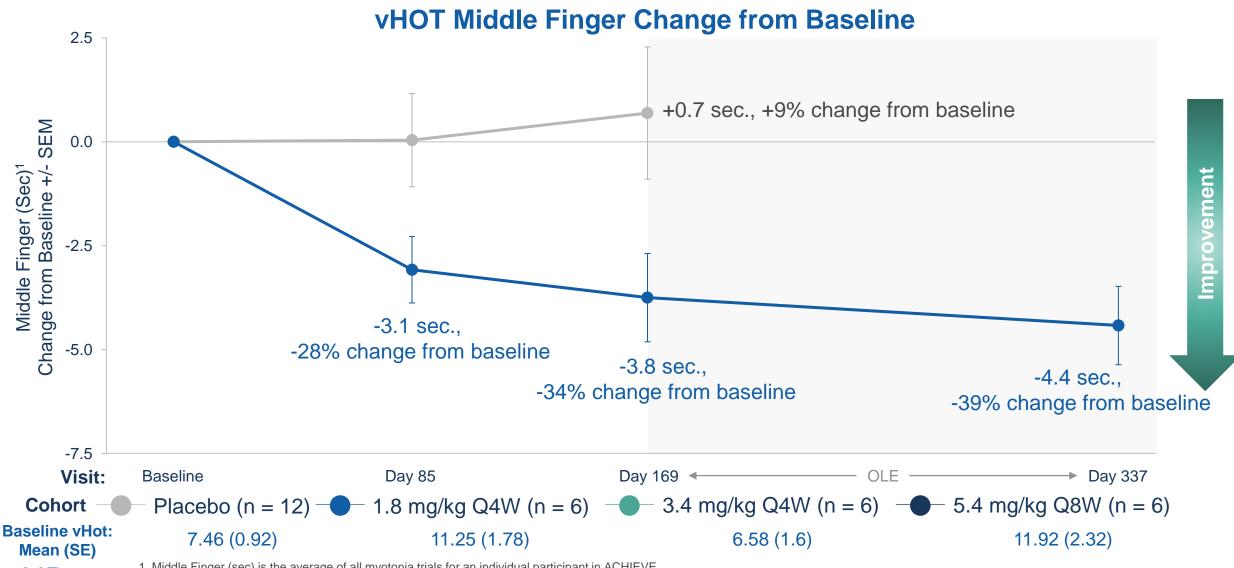




Continued Improvement in Functional Myotonia at 6 and 12 Months

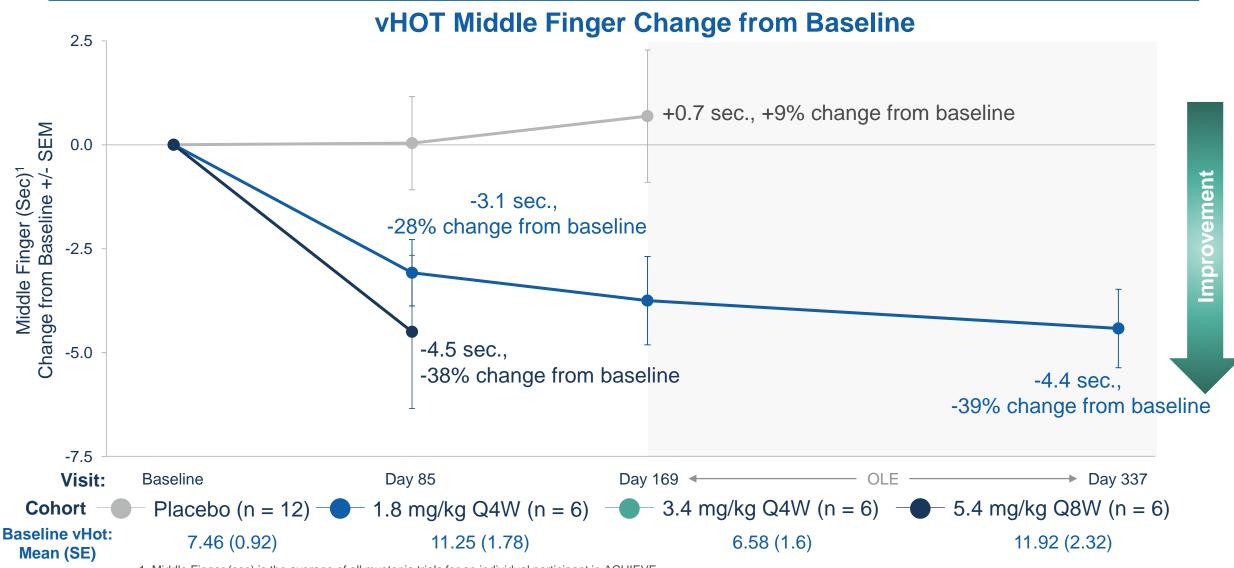
1.8 mg/kg Q4W myotonia benefit increased from 3.1 seconds at 3 Months to 4.4 seconds at 12 Months

PRO

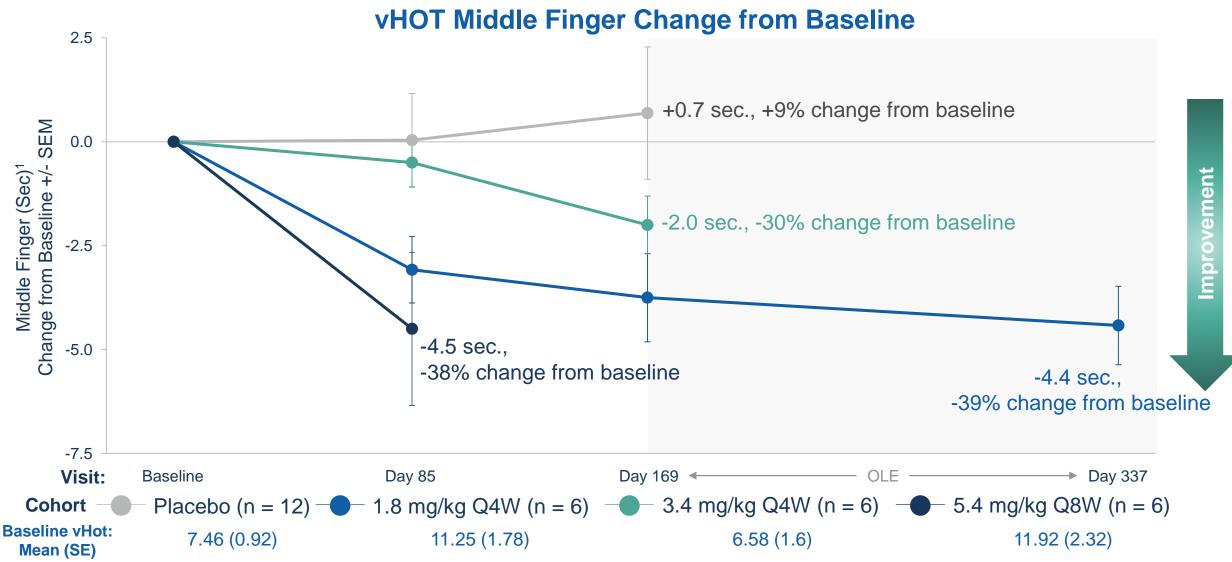


Continued Improvement in Functional Myotonia at 6 and 12 Months

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





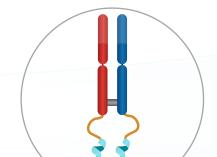
DYNE-101 Designed to Address the Foundational Spliceopathy of DM1 to Enable Comprehensive Functional Improvement

Robust Delivery

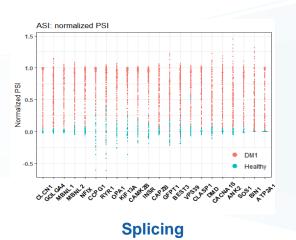
Validated Biomarker

Early Indicator of Functional Improvement

Broad Functional Improvement



FORCE Platform



Myotonia

Muscle Strength:

Quantitative Muscle Testing



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

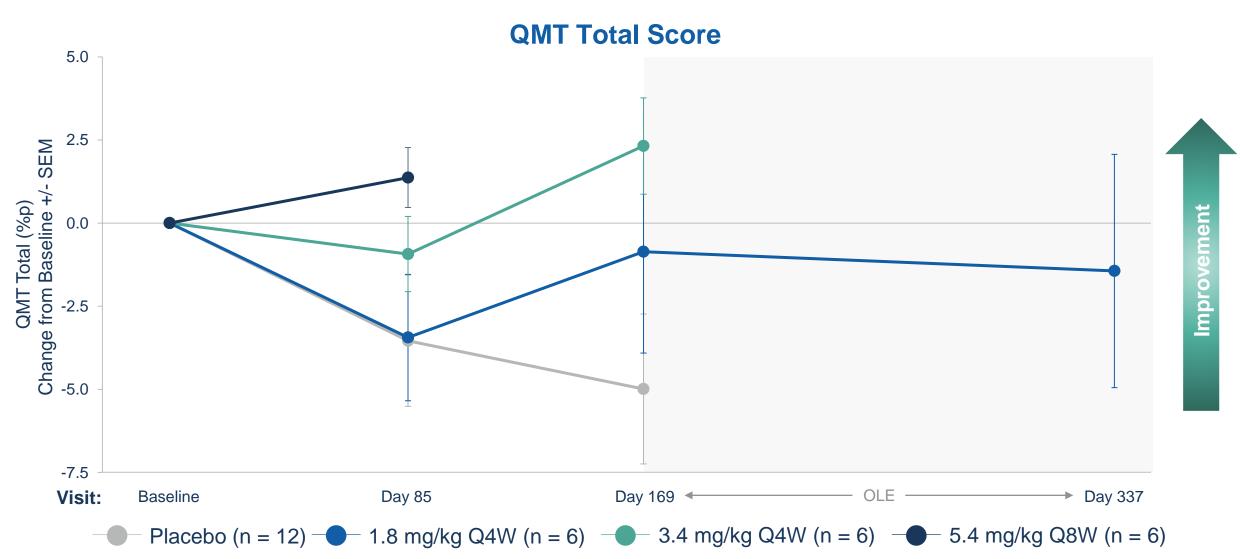


Patient Reported Outcomes:

Myotonic Dystrophy Health Index (MDHI); DM1-ACTIV^c

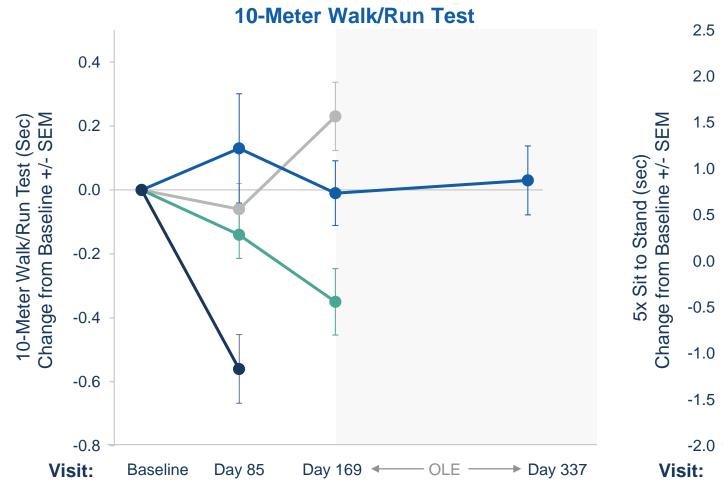


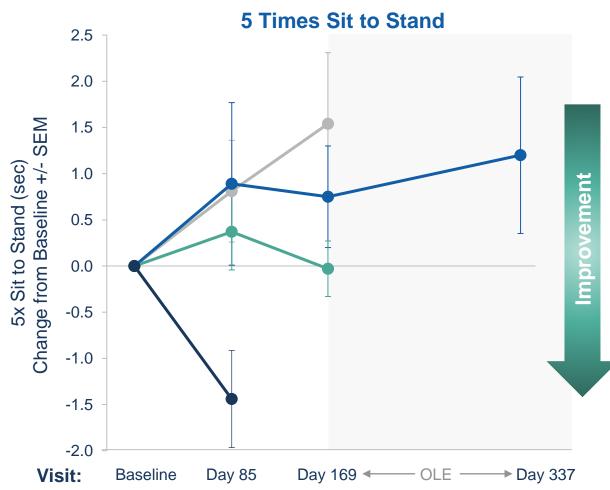
Measured by Quantitative Muscle Testing (QMT)





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







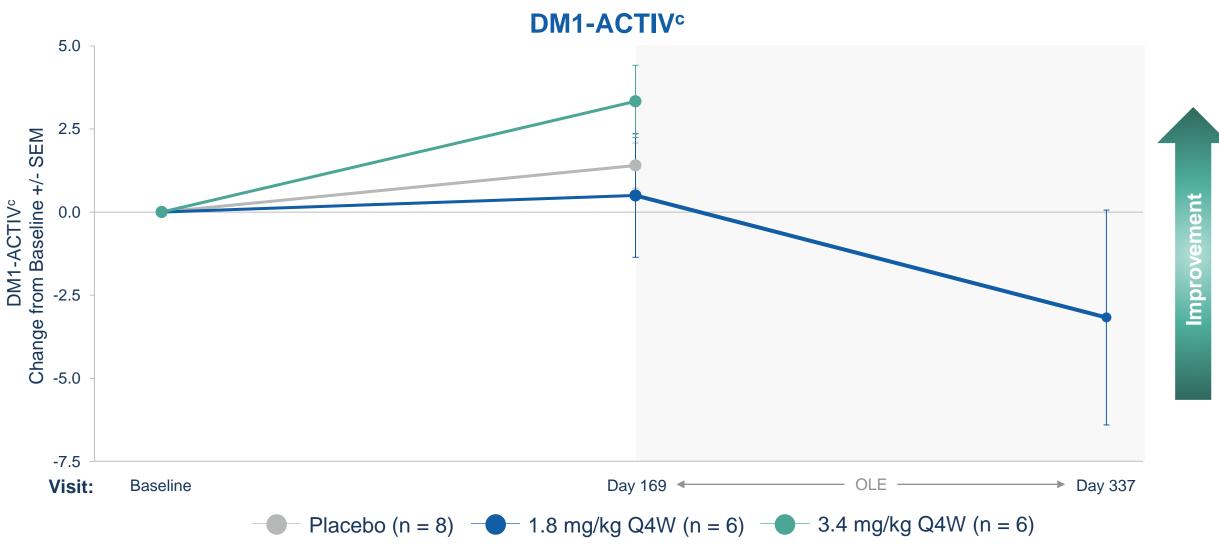




Placebo (n = 12) — 1.8 mg/kg Q4W (n = 6) — 3.4 mg/kg Q4W (n = 6) — 5.4 mg/kg Q8W (n = 6)



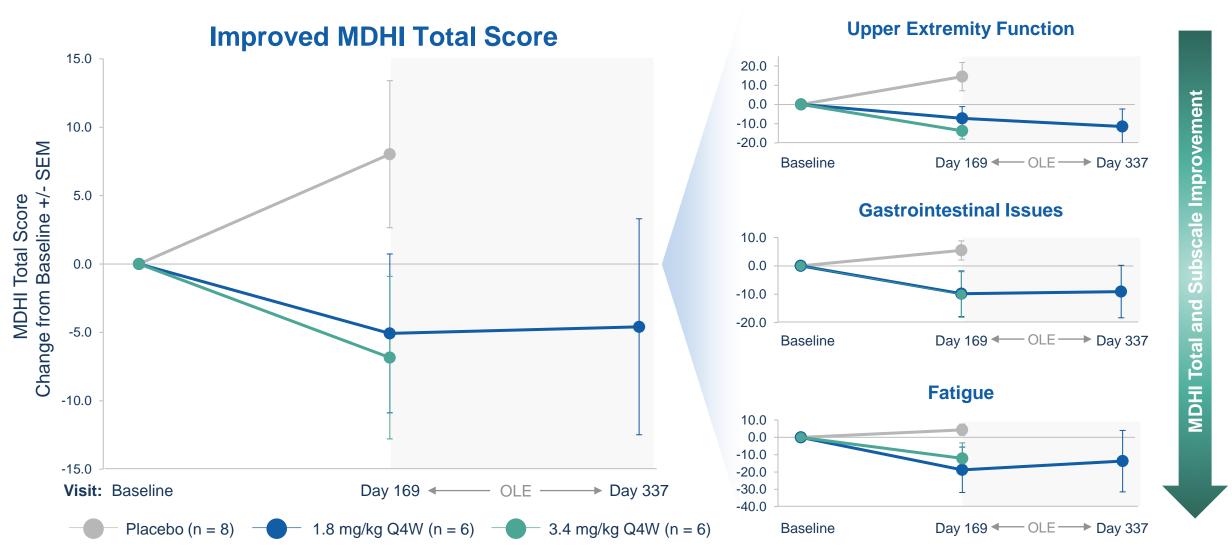






DYNE-101 Demonstrated Clinical Benefit Based on Well-Validated PRO

Showed Benefit in 17 out of 17 MDHI Subscales





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





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 date¹; 6.8 mg/kg Q8W cohort fully enrolled

Pursuing expedited approval based on recent regulatory interactions and strength of results

Update on path to registration for DYNE-101 expected by YE 2024



1. Data as of May 8, 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)



Potential Best-in-class Targeted Exon Skipping

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





DMD Community Has Urgent Need for Improved Treatment Options



"A potentially transformative treatment for me would be halting the progression of DMD and that would change everything for me and so many other people with it.

And because right now the progression of it, yeah, it's very tough. Great people are dying every day from it. It's always a big surprise, people die so suddenly from this. So, I think halting the progression would really change everything."

Alan, living with DMD



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 nonambulant

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

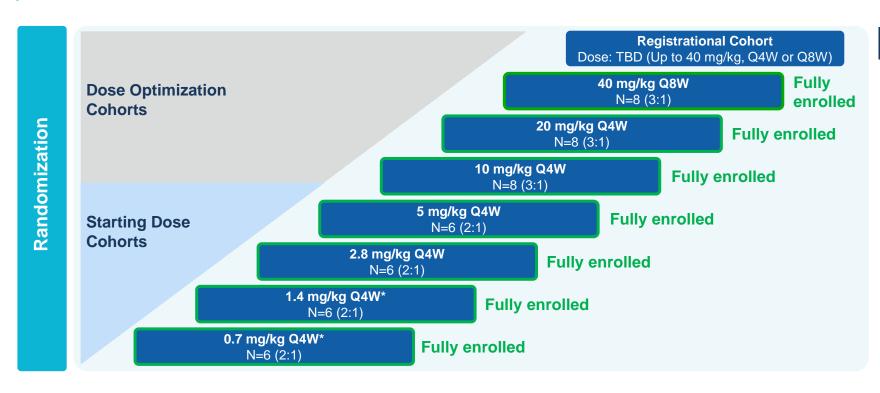
- Multiple Ascending Dose (MAD): 24 weeks
- Open-Label Extension (OLE): 24 weeks
- Long-Term Extension (LTE): 96 weeks



DELIVER Trial Design



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*
- Patients in MAD study escalated to highest tolerable dose in OLF and LTF

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



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)
Age (years)	10.8 (2.2)	7.8 (3.3)	10.7 (2.9)	8.3 (2.8)	6.6 (2.2)
BMI (kg/m ²)	19.5 (3.4)	18.6 (2.3)	22.6 (6.3)	20.9 (1.6)	18.3 (3.2)
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)
Corticosteroid dosing regimen (n (%)) ¹ Daily Other	4 (66.7%) 2 (33.3%)	4 (66.7%) 3 (50.0%)	5 (83.3%) 1 (16.7%)	6 (100.0%) 0	8 (100.0%) 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%)
NSAA Total Score	22.2 (7.2)	22.8 (10.5)	20.3 (9.0)	21.0 (7.0)	25.3 (6.4)
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)
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)
Stride Velocity 95th Percentile (m/sec)	N/A	N/A	N/A	N/A	1.9 (0.5)



Safety Muscle Delivery Exon 51 Skipping Dystrophin by WB Function

DYNE-251 Safety Profile Is Favorable to Date

Summary of Treatment Emergent Adverse Events (TEAEs)¹

	Participants with ≥1 TEAE – n (%)							
TEAE Category	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	Overall¹ N=48
Any TEAE	6 (100%)	6 (100%)	3 (50%)	6 (100%)	7 (88%)	7 (88%)	4 (50%)	39 (81%)
Any related TEAE	3 (50%)	3 (50%)	0	5 (83%)	2 (25%)	3 (38%)	2 (25%)	18 (38%)
Any serious TEAE	0	0	1 (17%)	0	0	1 (13%)	0	2 (4%)
Any serious related TEAE	0	0	0	0	0	0	0	0
Any TEAE leading to withdrawal from study drug	0	0	0	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0	0	0	0

Most TEAEs Were Mild or Moderate in Intensity

- The 2 serious TEAEs are unrelated to study drug
 - Dehydration due to gastroenteritis (1)
 - Left femoral neck fracture (1)
- Most common TEAEs (>10% participant incidence)²
 - Headache (23%)
 - Pyrexia; fall (each 21%)
 - Nasopharyngitis; vomiting; infusion-related reaction³ (each 19%)
 - Cough (17%)
 - Upper respiratory tract infection (13%)

Additional Safety Data

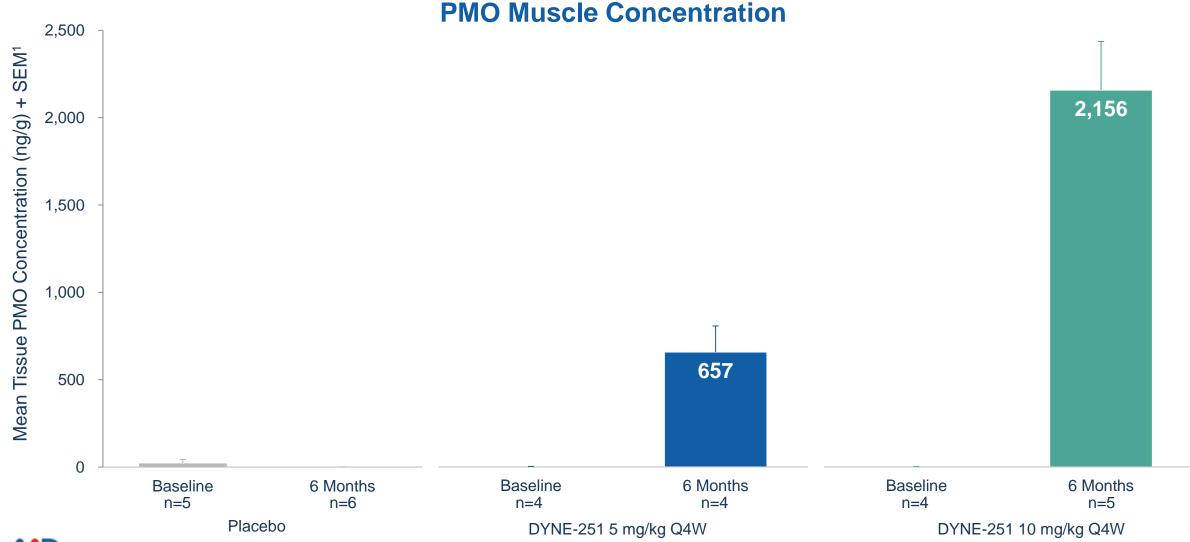
- No participants have demonstrated persistent related anemia or thrombocytopenia
- No participants have demonstrated kidney injury
- No participants have demonstrated clinically meaningful changes in electrolytes, including magnesium

~480 Doses Administered to Date Representing Over 35-patient Years of Follow-Up

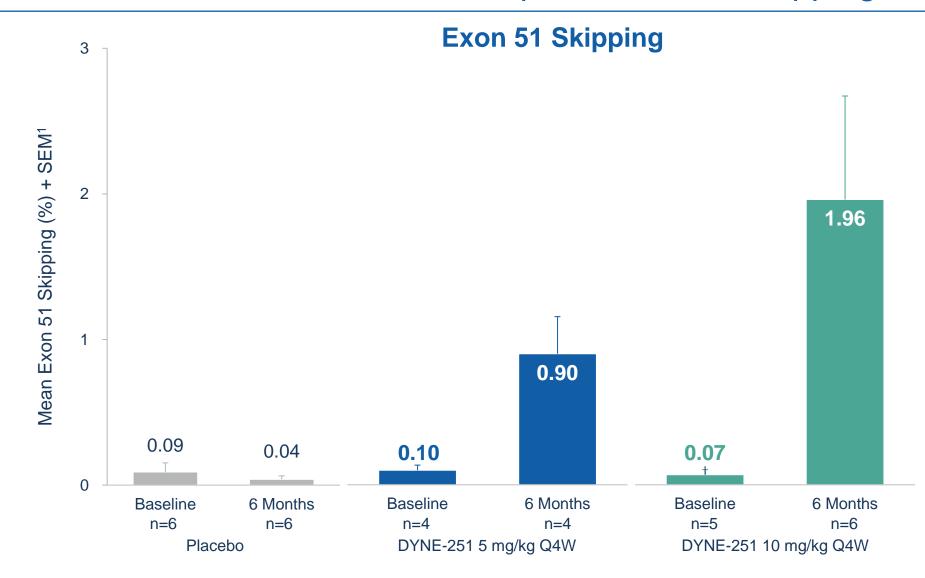


1. Data as of April 30, 2024. 2. All cohorts combined; preferred terms are reported. 3. All infusion related reactions have been mild or moderate in intensity; dosing has continued in all participants.

DYNE-251 Drove Dose Dependent Delivery of PMO to Muscle

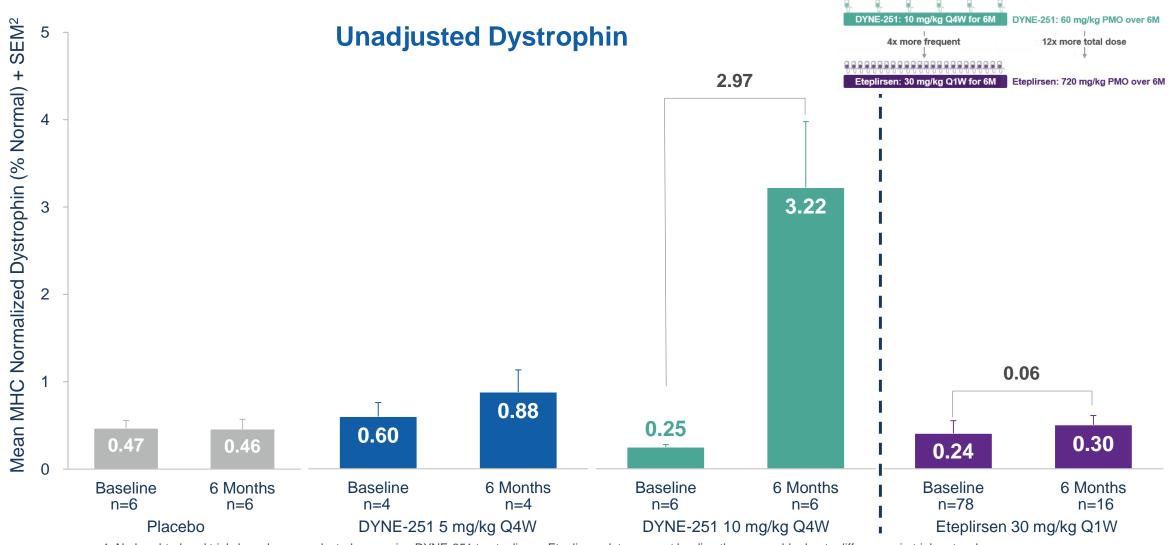






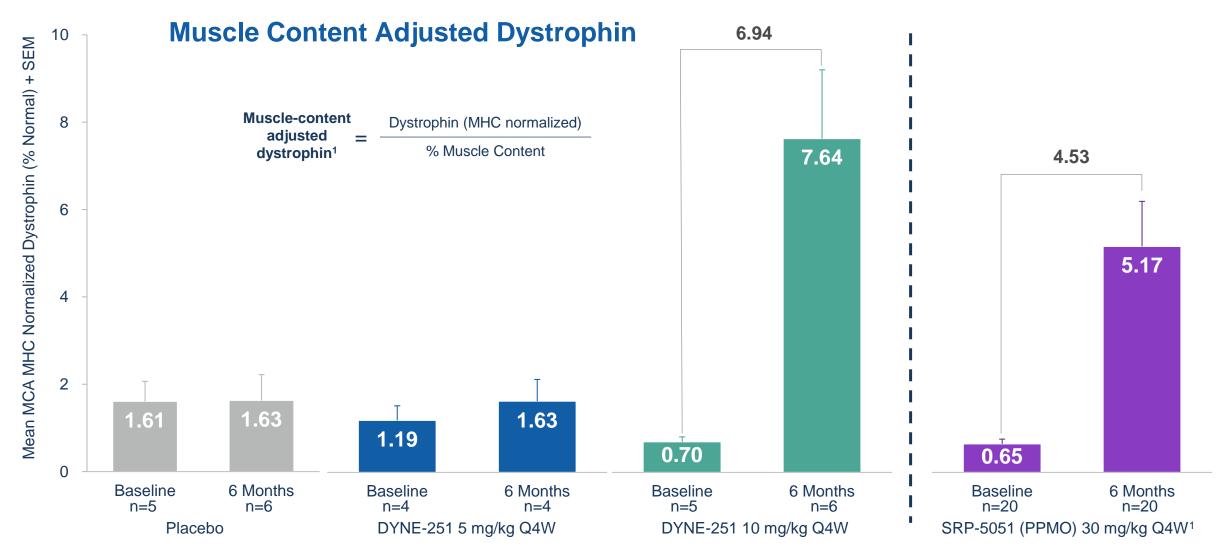


DYNE-251 Showed >10 Fold Higher Dystrophin at 6 Months than Eteplirsen Study with 12 Fold Lower PMO Dose Administered 4 Times Less Frequently ¹





DYNE-251 Achieved 7.6% Muscle Content Adjusted Dystrophin at 6 Months DYNE-251 dosed 10 mg/kg Q4W, SRP-5051 (PPMO) dosed 30 mg/kg Q4W

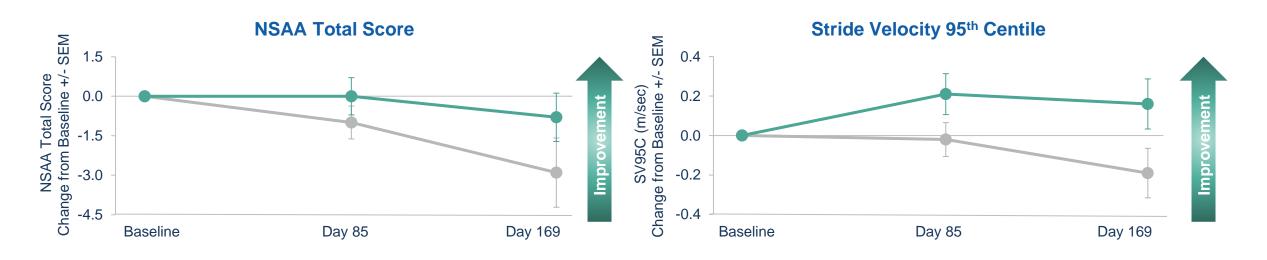


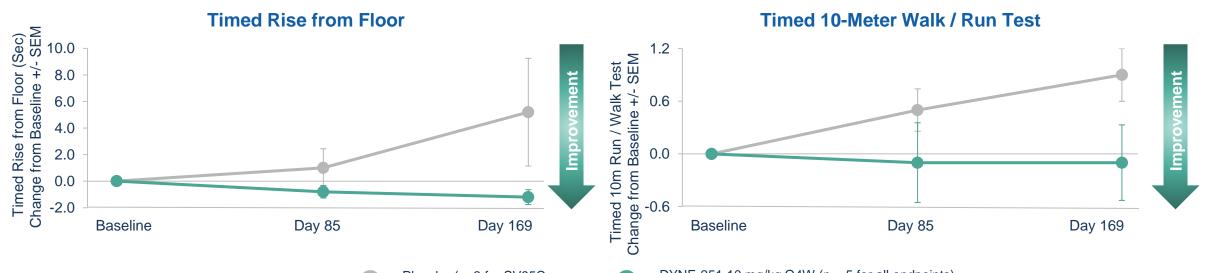


Safety Muscle Delivery Exon 51 Skipping Dystrophin by WB Function

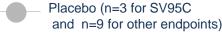
Encouraging Trends Across Multiple Functional Endpoints

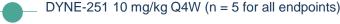
Baseline values inform interpretation of data; ongoing exploration of higher dose cohorts and longer time points









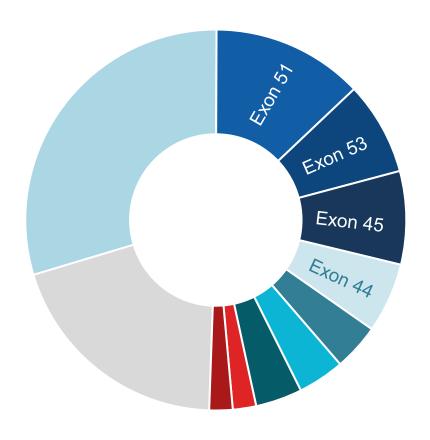


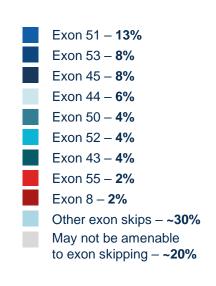
Opportunity to Build a Global DMD Franchise: Leading with DYNE-251, Payloads Identified for Exons 53, 45, 44

Approximately

80% of patients

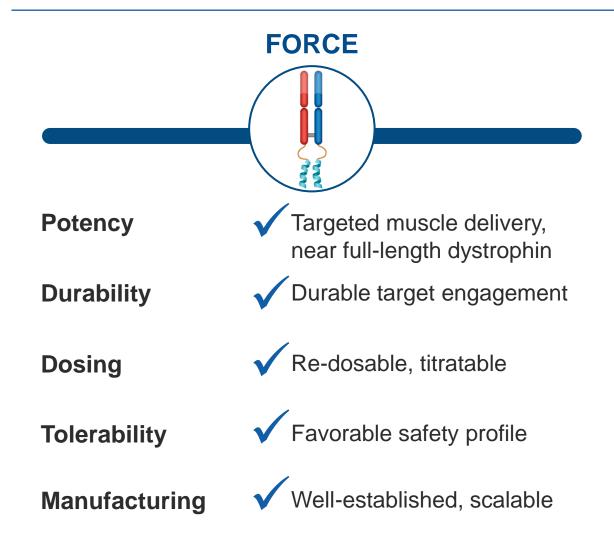
have genotypes amenable to exon skipping







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



- 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



DELIVER Data Demonstrated Potential for DMD Exon Skipping Franchise with Differentiated Efficacy and Safety Profile





At 10.0 mg/kg Q4W dose, DYNE-251 showed compelling profile vs. eteplirsen standard-of-care reported at 6 months¹:

- 3.2% unadjusted and 7.6% muscle content adjusted dystrophin expression
- Trends in improvement in functional outcomes, including NSAA and SV95C



Favorable safety profile to date²; 40 mg/kg Q8W cohort fully enrolled



Supports further development of DMD global franchise

Pursuing expedited approval based on recent regulatory interactions and strength of results

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



Program



Opening remarks
John Cox, President & CEO



DYNE-101 ACHIEVE Trial in DM1 Data DYNE-251 DELIVER Trial in DMD Data

Wildon Farwell, M.D., MPH, Chief Medical Officer

Q&A



Closing Remarks
John Cox, President & CEO



Driving Towards Potentially Transformative DM1 and DMD Therapies





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

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

Favorable Safety & Tolerability Profile Supporting Dose Escalation

Fully Enrolled Through 6.8 mg/kg

Fully Enrolled Through 40 mg/kg

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



Advancing Robust Portfolio Focused on Muscle Diseases

Pipeline Update by YE 2024 Including FSHD and Other Pipeline Programs

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		
	Exon 53			
	Exon 45			US: ~12,000-15,000 Europe: ~25,000
	Exon 44			•
	Other Exons			
Facioscapulohumeral Muscular Dystrophy (FSHD)	DUX4	DYNE-301		US: ~16,000-38,000 Europe: ~35,000

Pipeline Expansion Oppo	ortunities			
Rare Skeletal				
CNS				
Cardiac				
Metabolic				

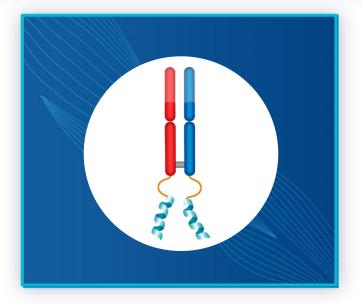




Building the World's Leading Muscle Disease Company



Win in DM1, DMD, FSHD



Own Muscle Delivery & Leverage FORCE



Dynamo Culture











FORCE

to Deliver for Patients





ACHIEVE & DELIVER CLINICAL UPDATE | MAY 20, 2024