Advancing Functional Improvement in DM1

DYNE-101 U.S. Accelerated Approval and Clinical Update

JUNE 17, 2025

Sarah, *living with DM1*

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Program

Opening Remarks

John Cox, President & CEO

Updated Plan for U.S. Accelerated Approval and New Clinical Data for DYNE-101

Doug Kerr, M.D., Ph.D., Chief Medical Officer

Closing Remarks

John Cox, President & CEO

Available for Q&A

Erick Lucera, Chief Financial Officer

Today's Update

Breakthrough Therapy Designation

- FDA granted Breakthrough Therapy Designation for DYNE-101 in DM1 following Type C Meeting

Accelerated Approval Pathway with vHOT

- Dyne and FDA agreed that the next step toward Accelerated Approval was to submit for review the revised protocol for the Registrational Expansion Cohort of the ACHIEVE trial with vHOT as primary endpoint
- Revised protocol submitted to FDA in June

New Long-Term Data from ACHIEVE Trial

- Robust and sustained functional improvement across multiple measures at 6 and 12 months at registrational dose
- Data support vHOT improvement as early indicator of clinical benefit with DYNE-101
- Continued favorable safety profile[1]

Data from Registrational Expansion Cohort, MAD, and LTE portions of ACHIEVE trial intended to support a potential U.S. Accelerated Approval

Data from the Registrational Expansion Cohort are planned for mid-2026 to support a potential U.S. Accelerated Approval submission in late 2026

1. Safety data as of April 23, 2025; vHOT = video hand opening time; MAD = multiple ascending dose; LTE = long-term extension.

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DM1 is a Devastating Neuromuscular Splicing Disorder

Overview

- Mutation in the *DMPK* gene leads to mis-splicing of multiple genes
- Onset at any point, depending on DM1 phenotype
- Life expectancy of 45 - 60 years

Clinical Presentation

- Muscle weakness & myotonia
- CNS manifestations including fatigue, cognition, and sleep
- Gastrointestinal issues
- Cardiac arrhythmia
- Pulmonary abnormalities

Population

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

NO approved therapies

OUR APPROACH

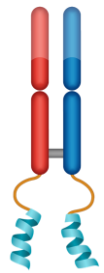
Functional Improvement via Splicing Correction in Nucleus

Restore normal RNA splicing to achieve **functional improvement** for those living with DM1

Note: DM1 = myotonic dystrophy type 1; 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** → **Early clinical effect** → **Broad functional improvement**



DYNE-101

Differentiated MOA

Myotonia:
Video Hand Opening Time (vHOT)

Muscle Strength:
Quantitative Muscle Testing

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

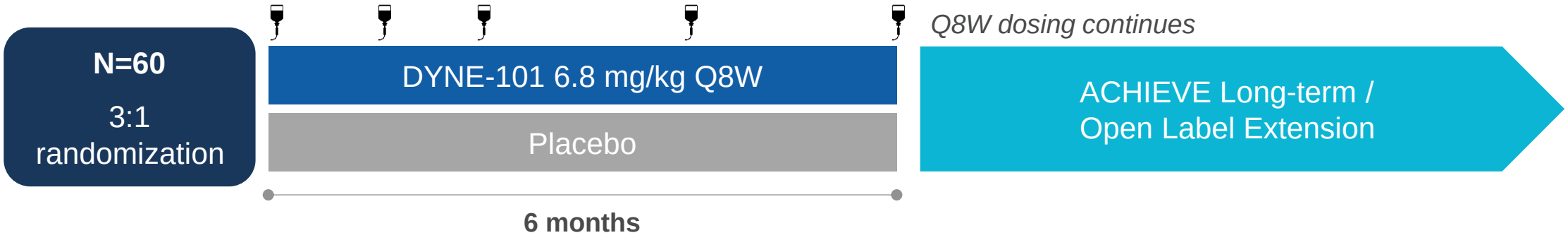
Patient Reported Outcomes:
Myotonic Dystrophy Health Index (MDHI)

1. Image depicts the intended DYNE-101 mechanism of action (MOA); DM1 = myotonic dystrophy type 1.

Revised Registrational Expansion Cohort to Support Potential U.S. Accelerated Approval

- ✓ ACHIEVE MAD cohorts complete; all cohorts now at 6.8 mg/kg Q8W in long-term / open label extension
- ACHIEVE Registrational Expansion Cohort **currently enrolling**
  - Primary endpoint: Change from baseline in middle finger myotonia as measured by vHOT at 6 months compared to placebo[1]
  - Secondary endpoints include: CASI-22, QMT, 10MWR, 5xSTS, and MDHI at 6 months
- Global footprint, including **addition of U.S. sites**

ACHIEVE Registrational Expansion Cohort



Data planned for mid-2026 to support a potential Accelerated Approval submission in late 2026

1. Average baseline vHOT for the 56 patients enrolled in the multiple ascending dose portion of ACHIEVE was 9.2 seconds. MAD = multiple ascending dose; 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 test; MDHI = Myotonic Dystrophy Health Index.

New Data Support the Potential for Accelerated Approval of DYNE-101 with vHOT as Primary Endpoint

Accelerated Approval allows FDA to approve drugs for serious conditions with an unmet medical need based on a surrogate or intermediate clinical endpoint, which is reasonably likely to predict clinical benefit

Intermediate clinical endpoint	• A clinical measure with the potential to detect a drug effect earlier than other clinically meaningful endpoints and which is considered reasonably likely to predict clinical benefit
DYNE-101 Outcomes	• Data support improvement in vHOT as early indicator of clinical benefit with DYNE-101 • Sustained improvements increase confidence in 6-month results
DYNE-101 Safety Data	• Favorable safety profile[1]

1. Safety data as of April 23, 2025; vHOT = video hand opening time.

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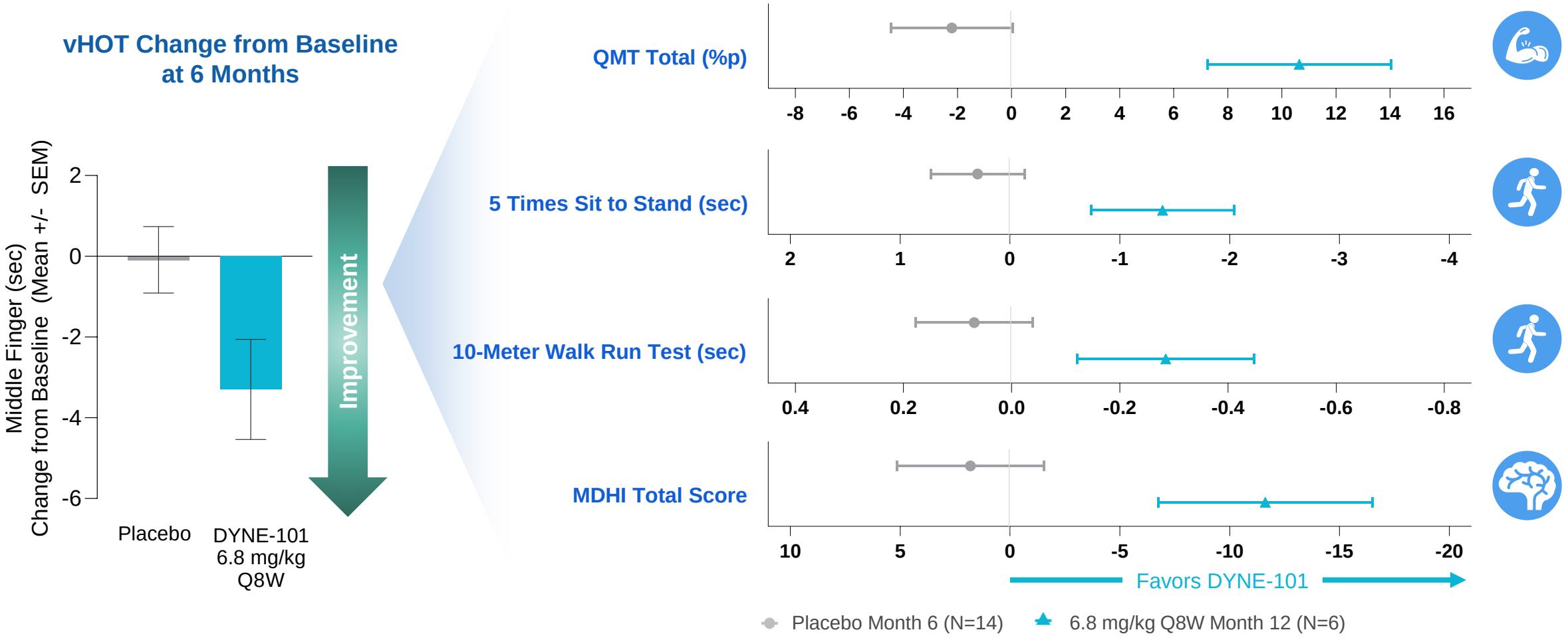
Data Support vHOT Improvement as an Early Indicator of Clinical Benefit with DYNE-101



With DYNE-101, all participants at highest 3 doses who improved in 6M vHOT improved in 12M strength, 5xSTS, and/or 10MWR

Notes: 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 ± SEM (standard error of the mean); 6 months = 169 days, 12 months = 337 days; vHOT = video hand opening time; QMT = quantitative muscle testing; 10MWR = 10-meter walk/run test; 5xSTS = 5 times sit to stand test; MDHI = Myotonic Dystrophy Health Index; %p = percent predicted.

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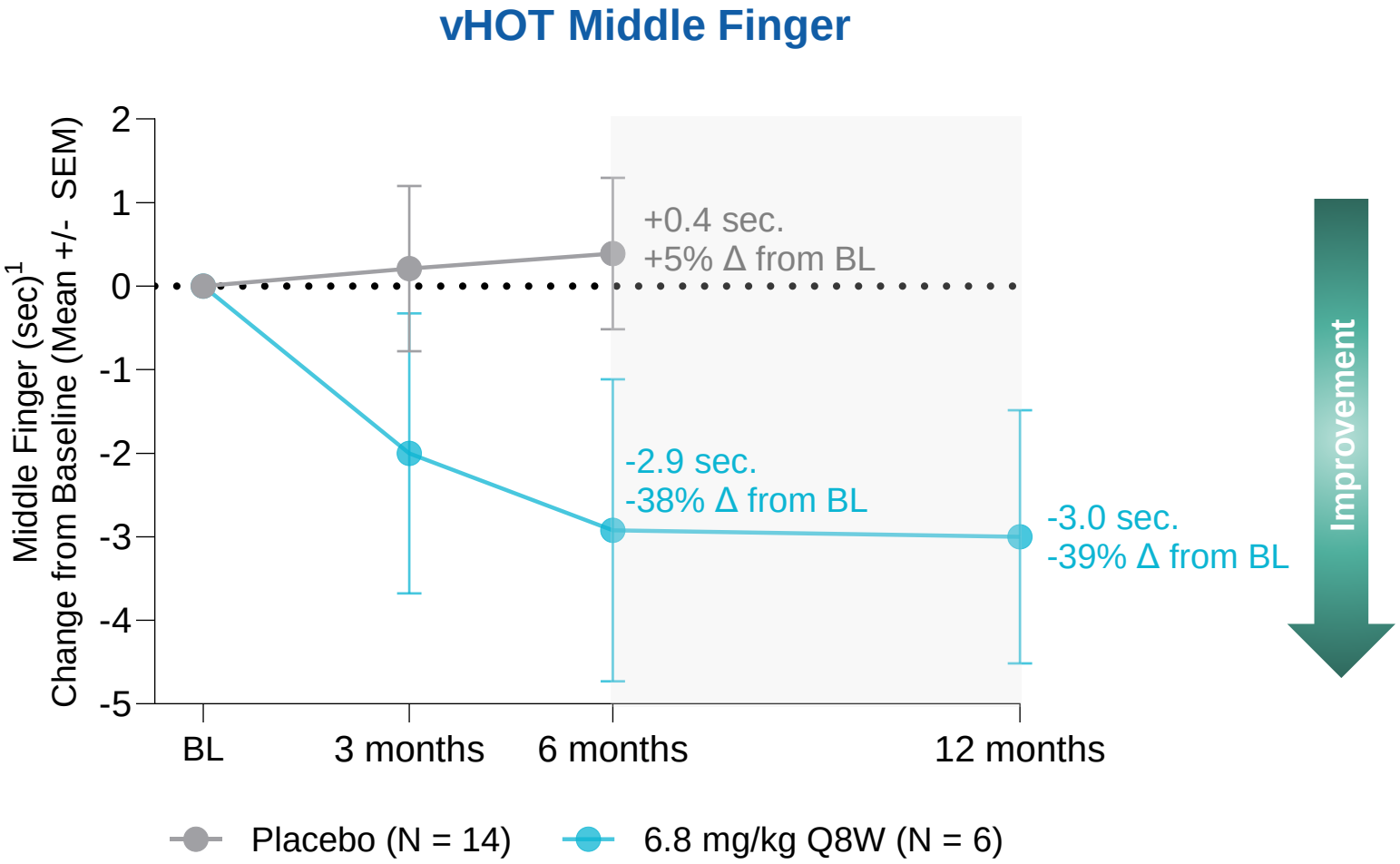
Robust and Sustained vHOT Improvement at 6 and 12 Months

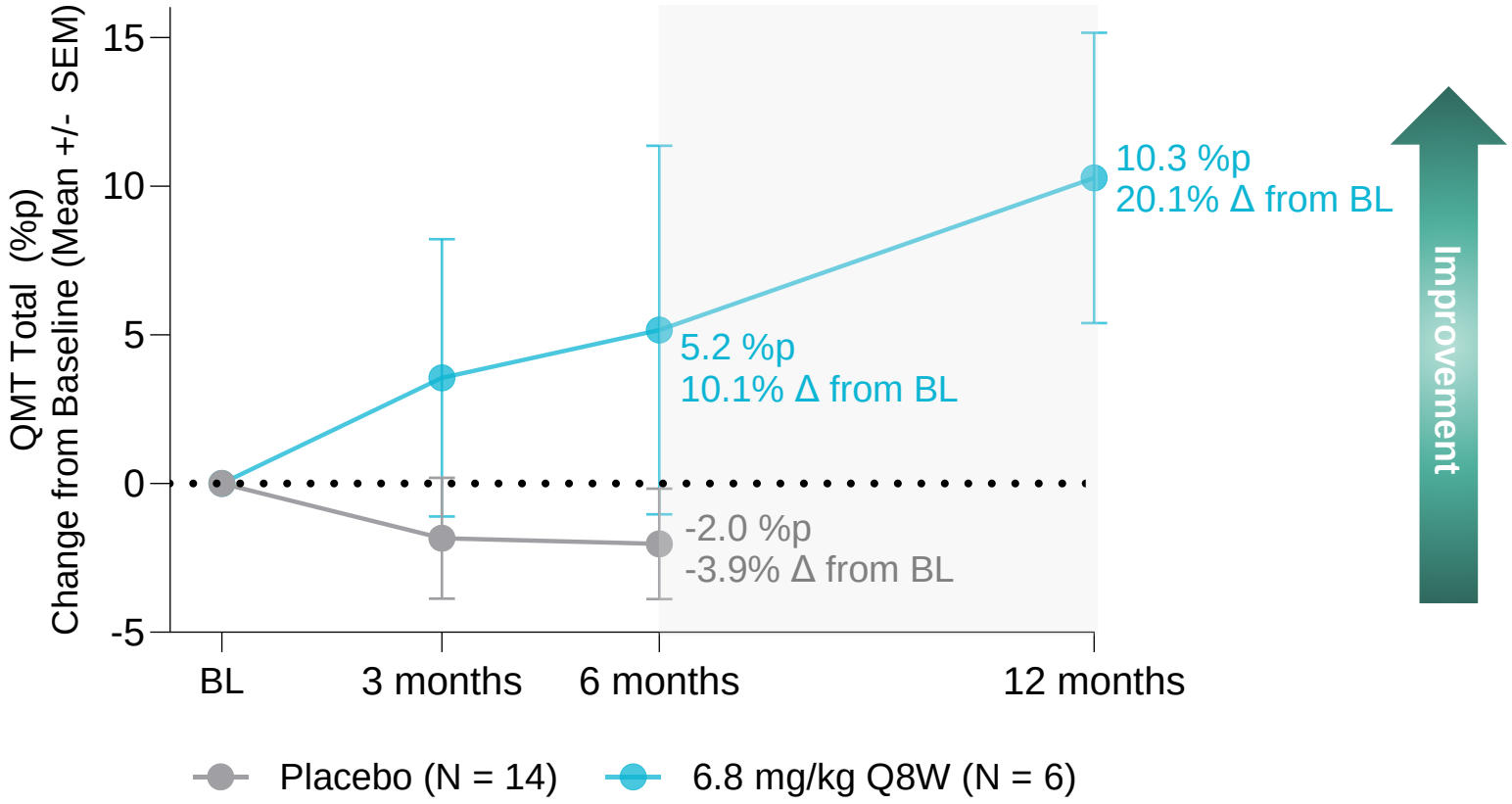


Baseline (sec), mean (SEM)	**7.5 (0.8)**	**7.8 (1.5)**

1. vHOT Middle Finger (sec) is the average of all myotonia trials for an individual participant in ACHIEVE; vHOT = video hand opening time; SEM = standard error of the mean; BL = baseline. 3 months = 85 days; 6 months = 169 days; 12 months = 337 days.

Strength Continues to Improve from Month 6 to Month 12

Quantitative Muscle Testing (QMT) Total Score

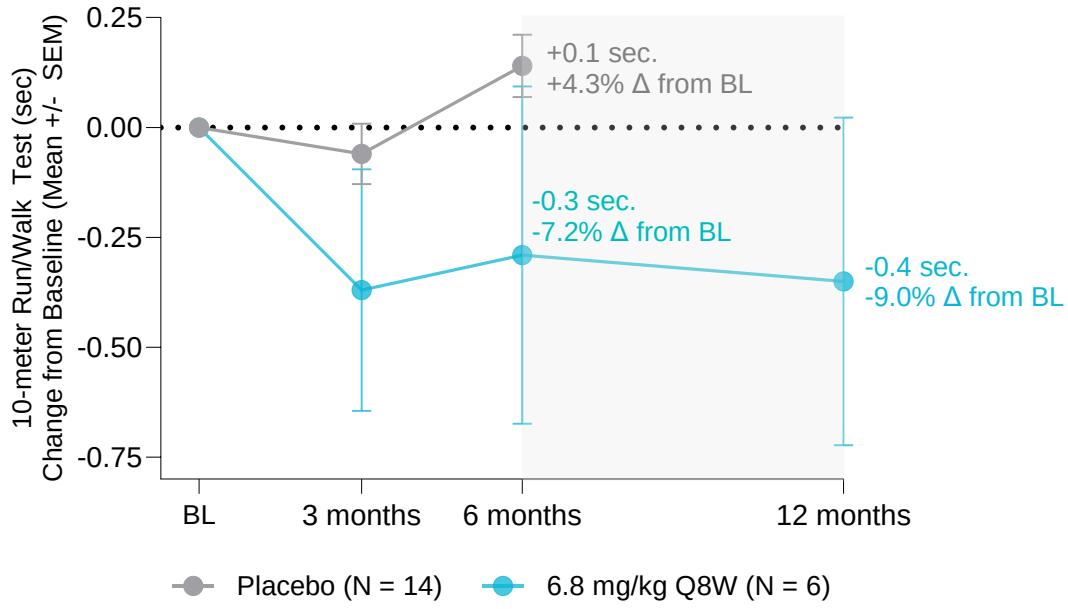


Baseline score, mean (SEM)	**51.5 (3.8)**	**51.3 (4.2)**

SEM = standard error of the mean; BL = baseline; %p = percent predicted; 3 months = 85 days; 6 months = 169 days; 12 months = 337 days.

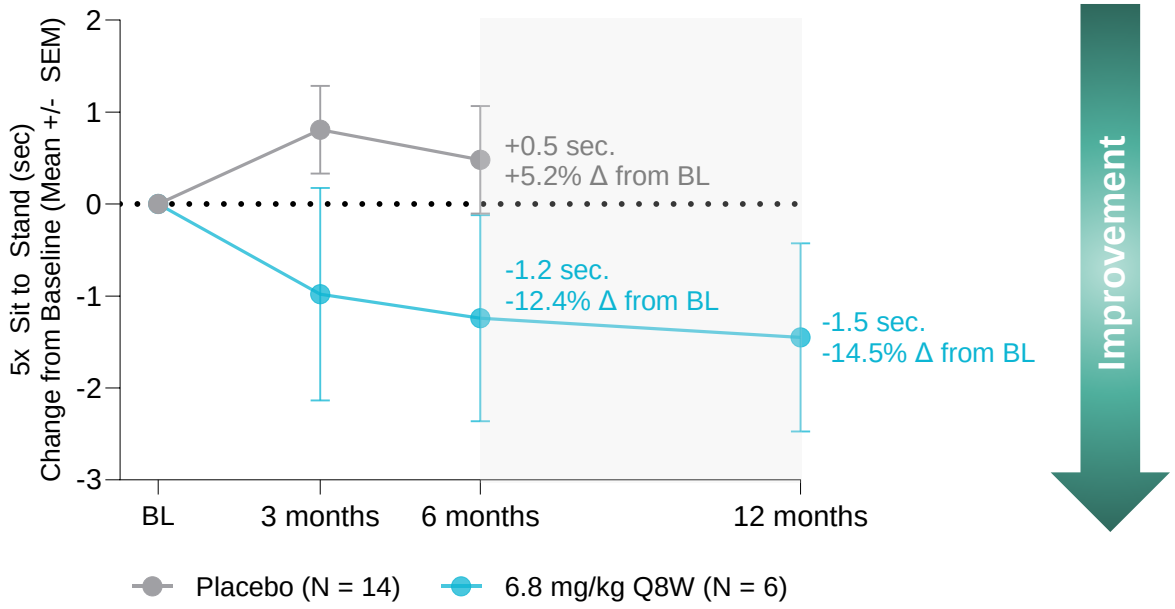
Robust Benefit Across Multiple Timed Function Tests Sustained at 6 and 12 Months

10-Meter Walk/Run Test



Baseline (sec), mean (SEM)	**3.3 (0.1)**	**3.9 (0.6)**

5 Times Sit to Stand Test

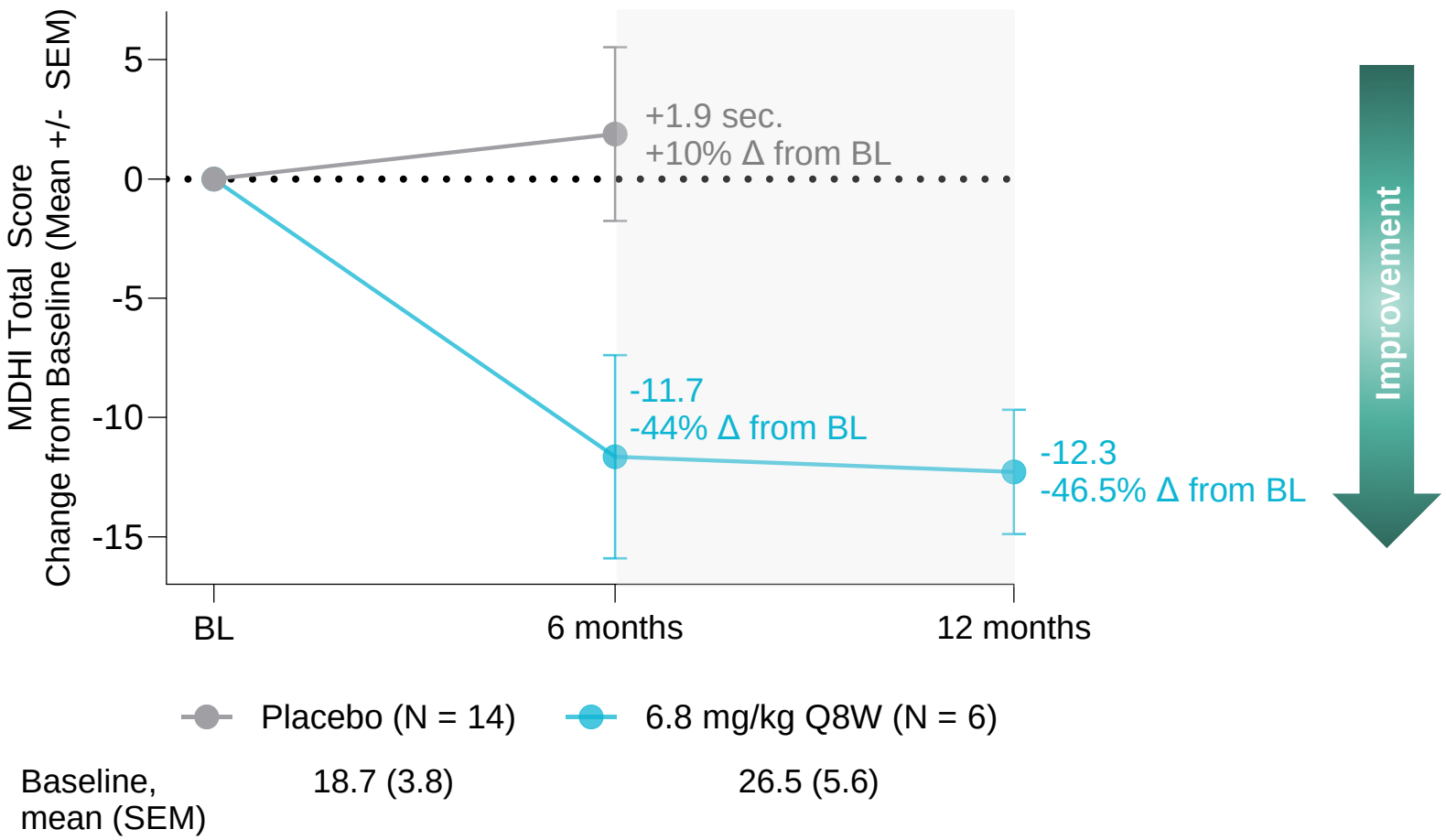


Baseline (sec), mean (SEM)	**9.2 (0.5)**	**10.0 (1.4)**

SEM = standard error of the mean; BL = baseline; 3 months = 85 days; 6 months = 169 days; 12 months = 337 days.

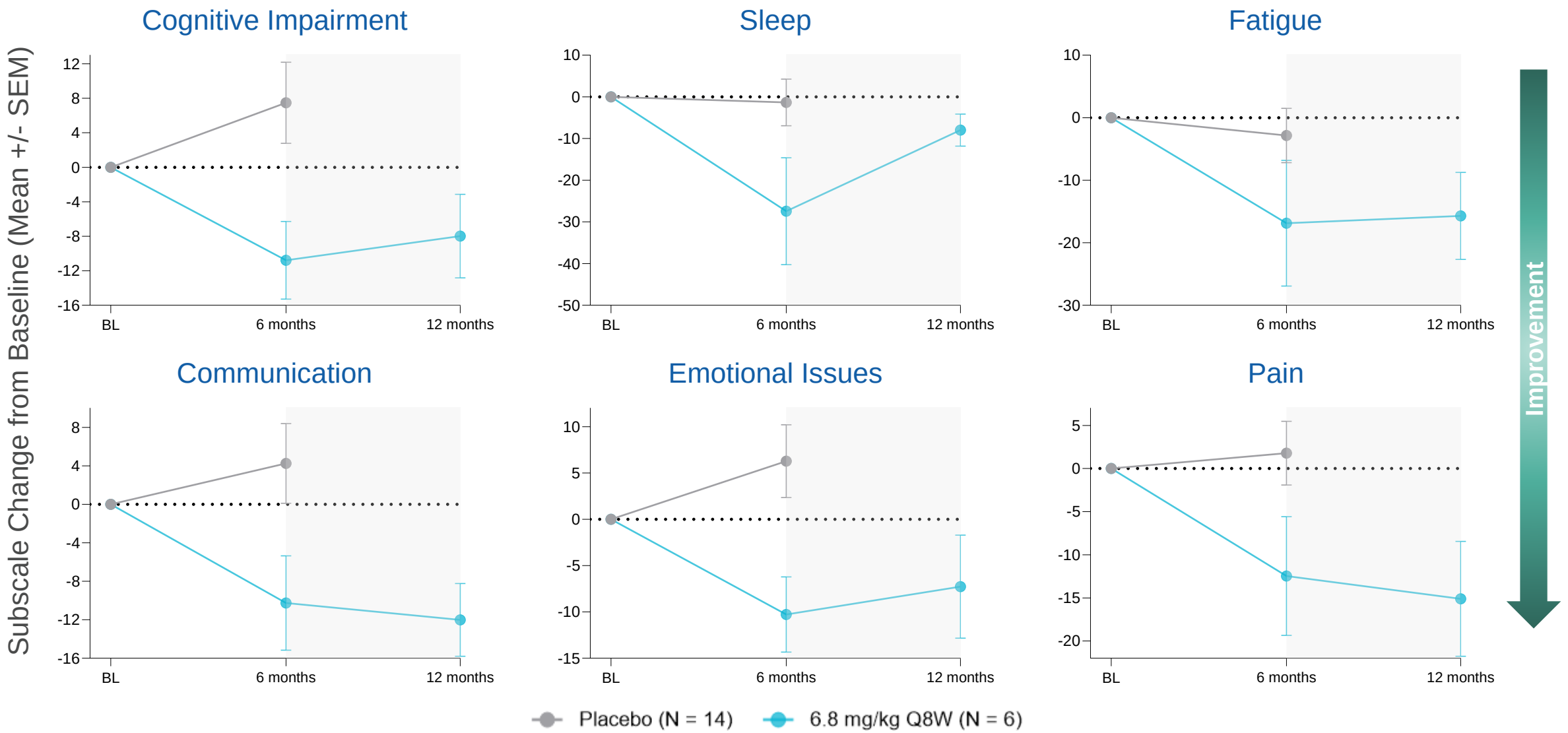
Deep Improvement in Patient Reported Outcome Sustained at 6 and 12 Months

Myotonic Dystrophy Health Index (MDHI) Total Score



SEM = standard error of the mean; BL = baseline; 3 months = 85 days; 6 months = 169 days; 12 months = 337 days.

Sustained Improvement in CNS-related MDHI Subscales Over Time



SEM = standard error of the mean; BL = baseline; Patient-reported outcomes (PRO) including Myotonic Dystrophy Health Index (MDHI) collected at baseline, 6 months (169 days) and 12 months (337 days).

New Data Support the Potential for Accelerated Approval of DYNE-101 with vHOT as Primary Endpoint

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DYNE-101 Outcomes

- Data support improvement in vHOT as early indicator of clinical benefit with DYNE-101
- Sustained improvements increase confidence in 6-month results

DYNE-101 Safety Data

- Favorable safety profile[1]

1. Safety data as of April 23, 2025; vHOT = video hand opening time.

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%)	10 (63%)	3 (38%)	6 (75%)	6 (75%)	34 (61%)
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 (41%)
  - Procedural pain (34%)
  - Influenza (30%)
  - Infusion-related reaction (29%)
  - Headache (27%)
  - Diarrhea (23%)

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

~1000 Doses of Study Drug Administered to Date Representing 93 Patient-Years of Follow-Up[1]

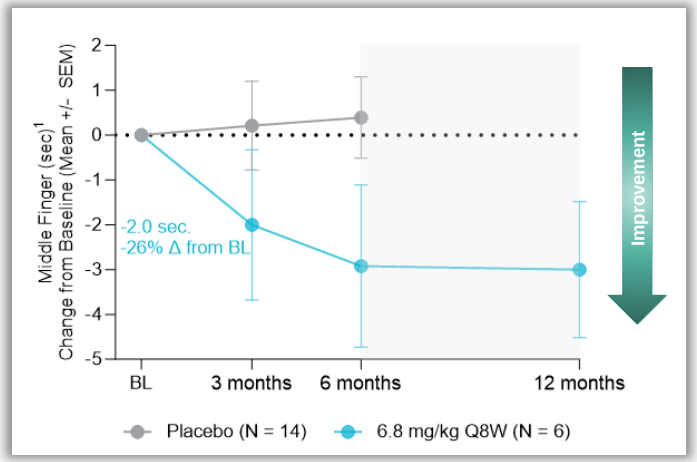
1. Data as of April 23, 2025; 2. Transient worsening of atrioventricular (AV) block in a participant with ongoing medical history of first-degree AV block; 3. Attributed to risk factors for pulmonary embolism; 4. All cohorts combined; preferred terms are reported.

vHOT is the Primary Endpoint to Support Potential Accelerated Approval of DYNE-101

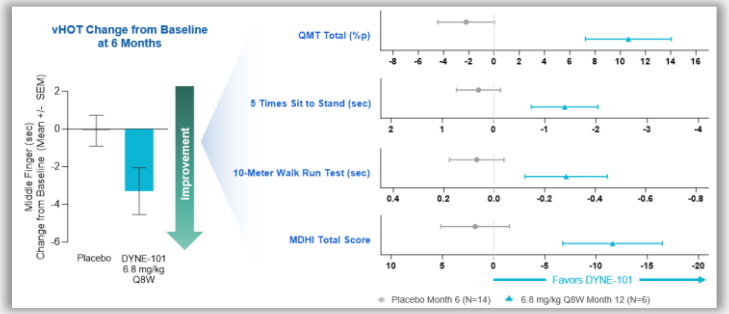
Myotonia is an early and common sign of DM1

Myotonia	
First symptom[1]	38.3%
Prevalence[2]	88%

DYNE-101 has demonstrated robust improvement in vHOT as early as 3 months



Data support vHOT as early indicator of clinical benefit with DYNE-101



1. Hilbert JE, et al. *J Neurol* 2013;260:2497-2504. N = 679 people with DM1 enrolled in the US National Registry.
2. Hagerman KA, et al. *Muscle Nerve* 2019;59:457-464. Data from the Christopher Project. N = 457 for DM1.
DM1 = myotonic dystrophy type 1; vHOT = video hand opening time; SEM = standard error of the mean.

Comprehensive Development Program for DYNE-101 in DM1

ACHIEVE

Demonstrated Proof of Concept in MAD and LTE

- ✓ Selected registrational dose of 6.8 mg/kg Q8W
- ✓ Data support vHOT improvement as early indicator of clinical benefit with DYNE-101
- ✓ Potential best-in-class profile across myotonia, strength, timed function tests, and patient reported outcomes, including CNS-related
- ✓ Favorable safety profile[1]; no serious related TEAEs

Registrational Expansion Cohort to Support U.S. Accelerated Approval

- 60 participants (3:1); 6.8 mg/kg Q8W
- Primary endpoint: Change from baseline in middle finger myotonia as measured by vHOT at 6 months, compared to placebo
- Secondary endpoints include: CASI-22, QMT, 10MWR, 5xSTS, and MDHI at 6 months
- Updated protocol submitted to FDA
- Enrollment completion planned for Q4 2025
- Data planned for mid-2026 to support potential U.S. Accelerated Approval submission in late 2026

Planned Phase 3 Study

- Planning to initiate confirmatory Phase 3 clinical trial in Q1 2026
- Ongoing engagement with global regulators to finalize trial design

1. Safety data as of April 23, 2025; DM1 = myotonic dystrophy type 1; MAD = multiple ascending dose; LTE = long term extension; CASI-22 = composite alternative splicing index; vHOT = video hand opening time; 10MWR = 10-meter walk/run test; QMT = quantitative muscle testing; 5xSTS = 5 times sit to stand test; MDHI = myotonic dystrophy health index.

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Summary

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Building Momentum Toward Two Potential Launches in 2027

DYNE-101 for DM1		**DYNE-251** for Exon 51 DMD	
Q4 2025	Complete enrollment planned for Registrational Expansion Cohort	**Q1 2025**	Completed enrollment of Registrational Expansion Cohort ✓
Mid-2026	Data planned for Registrational Expansion Cohort	**Late 2025**	Data planned for Registrational Expansion Cohort
Late 2026	Potential submission for U.S. Accelerated Approval	**Early 2026**	Potential submission for U.S. Accelerated Approval
2027	Potential U.S. launch	**2027**	Potential U.S. launch ***1st potential launch for Dyne***

DM1 = myotonic dystrophy type 1; DMD = Duchenne muscular dystrophy.

Aiming to Deliver Functional Improvement for People Living with Neuromuscular Diseases

LATE-STAGE PIPELINE	Two clinical programs in registrational 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 $677.5 million (as of 3/31/25) with expected runway into Q4 2026; all assets fully owned

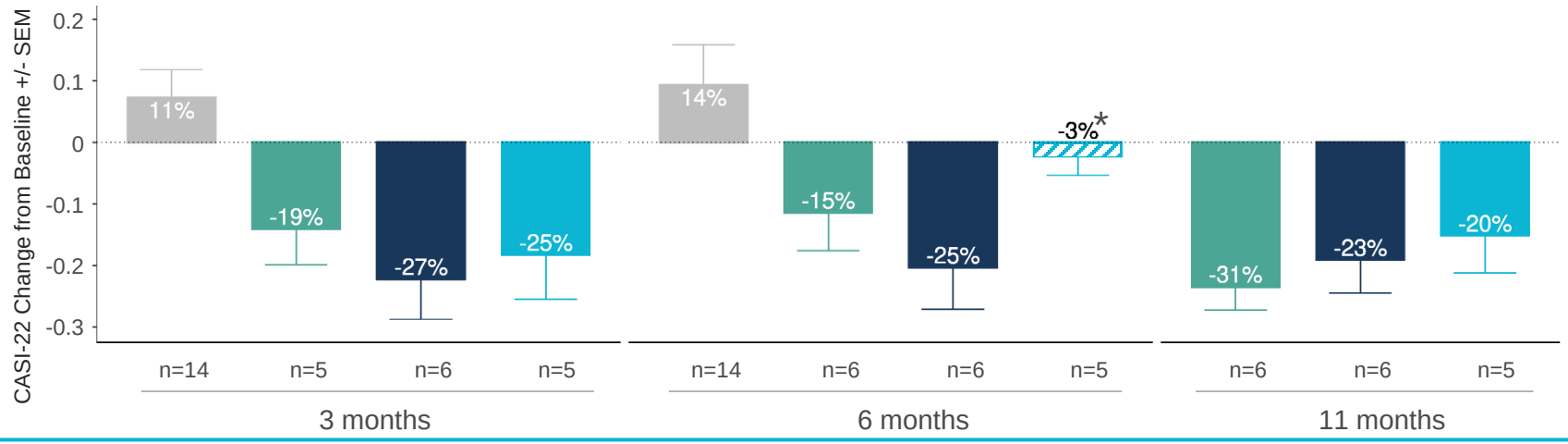
DM1 = myotonic dystrophy type 1; DMD = Duchenne muscular dystrophy; FSHD = facioscapulohumeral muscular dystrophy.

Q&A

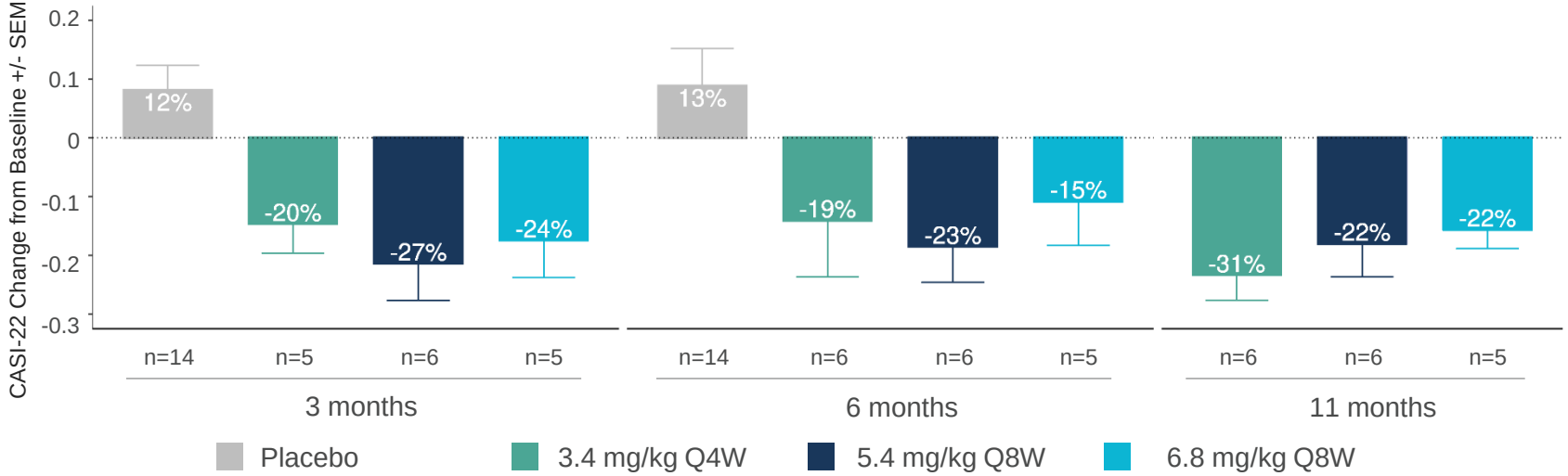
Appendix

Consistent Splicing Correction Maintained Through Month 11

Single aliquot
(original approach)



**Median of multiple aliquots
(revised approach)**



Splicing Improvement

Note: One post-baseline sample in 3.4 mg/kg Q4W and one baseline sample in 6.8 mg/kg treatment groups not included within splicing assay as the sample did not meet QC criteria; Percent values in bars represent percent mean change, calculated as mean change from baseline divided by baseline mean; Single aliquot approach takes valid result from aliquot of highest quality based on visual inspection of tissue samples; In multiple aliquot approach, all aliquots are tested and median taken across those with valid results, up to 4. CASI-22 = composite alternative splicing index; SEM = standard error of the mean; 3 months = 85 days; 6 months = 169 days; 11 months = 309 days.
* Data confounded by missing baseline data and intra-patient sample variability.

ACHIEVE Baseline Participant Characteristics: By Treatment

Mean (SD)	Placebo (N=14)	1.8 mg/kg Q4W (N=6)	3.4 mg/kg Q4W (N=6)	5.4 mg/kg Q8W (N=6)	6.8 mg/kg Q8W (N=6)
Age (years)	32.6 (9.6)	37.0 (10.5)	31.2 (4.4)	40.2 (6.5)	37.2 (9.7)
BMI (kg/m^2)	24.4 (4.7)	21.6 (5.8)	21.1 (1.8)	21.4 (2.5)	23.4 (5.6)
CASI-22	0.68 (0.20)	0.64 (0.25)	0.75 (0.12)	0.82 (0.16)	0.74 (0.25)
CTG Repeats	597 (246)	303 (163)	652 (258)	482 (236)	542 (191)
vHOT (sec) (middle finger)	7.5 (3.0)	11.3 (4.4)	6.6 (3.9)	11.9 (5.7)	7.8 (3.8)
QMT Total (% predicted)	51.5 (14.3)	48.1 (10.6)	42.0 (12.6)	46.6 (17.7)	51.3 (10.4)
10MWR (sec)	3.34 (0.48)	3.39 (0.55)	3.48 (0.67)	5.1 (2.40)	3.94 (1.56)
5 Times Sit to Stand (sec)	9.24 (2.03)	9.47 (2.04)	8.75 (1.88)	12.78 (6.79)	9.98 (3.33)
DM1-ACTIV^c Total	47 (3.82)	46 (4.59)	38 (4.65)	44 (6.99)	43.4 (5.23)
MDHI Total	18.7 (13.8)	23.5 (23.2)	30.2 (23.2)	14.8 (7.4)	26.5 (13.7)