FUNCTIONAL IMPROVEMENT

MOVING BEYOND DYSTROPHIN IN DMD

Dyne® THERAPEUTICS

Speakers

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Disclosures

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- Compensation for ad hoc advisory boards/consulting activity with Biogen, Novartis, Sarepta Therapeutics, PTC Therapeutics, Scholar Rock, Pfizer, Catalyst, Lupin, Santhera, Entrada Therapeutics, Avidity, Solid, Regenxbio, Insmed, Keros, Precisionbio, Gruenenthal, Mesoblast, Dyne Therapeutics, and Italfarmaco
- Associate Editor – Muscle and Nerve

Susan Apkon

- Site PI for Dyne Therapeutics, Capricor, Sarepta Therapeutics, Satellos, Biohaven, ScholarRock, Biogen

Agenda

Session Title	Speaker
Unmet needs in DMD	Aravindhan Veerapandiyan 
Resetting expectations for functional improvement	
DELIVER trial data: functional outcomes in focus	Susan Apkon 
Moving the needle in DMD	
Audience Q&A and close	Aravindhan Veerapandiyan

Unmet needs in DMD

Aravindhan Veerapandiyan, MD

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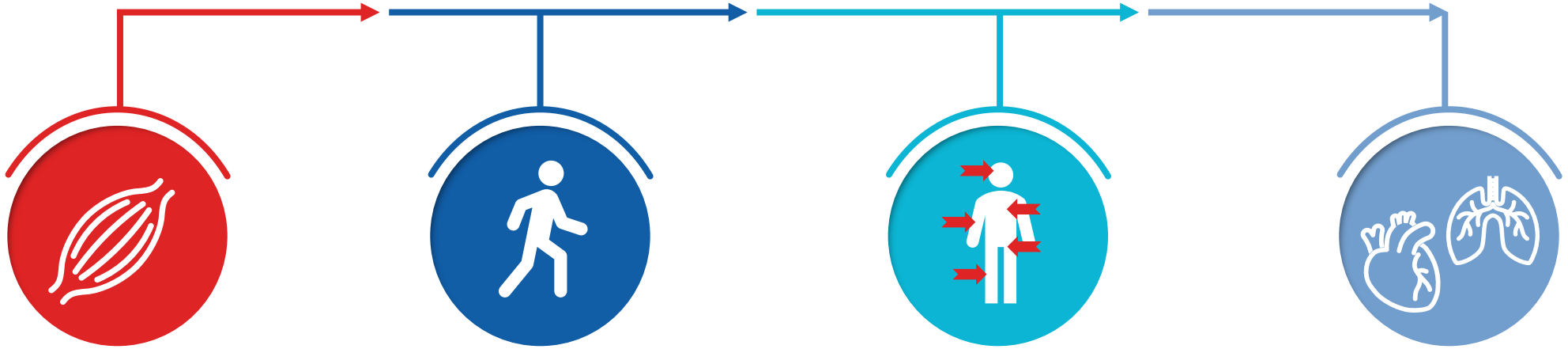
DMD is caused by dystrophin deficiency and manifests as a progressive multisystem disease, affecting muscle and the CNS

Greatly reduced or absent dystrophin protein expression[1]



Muscle weakness and gait abnormalities[2]

Progressive loss of upper and lower limb strength and function[2]

Multisystem involvement that affects skeletal, including pulmonary, smooth, and cardiac muscles and the CNS[3]

Cardiopulmonary failure as the leading cause of death[4]

CNS, central nervous system; DMD, Duchenne muscular dystrophy.

1. de Feraudy Y, et al. *Ann Neurol.* 2021;89:280–292; 2. Bushby K, et al. *Lancet Neurol.* 2010;9:77–93; 3. Ohlendieck K, Swandulla D. *Pflügers Arch.* 2022;473:1813–1839; 4. Birnkrant DJ, et al. *Lancet Neurol.* 2018;17:251–267.

Therapeutic approaches in DMD have evolved from supportive care to targeted approaches

Supportive standard of care[1–3]

~1990s[2]

- Corticosteroid therapy[1,2]
- Multidisciplinary management[3,4]

Dystrophin-producing therapies[1,2]

2016*

Exon skipping therapy[2]

- RNA-level dystrophin restoration

Gene therapy[1]

- Micro-dystrophin protein replacement

HDAC inhibitors[1]

2024[1]

- Target inflammation, fibrosis, muscle degeneration[5]

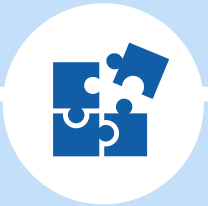
DMD, Duchenne muscular dystrophy; HDAC, histone deacetylase.
*The first exon skipping therapy was approved in 2016[2]; the first gene therapy was approved in 2023[1].

1. Komaki H. *Brain Dev*. 2025;47:104397; 2. D'Ambrosio ES, Mendell JR. *Neurotherapeutics*. 2023;20:1669–1681; 3. Bushby K, et al. *Lancet Neurol*. 2010;9:177–189; 4. Duan D, et al. *Nat Rev Dis Primers*. 2021;7:13; 5. Anjum AF, et al. *Curr Ther Res Clin Exp*. 2025;102:100787.

Despite progress, challenges remain with current treatments

Exon skipping and gene therapy

Dystrophin quantity and quality



- Low dystrophin expression levels[1]
  - <1% with approved exon 51 skipping therapy
- Micro-dystrophin functionality[1]
  - Shorter micro-dystrophin protein lacks key functional domains believed to support muscle health[2,3]

Effective distribution and durability of effect

- Limited delivery to muscle and the CNS[1,4]
- Modest clinical benefits with exon skipping[4]
- Unknown durability of effect with gene therapy[4]

All modalities

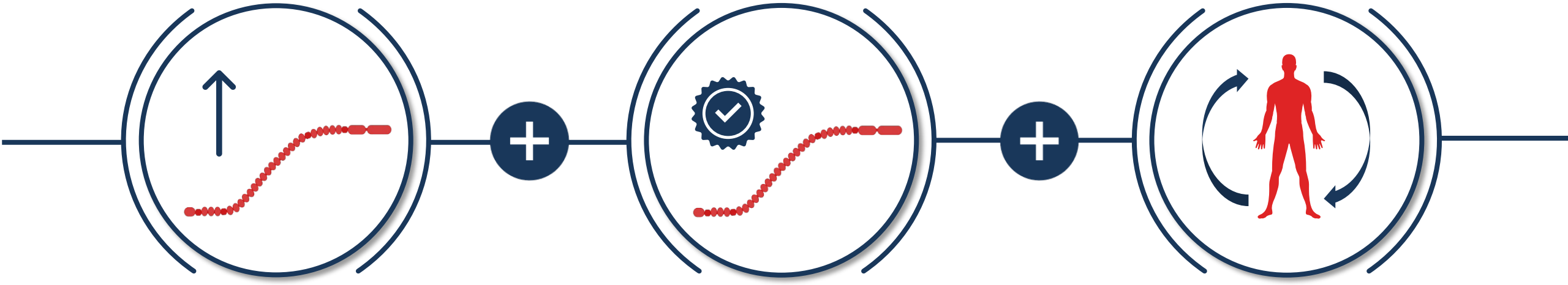
Treatment burden, safety, and access

- Access/clinical eligibility restrictions with gene therapy[4]
- Adverse events[1,5,6]
- Regular monitoring[5,7]
- Dosing
  - Inability to safely and effectively re-dose with gene therapy[1,8]
  - Frequent IV dosing with current exon skipping therapy[8]

CNS, central nervous system; IV, intravenous.

1. Chwalenia K, et al. *J Muscle Res Cell Motil*. 2025;46:293–300; 2. Harper S, et al. *Hum Mol Genet*. 2002;11:1807–1815; 3. Davies KE, Guiraud S. *Mol Ther*. 2019;27:486–488; 4. Gonzalez Castillo Z, et al. *J Transl Genet Genom*. 2025;9:338–351; 5. Montagna C, et al. *Int J Mol Sci*. 2025;26(:6742; 6. D'Ambrosio ES, Mendell JR. *Neurotherapeutics*. 2023;20:1669–1681; 7. Das P, et al. *Pharmacology*. 2025;110:1–13; 8. Komaki H. *Brain Dev*. 2025;47:104397.

Functional improvement in DMD requires therapeutic approaches that improve the quantity, quality, and distribution of dystrophin



Increased dystrophin production

Production of high-quality dystrophin

Broad and effective distribution of dystrophin restorative treatments to affected muscles and the CNS

Functional improvement

CNS, central nervous system; DMD, Duchenne muscular dystrophy.

Resetting expectations for functional improvement

Aravindhan Veerapandiyan, MD

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Dystrophin quantity, quality, and distribution underlies functional improvement in DMD

Beyond dystrophin: functional improvement in practice

- Preserving motor function and retaining independence are important to individuals with DMD and caregivers[1]
- Dystrophin deficiency manifests in a multisystemic manner – individuals can experience CNS, GI, bladder, cardiac, and respiratory manifestations[2]

Dystrophin: quantity, quality, and distribution

- Increased dystrophin production
- Production of high-quality dystrophin
- Broad and effective distribution of dystrophin restorative treatments to affected muscles (skeletal, smooth, and cardiac) and the CNS

CNS, central nervous system; DMD, Duchenne muscular dystrophy; GI, gastrointestinal.

1. Gillman A, et al. *Front Neurol. 2025;*16:1509174; 2. Ohlendieck K, Swandulla D. *Pflügers Arch.* 2022;473:1813–1839.

How is meaningful change in functional improvement defined?

In clinical trials…

MCID
Minimal clinically important difference

The smallest difference that reflects a change that is meaningful for an individual and would impact their healthcare management[1]

May be measured as:

- **Velocity** e.g. in 10MWR, 4SC, TTR, SV95C[2,3]
- **Points/score** e.g. in PUL, NSAA[4,5]

By those affected by DMD…

ADLs
Activities of daily living

Ability to perform ADLs, maintain independence, and participate in hobbies[6]

In qualitative evaluation of meaningful change on functional assessments:*

- Patients interpret change by tasks[6]
- A single point may reflect real functional loss[6]

*The study utilized a non-interventional, descriptive, cross-sectional qualitative design consisting of 69 semi-structured interviews with individuals with DMD and their caregivers, as well as two interviews with neuromuscular expert physiotherapists. NSAA and PUL were used to measure motor performance in ambulatory and non-ambulatory individuals, respectively.

10MWR, 10-meter walk/run; 4SC, 4 stair climb; ADL, activities of daily living; MCID, minimal clinically important difference; NSAA, North Star Ambulatory Assessment; PUL, performance upper limb; SV95C, stride velocity 95th centile; TTR, time to rise.

1. Cook CE, et al. *J Man Manip Ther*. 2008;16:E82–83; 2. Duong T, et al. *J Neuromuscul Dis*. 2021;8:939–48; 3. EMA Qualification Opinion. July 2023. Accessed February 16, 2026. https://www.ema.europa.eu/en/documents/scientificguideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf; 4. Naarding KJ, et al. *J Neuromuscul Dis*. 2022;9:555–569; 5. Ayyar Gupta V, et al. *PLoS One*. 2023;18:e0283669; 6. Gillman A, et al. *Front Neurol. 2025;*16:1509174.

Clinical measures can translate into meaningful outcomes for individuals with DMD

10MWR, 10-meter walk/run; 4SC, 4 stair climb; DMD, Duchenne muscular dystrophy; FVC%p, forced vital capacity percent predicted; LVEF, left ventricular ejection fraction; NSAA, North Star Ambulatory Assessment; PUL, performance upper limb; SV95C, stride velocity 95th centile; TTR, time to rise.

1. Arora H, et al. *Muscle Nerve.* 2018;58:631–638; 2. Servais L, et al. *Nat Med.* 2023;29:2391–2392; 3. McDonald CM, et al. *Lancet.* 2018;391:451–461; 4. Gillman A, et al. *Front Neurol.* 2025;16:1509174; 5. Lechner A, et al. *ERJ Open Res.* 2023;9:00176–2023; 6. Phillips MF, et al. *Am J Respir Crit Care Med.* 2001;164:2191–2194.

What are the treatment goals for individuals with DMD and their families?

Preserve daily function

- Maintain ability to walk, use arms and hands, and perform self-care[1,2]
- Delay loss of independence in school, work, and social life[1,2]
- Address under-recognized neurobehavioral symptoms that impact quality of life[3]

Protect vital organs

- Prevent or delay cardiomyopathy[4]
- Preserve breathing capacity[4]

Change the disease trajectory

- Delay irreversible milestones – loss of ambulation, need for ventilation, progressive heart and respiratory failure[1,4,5]

1. Brown V, et al. *J Patient Rep Outcomes*. 2023;7:129; 2. Gillman A, et al. *Front Neurol. 2025;*16:1509174; 3. Geuens S, et al. *J Neuromuscul Dis*. 2024;11:791–799; 4. Birnkrant DJ, et al. *Lancet Neurol.* 2018;17:251–267;
5. Duan D, et al. *Nat Rev Dis Primers*. 2021;7:13.

DELIVER trial data: Functional outcomes in focus

Susan Apkon, MD

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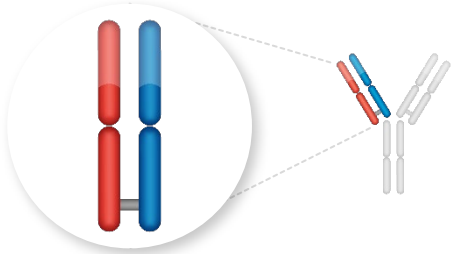
Zeleciment rostudirsen (z-rostudirsen or DYNE-251) leverages the FORCE™ platform for broad delivery of an exon 51-skipping PMO to tissues impacted by DMD

ANTIBODY

Proprietary Fab against TfR1 to enable targeted delivery to muscle and CNS

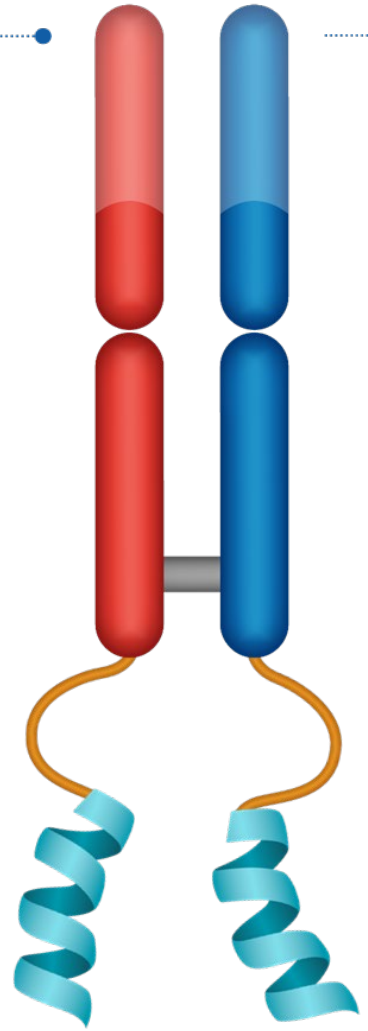


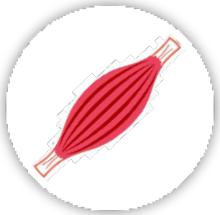
LINKER

Connects Fab and payload

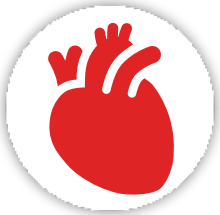
PAYLOAD

PMO designed to enable production of near full-length dystrophin





Skeletal (including diaphragm) and smooth muscle



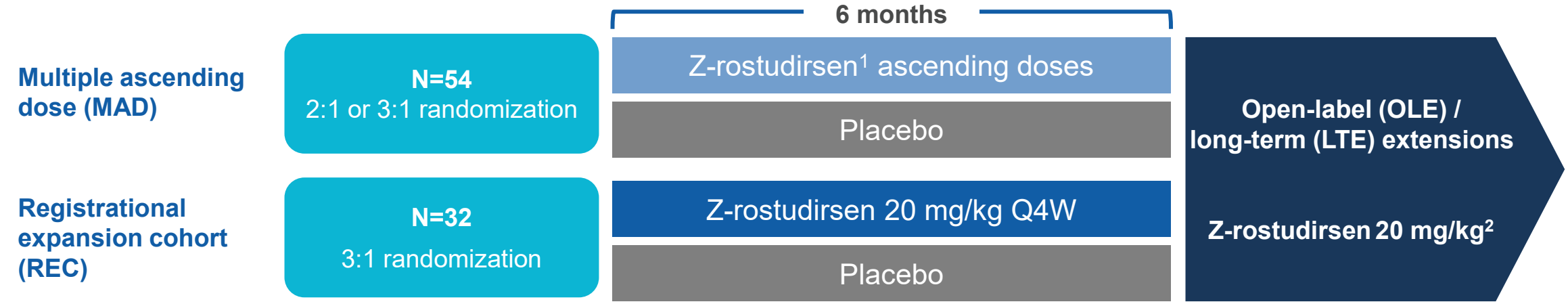
Cardiac muscle

CNS

Zeleciment rostudirsen (z-rostudirsen, also known as DYNE-251) is an investigational medicine or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Note: Figure depicts oligonucleotide payload. CNS, central nervous system; DMD, Duchenne muscular dystrophy; Fab, fragment antibody-binding; PMO, phosphorodiamidate morpholino oligomer; TfR1, transferrin receptor 1.

DELIVER study design

DELIVER (N=86)



Select inclusion/exclusion criteria

Inclusion criteria

- Ambulatory or non-ambulatory
- Age 4 to 16 years inclusive
- Stable dosage of glucocorticoids for at least 12 weeks

Exclusion criteria

- Exon-skipping/dystrophin-modifying therapy or givinostat within 12 weeks of randomization
- Gene therapy at any time

Endpoints

Primary endpoints

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

Key functional endpoints

- TTR velocity, 10MWR velocity, NSAA, SV95C, PUL2.0, FVC%p

Zeleciment rostudirsen (z-rostudirsen, also known as DYNE-251) is an investigational medicine or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

1. Z-rostudirsen doses in the MAD cohorts ranged from 0.7 mg/kg to 40 mg/kg every 4 or 8 weeks. 2. Transition to 20 mg/kg dose occurred at non-uniform times during OLE or LTE; for participants initiated at 40 mg/kg, transition started either in the placebo-controlled period or OLE.

10MWR, 10-meter walk/run; FVC%p, forced vital capacity percent predicted; NSAA, North Star Ambulatory Assessment; PUL2.0, performance upper limb v2.0; Q4W, every 4 weeks; SV95C, stride velocity 95th centile; TTR, time to rise.

Dyne Therapeutics. Positive Topline Results from Phase 1/2 DELIVER Trial of Zeleciment Rostudirsen (DYNE-251) in DMD to Support Potential U.S. Accelerated Approval. Available from: https://investors.dyne-tx.com/static-files/2e54fea2-98b4-44a4-acaf-6277e0ce965e.

DELIVER baseline participant characteristics were generally well balanced across cohorts

	Placebo (MAD+REC) N=24[5] Mean (SD) or n (%)	Z-rostudirsen			
		20 mg/kg Q4W (REC) N=24 Mean (SD) or n (%)	10 → 20 mg/kg[6] Q4W (MAD) N=6 Mean (SD) or n (%)	20 mg/kg Q4W (MAD) N=6 Mean (SD) or n (%)	Overall (MAD+REC) N=86 Mean (SD) or n (%)
Age (years)	8.2 (2.5)	7.8 (3.6)	6.8 (2.5)	7.7 (2.5)	8.3 (3.3)
BMI (kg/m^2)	19.8 (4.7)	17.6 (4.5)	17.9 (3.7)	17.5 (2.9)	18.7 (4.3)
Age of symptom onset (years)	3.4 (1.8)	2.5 (1.7)	3.0 (1.8)	2.0 (0.9)	2.8 (1.7)
Most recent corticosteroid dosing regimen, n (%)[1] Daily Other	 20 (83.3) 4 (16.7)	 20 (83.3) 4 (16.7)	 6 (100) 0	 6 (100) 0	 73 (84.9) 13 (15.1)
Duration of corticosteroid treatment (years)[2]	2.1 (2.4)	2.4 (2.5)	1.5 (2.0)	2.4 (2.2)	2.6 (2.6)
Prior DMD therapy, n (%) Eteplirsen Other	 4 (16.7) 2 (8.3)	 2 (8.3) 5 (20.8)	 0 0	 0 2 (33.3)	 15 (17.4) 15 (17.4)
PUL2.0 total score[3]	36.3 (4.0)	36.3 (5.0)	37.2 (5.9)	33.8 (3.5)	36.4 (4.2)
FVC%p	92.7 (17.6)	90.0 (22.2)	89.8 (22.7)	90.7 (11.2)	87.5 (19.2)
Ambulant (%)	19 (79.2)	21 (87.5)	5 (83.3)	6 (100)	75 (87.2)
TTR velocity (rise/sec)[4]	0.20 (0.10)	0.22 (0.12)	0.23 (0.06)	0.17 (0.14)	0.20 (0.1)
10MWR velocity (m/sec)[4]	2.0 (0.5)	1.8 (0.5)	2.5 (0.7)	1.5 (0.6)	1.9 (0.6)
NSAA total score[4]	21.6 (6.3)	20.6 (5.0)	26.6 (5.4)	15.0 (5.3)	20.6 (7.0)
SV95C (m/sec)[4]	1.7 (0.5)	1.5 (0.4)	2.0 (0.3)	1.4 (0.5)	1.6 (0.5)

Zelecirment rostudirsen (z-rostudirsen, also known as DYNE-251) is an investigational medicine or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
1. Most recent corticosteroid regimen refers to corticosteroid at time of randomization. 2. Cumulative duration of previous and most recent corticosteroid treatment at the time of randomization. 3. Missing values imputed.
4. Ambulant participants; out-of-threshold and/or missing values imputed. 5. All placebo participants pooled from MAD and REC. 6. Participants transitioned from 10 mg/kg Q4W to 20 mg/kg Q4W after 6 months.
10MWR, 10-meter walk/run; BMI, body mass index; DMD, Duchenne muscular dystrophy; FVC%p, forced vital capacity percent predicted; kg, kilogram; m, meter; MAD, multiple ascending dose; NSAA, north star ambulatory assessment; PUL2.0, performance upper limb v2.0; Q4W, every 4 weeks; REC, registrational expansion cohort; SD, standard deviation; SV95C, stride velocity 95th centile; TTR, time to rise.
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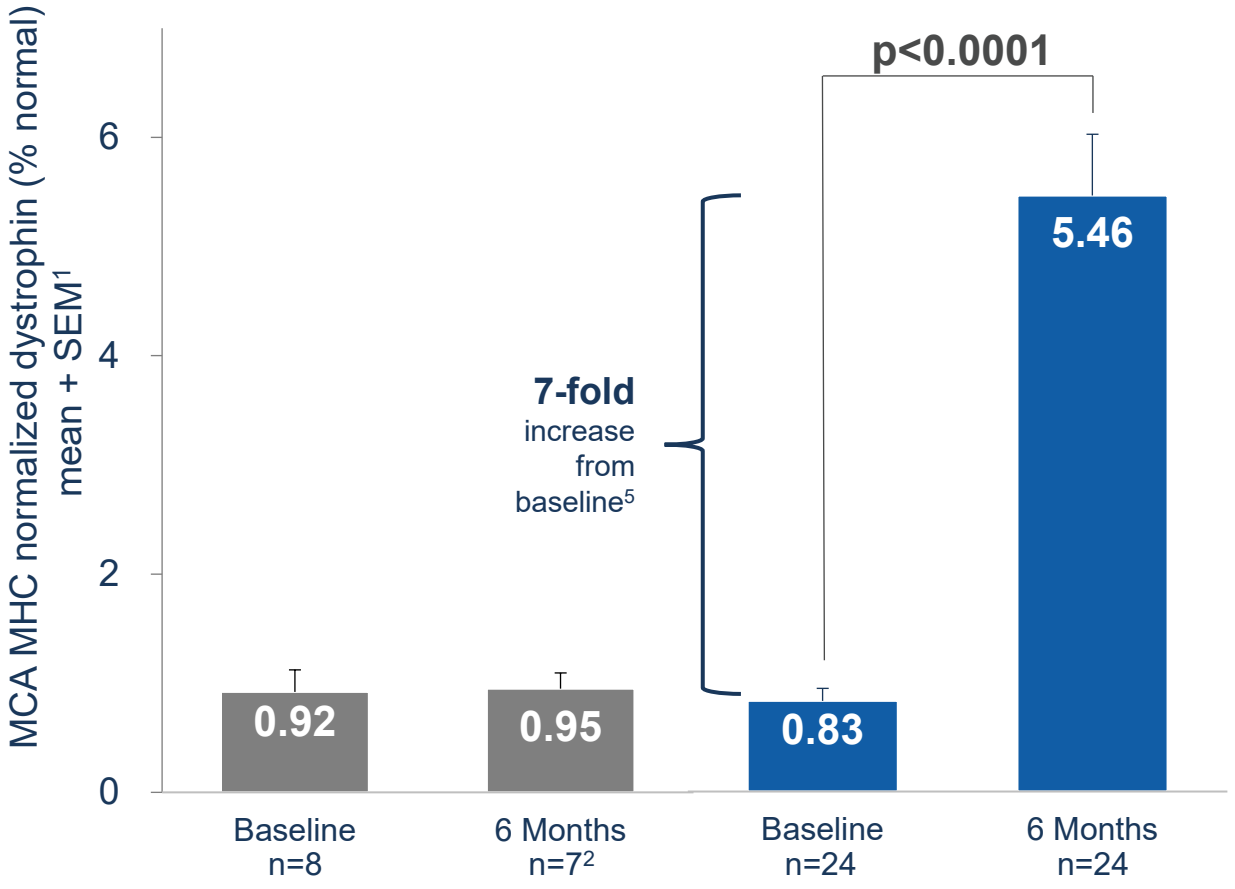
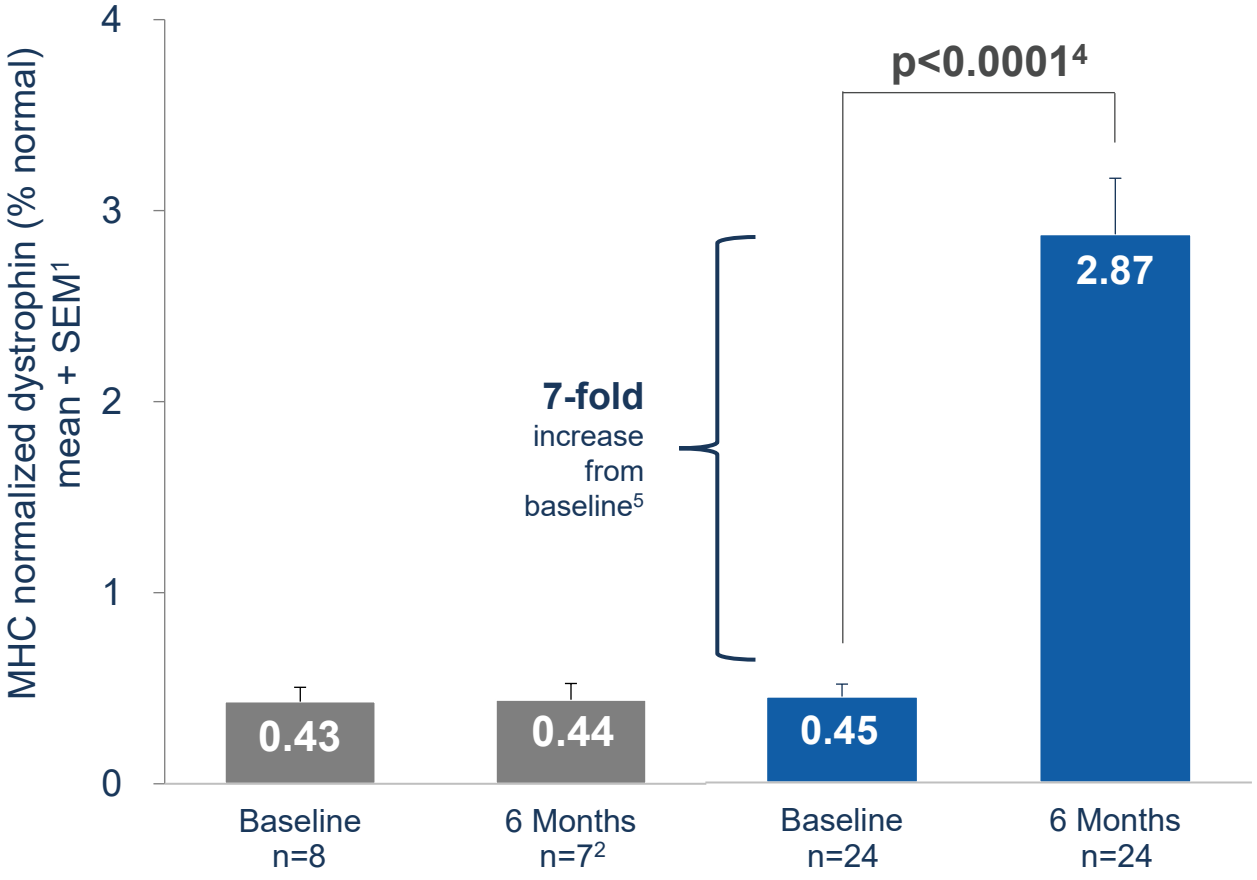
Dystrophin expression with z-rostudirsen relative to baseline at 6 months

Muscle content-adjusted dystrophin[3] (REC)



Unadjusted dystrophin (REC)



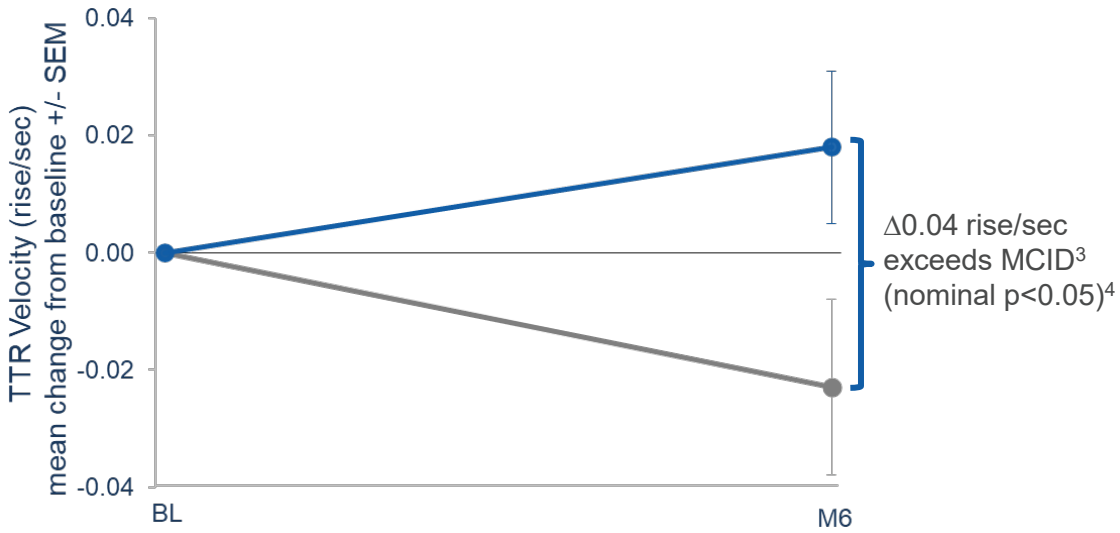
Placebo Z-rostudirsen 20 mg/kg Q4W (REC)

Zelecirnent rostudirsen (z-rostudirsen, also known as DYNE-251) is an investigational medicine or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

1. Biopsies taken approximately 28 days after most recent dose. 2. One REC placebo participant sample could not be analyzed at Week 25. 3. Muscle content-adjusted dystrophin = MHC normalized dystrophin / % muscle content.
4. Prespecified nominal p-value with no adjustment for multiplicity. 5. Based on geometric mean.
6 months = Week 25 for DELIVER. MCA, muscle content-adjusted; MHC, myosin heavy chain; Q4W, every 4 weeks; REC, registrational expansion cohort; SEM, standard error of the mean.
Dyne Therapeutics. Positive Topline Results from Phase 1/2 DELIVER Trial of Zelecirnent Rostudirsen (DYNE-251) in DMD to Support Potential U.S. Accelerated Approval. Available from: https://investors.dyne-tx.com/static-files/2e54fea2-98b4-44a4-acaf-6277e0ce965e.

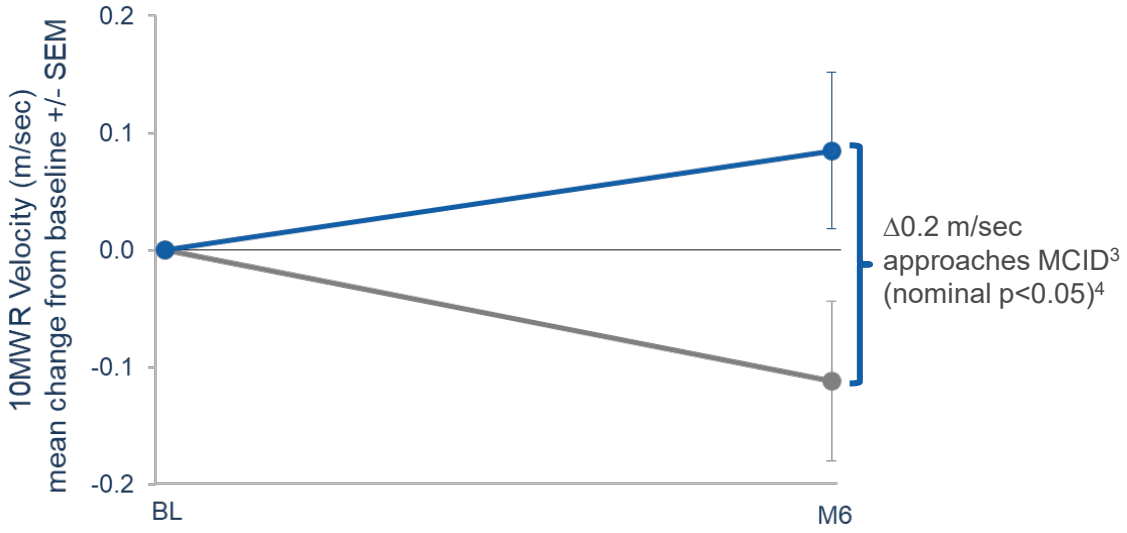
Increase in TTR velocity and 10MWR velocity at 6 months

Time to rise[1] (TTR) velocity[2]



Improvement

10-meter walk/run (10MWR) velocity[2]



Placebo (REC+MAD) (n=18)

Z-rostudirsen 20 mg/kg Q4W (REC) (n=21)

Placebo (REC+MAD) (n=18)

Z-rostudirsen 20 mg/kg Q4W (REC) (n=21)

Zelecimet rostudirsen (z-rostudirsen, also known as DYNE-251) is an investigational medicine or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

1. Also referred to as rise from floor (RFF). 2. Ambulant participants; out-of-threshold or missing values imputed. 3. Duong T et al. *J Neuromusc Dis.* 2021; 8(6):939–948; RFF velocity MCID = 0.023 rise/sec; 10MWR velocity MCID = 0.212 m/sec. 4. Post-hoc analysis; prespecified statistical analysis plan did not include formal hypothesis testing for any functional endpoint.

BL, baseline; M6 = 169 days; M, month; sec, seconds; SEM, standard error of mean; MCID, minimal clinically important difference; REC, registrational expansion cohort; MAD, multiple ascending dose; Q4W, every 4 weeks.

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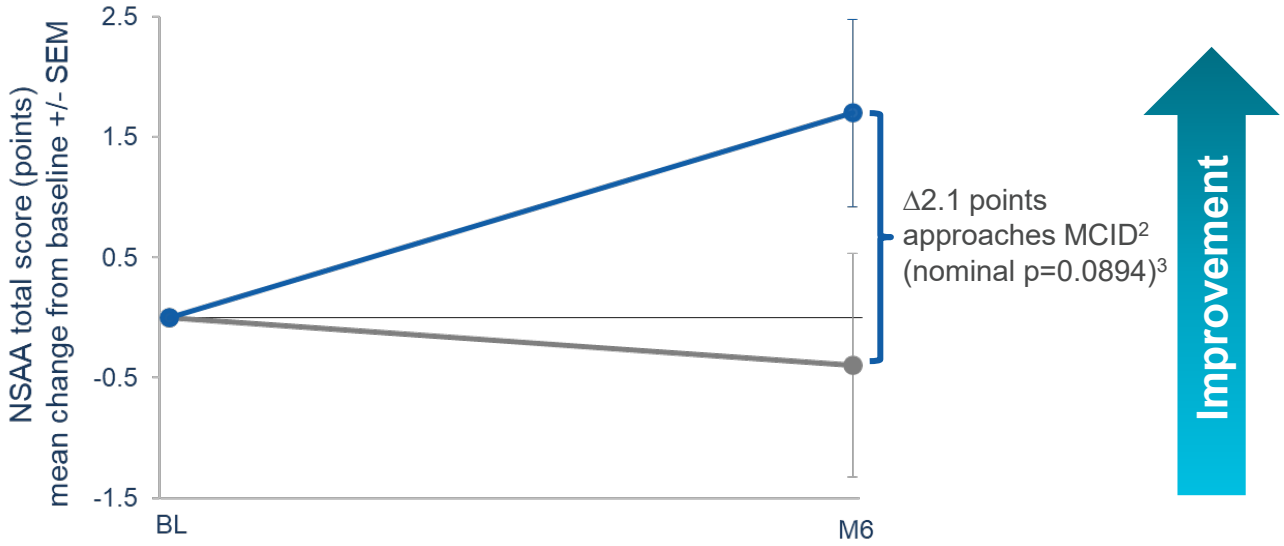
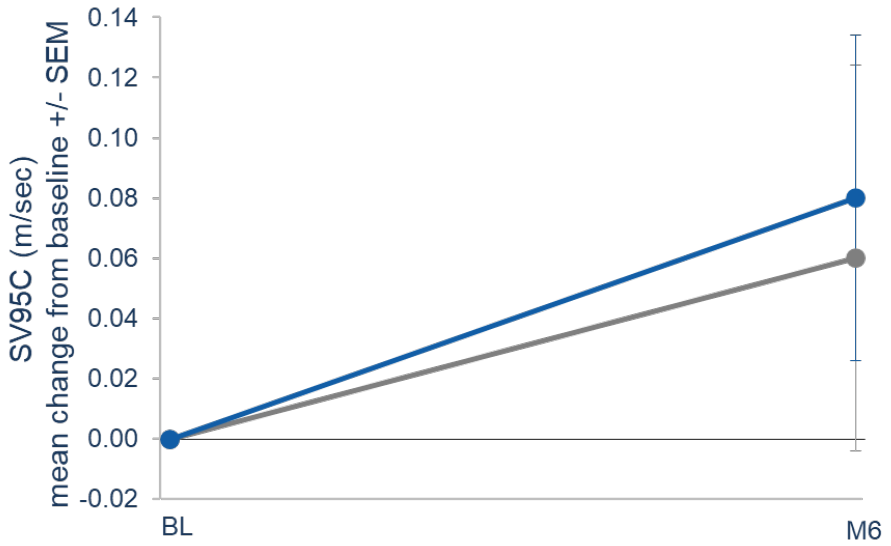
Increase in NSAA and SV95C at 6 months

North Star Ambulatory Assessment (NSAA)[1]



Stride Velocity 95th Centile (SV95C)[1]



Placebo (REC+MAD) (n=18)

Z-rostudirsen 20 mg/kg Q4W (REC) (n=21)

Placebo (REC+MAD)[4] (n=12)

Z-rostudirsen 20 mg/kg Q4W (REC) (n=20)

Zeleciment rostudirsen (z-rostudirsen, also known as DYNE-251) is an investigational medicine or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

1. Ambulant participants; missing values imputed. 2. Ayyar Gupta et al. *PLoS One*. 2023 Apr 26;18(4):e0283669; NSAA MCID ≥2.3 points. 3. Post-hoc analysis; prespecified statistical analysis plan did not include formal hypothesis testing for any functional endpoint. 4. Placebo impacted by single participant with change from baseline of 0.46 m/sec at 6M; if this participant were excluded, mean change from baseline at 6M for placebo would be approximately 0.02 m/sec. BL, baseline; M6 = 169 days; M, month; sec, seconds; SEM, standard error of mean; MCID, minimal clinically important difference; REC, registrational expansion cohort; MAD, multiple ascending dose; Q4W, every 4 weeks.

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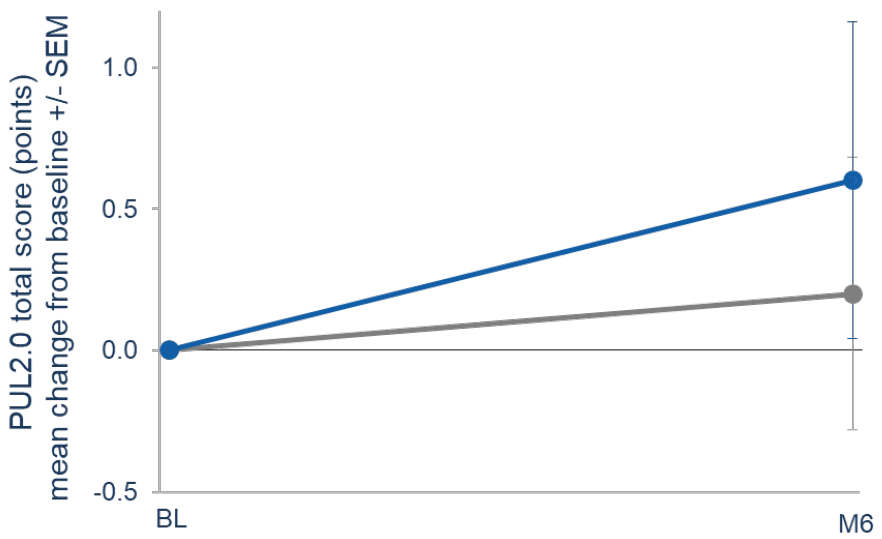
PUL2.0 and FVC%p at 6 months in ambulant and non-ambulant participants

Performance upper limb v2.0 (PUL2.0)[1]

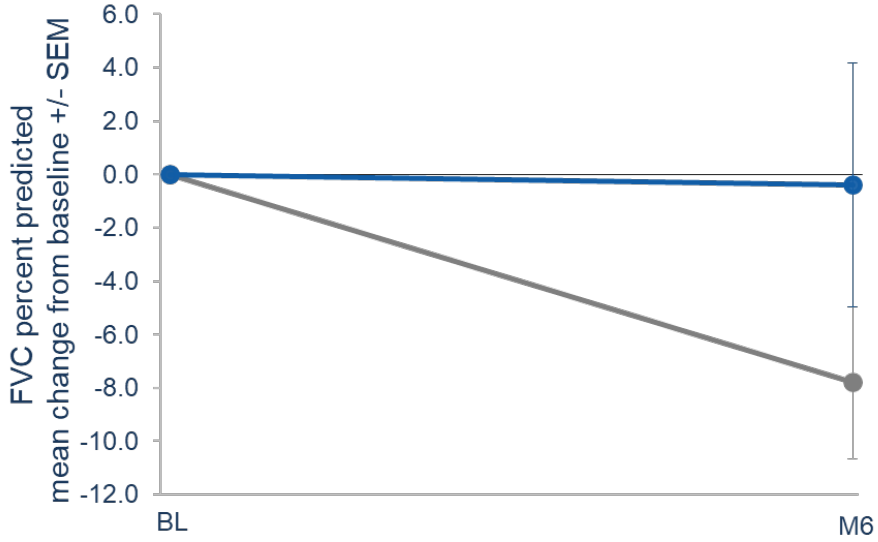


Placebo (REC+MAD) (n=23)

Z-rostudirsen 20 mg/kg Q4W (REC) (n=22)

Improvement

Forced vital capacity percent predicted (FVC%p)[1]



Placebo (REC+MAD) (n=20)

Z-rostudirsen 20 mg/kg Q4W (REC) (n=15)

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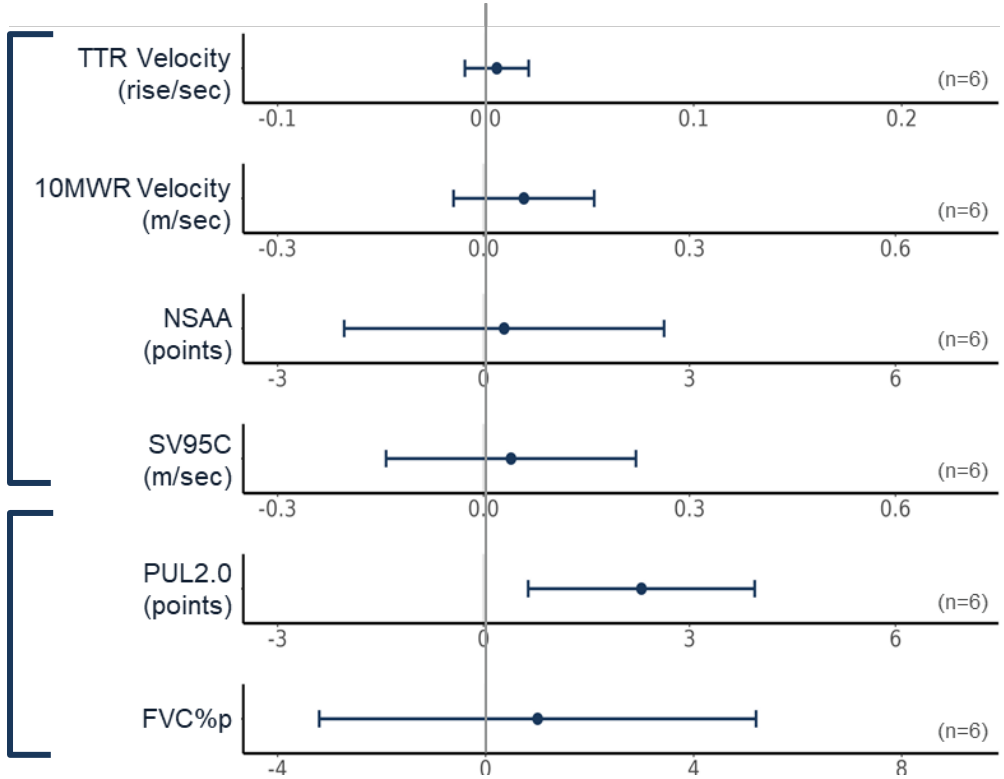
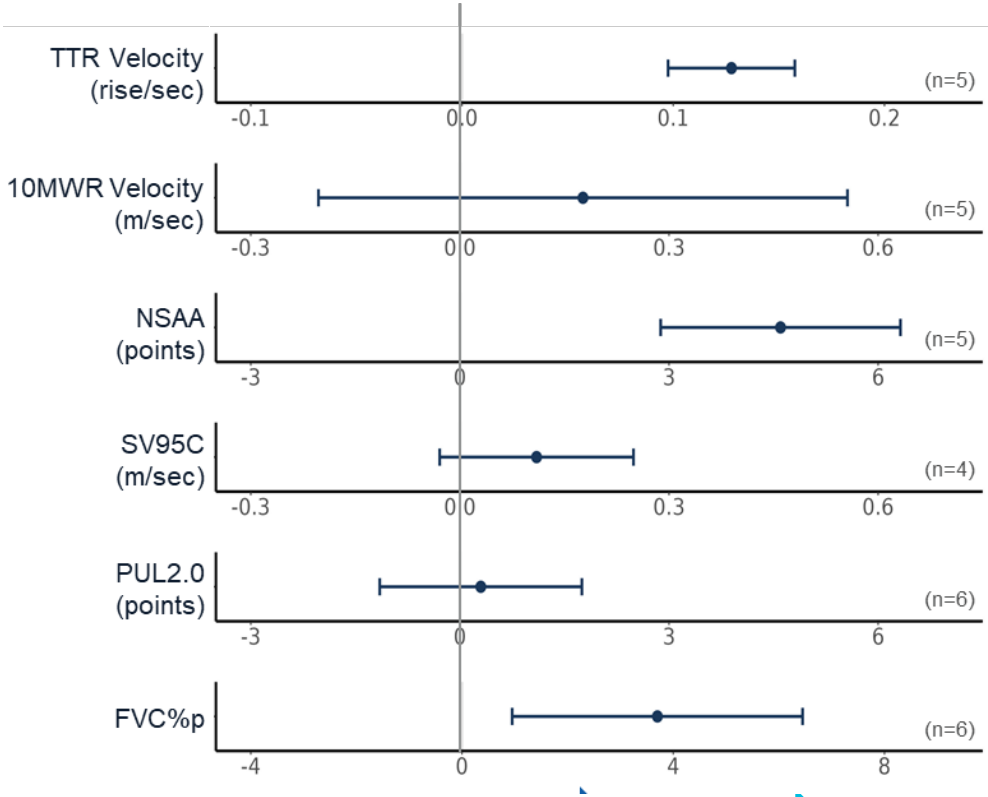
1. Ambulant and non-ambulant participants; missing values imputed for PUL2.0. BL, baseline; M6 = 169 days; M, month; sec, seconds; SEM, standard error of mean; REC, registrational expansion cohort; MAD, multiple ascending dose; Q4W, every 4 weeks.
Dyne Therapeutics. Positive Topline Results from Phase 1/2 DELIVER Trial of Zeleciment Rostudirsen (DYNE-251) in DMD to Support Potential U.S. Accelerated Approval. Available from: https://investors.dyne-tx.com/static-files/2e54fea2-98b4-44a4-acaf-6277e0ce965e.

Functional improvement compared with baseline across all 6 measures up to 24 months in the OLE/LTE

18-month CFB[1]
20 mg/kg Q4W
MAD Cohort



24-month CFB[1]
10 → 20 mg/kg Q4W[2]
MAD Cohort



Ambulatory participants

Ambulatory & non-ambulatory participants

Improvement

Improvement

Zeleciment rostudirsen (z-rostudirsen, also known as DYNE-251) is an investigational medicine or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

1. Mean change from baseline +/- SEM; TTR velocity, 10MWR velocity, NSAA, and SV95C analyzed from ambulant participants; PUL2.0 and FVC%p analyzed from ambulant and non-ambulant participants; Out-of-threshold and/or missing values imputed except for FVC%p.
2. Participants transitioned from 10 mg/kg Q4W to 20 mg/kg Q4W after 6M; all participants treated with 20 mg/kg Q4W for at least 12M in the 24M assessment. 10MWR, 10-meter walk/run; CFB, change from baseline; FVC%p, forced vital capacity percent predicted; LTE, long-term extension; m, meters; MAD, multiple ascending dose; NSAA, North Star Ambulatory Assessment; OLE, open-label extension; PUL2.0, performance upper limb v2.0; Q4W, every 4 weeks; sec, second; SEM, standard error of the mean; SV95C, stride velocity 95th centile; TTR, time to rise.
Dyne Therapeutics. Positive Topline Results from Phase 1/2 DELIVER Trial of Zeleciment Rostudirsen (DYNE-251) in DMD to Support Potential U.S. Accelerated Approval. Available from: https://investors.dyne-tx.com/static-files/2e54fea2-98b4-44a4-acaf-6277e0ce965e.

Summary of DELIVER data

Endpoint	Patient population	Muscle system	6-month functional improvement vs. placebo*	24-month functional improvement vs. baseline†
TTR velocity	Ambulatory	Trunk & lower limbs	✓	✓
10MWR velocity	Ambulatory	Lower limbs	✓	✓
NSAA	Ambulatory	Upper limbs, trunk & lower limbs	✓	✓
SV95C	Ambulatory	Lower limbs	✓	✓
PUL2.0	Ambulatory & non-ambulatory	Upper limbs	✓	✓
FVC%p	Ambulatory & non-ambulatory	Diaphragm & trunk	✓	✓

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*Reflects results from 6-month placebo-controlled Registrational Expansion Cohort of DELIVER trial with 20 mg/kg Q4W z-rostudirsen. Check mark represents numerically higher value relative to placebo. †Reflects 24-month results from the long-term portions of the DELIVER trial for participants who transitioned from 10 mg/kg Q4W to 20 mg/kg Q4W after 6M; all participants treated with 20 mg/kg Q4W for at least 12M in the 24M assessment. Check mark represents numerically higher value relative to baseline.

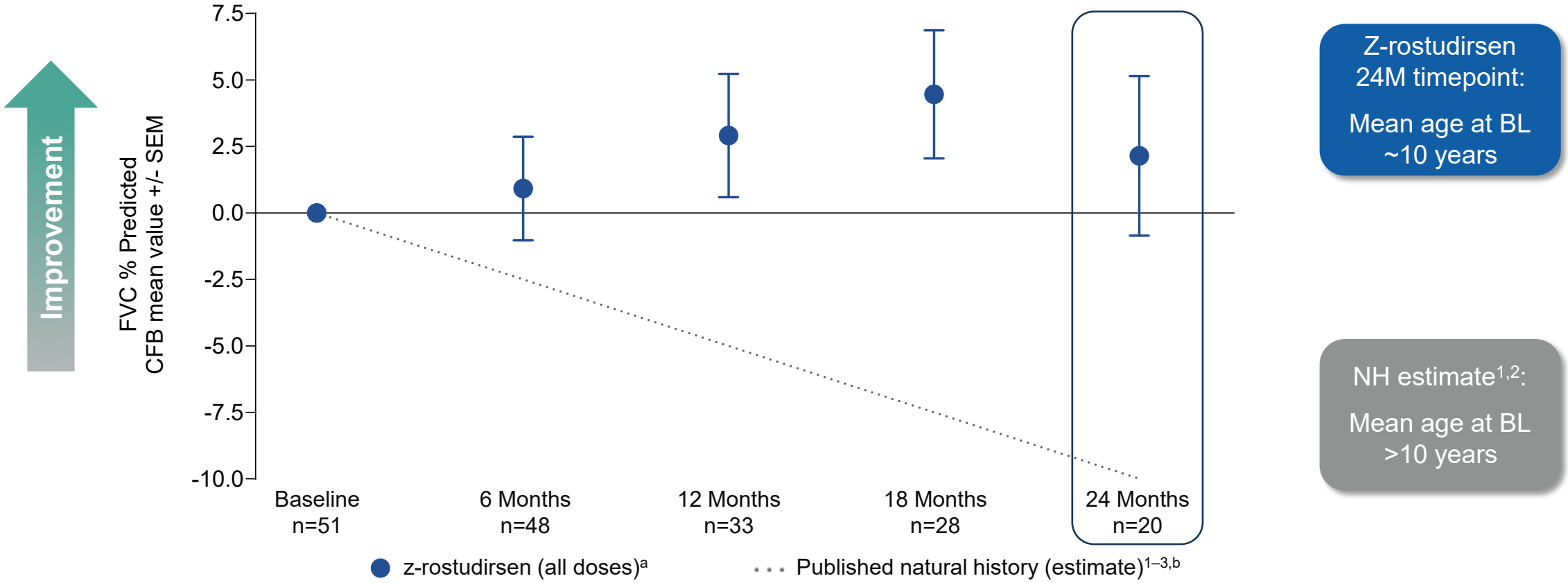
Considerations regarding dose escalation over time in a MAD study

Each timepoint represents a group of participants at varied dose levels and duration	
Dose levels	• Doses were escalated sequentially • Later timepoints included participants starting at low doses and who may have dose escalated through multiple doses
Dose duration	• Each timepoint reflects a group of participants with varying amounts of time on any specific dose

Considerations
• Most participants accrued substantial time on doses lower than 20 mg/kg Q4W prior to escalation • The observed long-term efficacy may not reflect the effect of continuously maintaining 20 mg/kg Q4W • There may be an underestimate of the true effect

MAD, multiple ascending dose; Q4W, every 4 weeks.

Long-term lung function with z-rostudirsen compared to published natural history data



Z-rostudirsen 24M timepoint:

Mean age at BL ~10 years

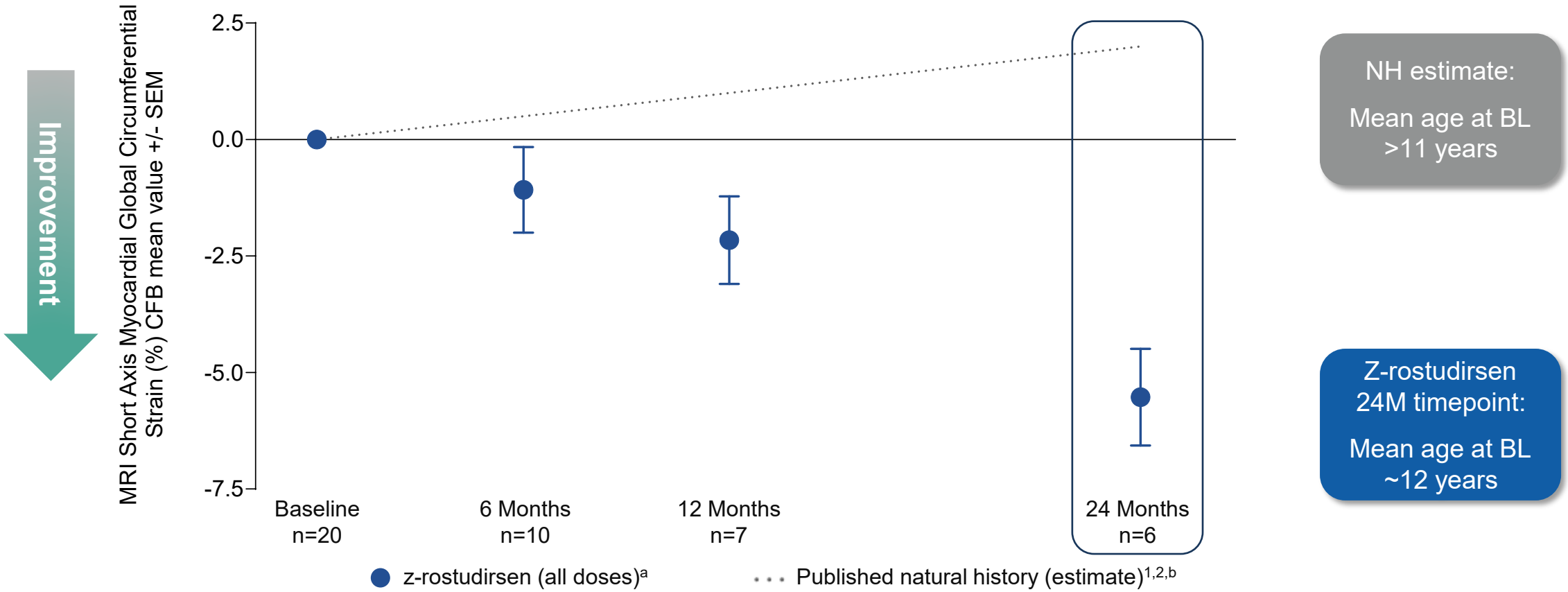
NH estimate[1,2]:

Mean age at BL >10 years

- The majority of participants at the 24M timepoint initiated treatment at the 0.7–2.8 mg/kg Q4W dose levels. One participant initiated treatment at 20 mg/kg Q4W
- All participants at the 24M timepoint received 20 mg/kg Q4W z-rostudirsen for ≥9 months

Results are reported as mean CFB through 24 months and presented with SEM.
a. Shown are all DELIVER participants (REC + MAD) randomized to z-rostudirsen treatment at baseline (any dose, including dose escalation[s] or de-escalation) and for whom FVC%p data were available. b. Based on 2-year published natural history data; assumes ~5%/year decline in FVC%p.
BL, baseline; CFB, change from baseline; FVC%p, forced vital capacity percent predicted; MAD, multiple ascending dose; NH, natural history; REC, registrational expansion cohort; SEM, standard error of the mean.
1. Mayer OH, et al. *Pediatr Pulmonol.* 2015;50:487–494; 2. McDonald CM, et al. *Neuromuscul Disord.* 2018;28:897–909; 3. Meier T, et al. *Neuromuscul Disord.* 2017;27:307–314.

CMR-based circumferential strain in z-rostudirsen-treated participants compared to published natural history data



NH estimate:

Mean age at BL >11 years

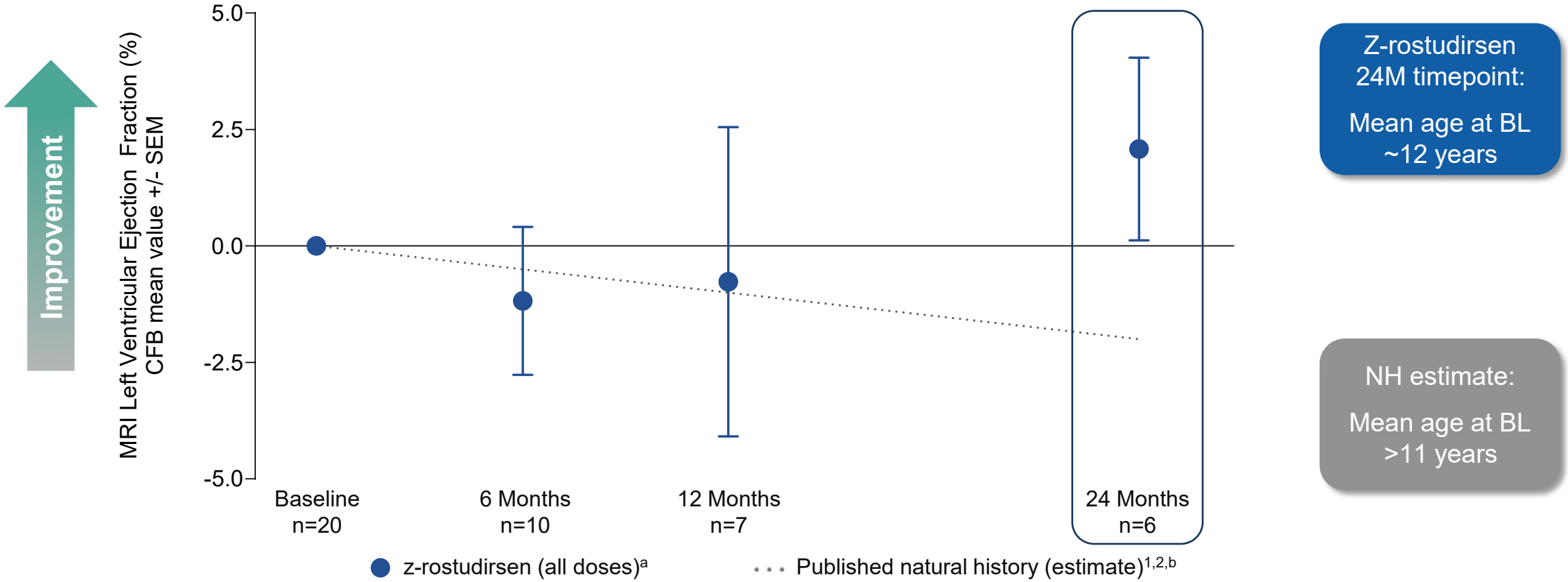
Z-rostudirsen 24M timepoint:

Mean age at BL ~12 years

- The majority of participants at the 24M timepoint initiated treatment at the 0.7–2.8 mg/kg Q4W dose levels. One participant initiated treatment at 20 mg/kg Q4W
- All participants at the 24M timepoint received 20 mg/kg Q4W z-rostudirsen for ≥6 months

Results are reported as mean CFB through 24 months and presented with SEM.
a. Shown are all DELIVER participants (REC + MAD) randomized to z-rostudirsen treatment at baseline (any dose, including dose escalation[s] or de-escalation) and for whom circumferential strain data were available. b. Based on 2-year published natural history data; assumes ~1%/year decline in strain.
BL, baseline; CFB, change from baseline; CMR, cardiac magnetic resonance; MAD, multiple ascending dose; MRI, magnetic resonance imaging; NH, natural history; REC, registrational expansion cohort; SEM, standard error of the mean.
1. Batra A, et al. *BMC Cardiovasc Disord.* 2022;22:260, *2.* Hagenbuch SC, et al. *Am J Cardiol.* 2010;105:1451–1455.

CMR-based left ventricular ejection fraction in z-rostudirsen-treated participants compared to published natural history data



Z-rostudirsen 24M timepoint:

Mean age at BL ~12 years

NH estimate:

Mean age at BL >11 years

- The majority of participants at the 24M timepoint initiated treatment at the 0.7–2.8 mg/kg Q4W dose levels. One participant initiated treatment at 20 mg/kg Q4W
- All participants at the 24M timepoint received 20 mg/kg Q4W z-rostudirsen for ≥6 months

Results are reported as mean CFB through 24 months and presented with SEM.
a. Shown are all DELIVER participants (REC + MAD) randomized to z-rostudirsen treatment at baseline (any dose, including dose escalation[s] or de-escalation) and for whom left ventricular ejection fraction data were available.
b. Based on 2-year published natural history data; assumes ~1%/year decline in LVEF.
BL, baseline; CFB, change from baseline; CMR, cardiac magnetic resonance; LVEF, left ventricular ejection fraction; MAD, multiple ascending dose; MRI, magnetic resonance imaging; NH, natural history; REC, registrational expansion cohort; SEM, standard error of the mean.
1. Batra A, et al. *BMC Cardiovasc Disord.* 2022;22:260, *2.* Hagenbuch SC, et al. *Am J Cardiol.* 2010;105:1451–1455.

Safety profile of z-rostudirsen 20 mg/kg Q4W

Summary of treatment-emergent adverse events (TEAEs)[1]

Study period	Placebo-controlled (PC) period (0 to 6M)		All study periods (0 to ≤36M)
Participants with ≥1 TEAE – n (%)	Placebo (MAD+REC) N=24[2]	Z-rostudirsen 20 mg/kg Q4W (MAD+REC) N=30[3]	Z-rostudirsen Pooled doses[4] (MAD+REC) N=85[5]
Any TEAE	22 (91.7)	29 (96.7)	80 (94.1)
Any related TEAE	3 (12.5)	10 (33.3)	41 (48.2)
Any serious TEAE	1 (4.2)	2 (6.7)	10 (11.8)
Any serious related TEAE	0	0	4 (4.7)
Any TEAE leading to withdrawal from study	0	0	0
Any TEAE leading to death	0	0	0

Most related TEAEs were mild or moderate

Potentially related serious TEAEs

- 2 participants at 20 mg/kg Q4W (registrational dose)
  - Pyrexia (fever) and malaise[6]
- 2 participants at 40 mg/kg Q4W
  - Acute kidney injury; thrombocytopenia[7]
  - Pancytopenia[8]

Most frequent related TEAEs ≥10%[9]

- Pyrexia (fever) (18%)
- Headache (13%)

Additional safety data at 20 mg/kg Q4W

- No participants have persistent related anemia[10] or thrombocytopenia

1,441 doses of z-rostudirsen administered to date representing 113 patient-years of follow-up (up to 36 months)[1]
1,062 doses of z-rostudirsen at 20 mg/kg dose level administered to date[1]

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1. Data as of August 19, 2025; all participants, placebo-controlled period, OLE, and LTE. 2. All placebo participants pooled from MAD and REC. 3. All participants randomized to z-rostudirsen 20 mg/kg Q4W in MAD and REC cohorts.
4. All doses of z-rostudirsen from MAD and REC at doses ranging from 0.7 mg/kg to 40 mg/kg every 4 or 8 weeks. 5. One participant randomized to placebo in REC not yet dosed with z-rostudirsen as of August 19, 2025. 6. One participant with same day onset of pyrexia and malaise in OLE and separate single event of pyrexia in LTE; one participant with single event of pyrexia in LTE; both participants fully recovered and have continued to receive z-rostudirsen without interruption. 7. Events had same day of onset in a single participant with a non-serious related TEAE of anemia in the context of fever, hemolysis, diarrhea, and positive blood in stool; together these events were consistent with hemolytic uremic syndrome with a possible infectious etiology. 8. Participant has a history of hemolytic anemia of unidentified etiology; presented with fever and tonsilitis; symptoms resolved without therapeutic intervention. 9. All cohorts combined; preferred terms reported. 10. No participants have persistent related anemia with Hgb levels <11.2 g/dL (threshold for anemia in children [ref: Powers JM. Approach to the child with anemia. UpToDate, Connor RF (Ed), Wolters Kluwer. Accessed December 2, 2025]).
Hgb, hemoglobin; LTE, long-term extension; M, months; MAD, multiple ascending dose; OLE, open-label extension; Q4W, every 4 weeks; REC, registrational expansion cohort; TEAE, treatment-emergent adverse event.
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Summary

Investigational z-rostudirsen appears to show broad multisystem functional improvement in clinical measures across muscles of the upper and lower limb, the trunk, and cardiac and pulmonary muscles

The DELIVER REC met the primary endpoint, demonstrating a statistically significant increase in mean muscle content-adjusted dystrophin at 6 months compared with baseline

At 6 months, functional improvement was observed across multiple measures of muscle strength and function relative to baseline and placebo, including TTR velocity, 10MWR velocity, NSAA, and PUL2.0

Functional improvement was also seen over the longer term (up to 24 months) across these clinical measures, including measures of cardiac and pulmonary function

Z-rostudirsen demonstrated a favorable safety and tolerability profile based on data from 86 participants enrolled in DELIVER and followed for up to 36 months[1]

Data from the DELIVER trial support the potential of z-rostudirsen to address the unmet needs of individuals with DMD pathogenic variants amenable to exon 51 skipping

Zeleciment rostudirsen (z-rostudirsen, also known as DYNE-251) is an investigational medicine or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

1. Data as of August 19, 2025.

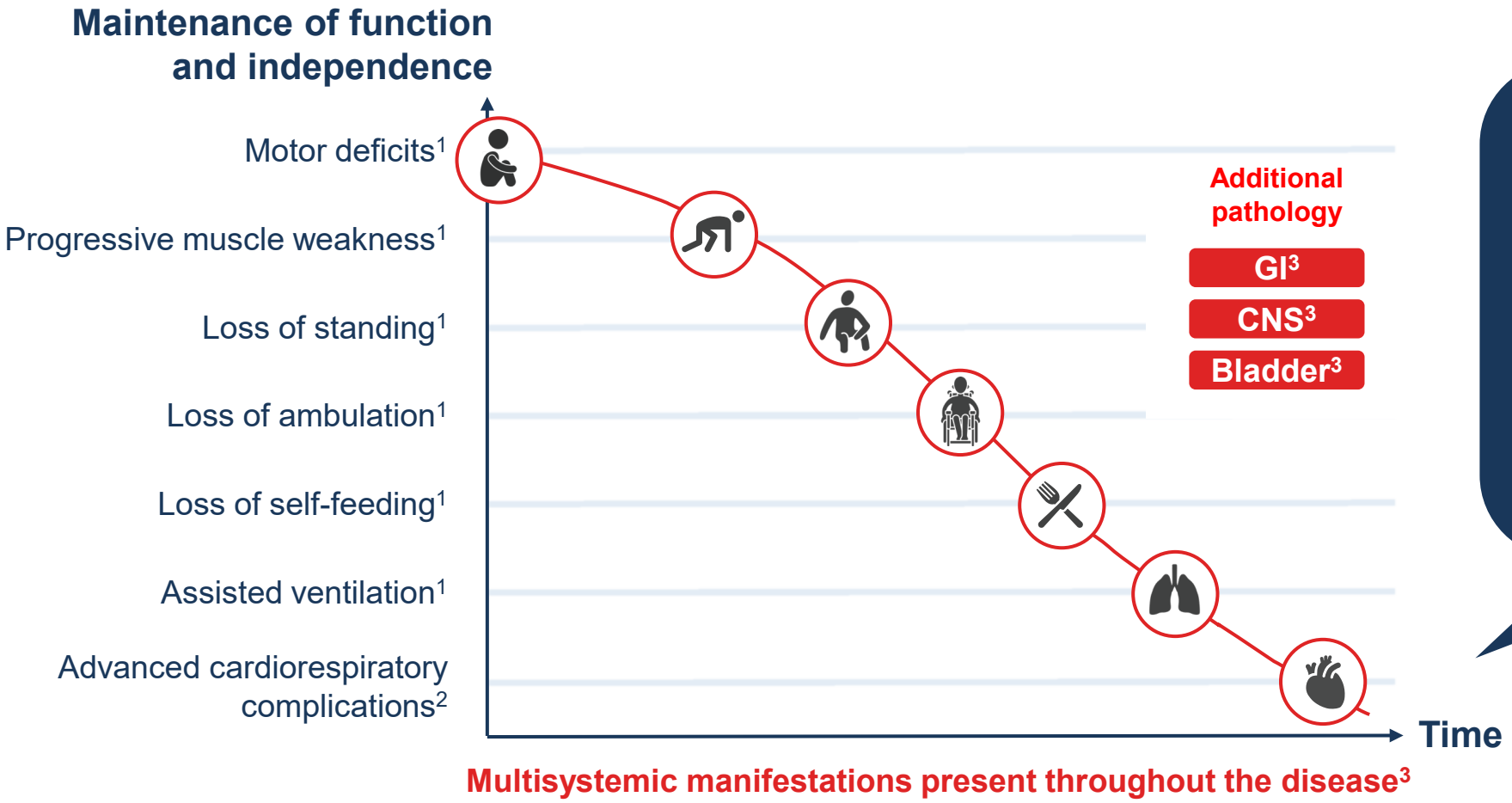
10MWR, 10-meter walk/run; DMD, Duchenne muscular dystrophy; NSAA, North Star Ambulatory Assessment; PUL, performance upper limb; REC, registrational expansion cohort; TTR, time to rise.

Moving the needle in DMD

Susan Apkon, MD

Dyne THERAPEUTICS

DMD is a multisystemic disease of progressive losses



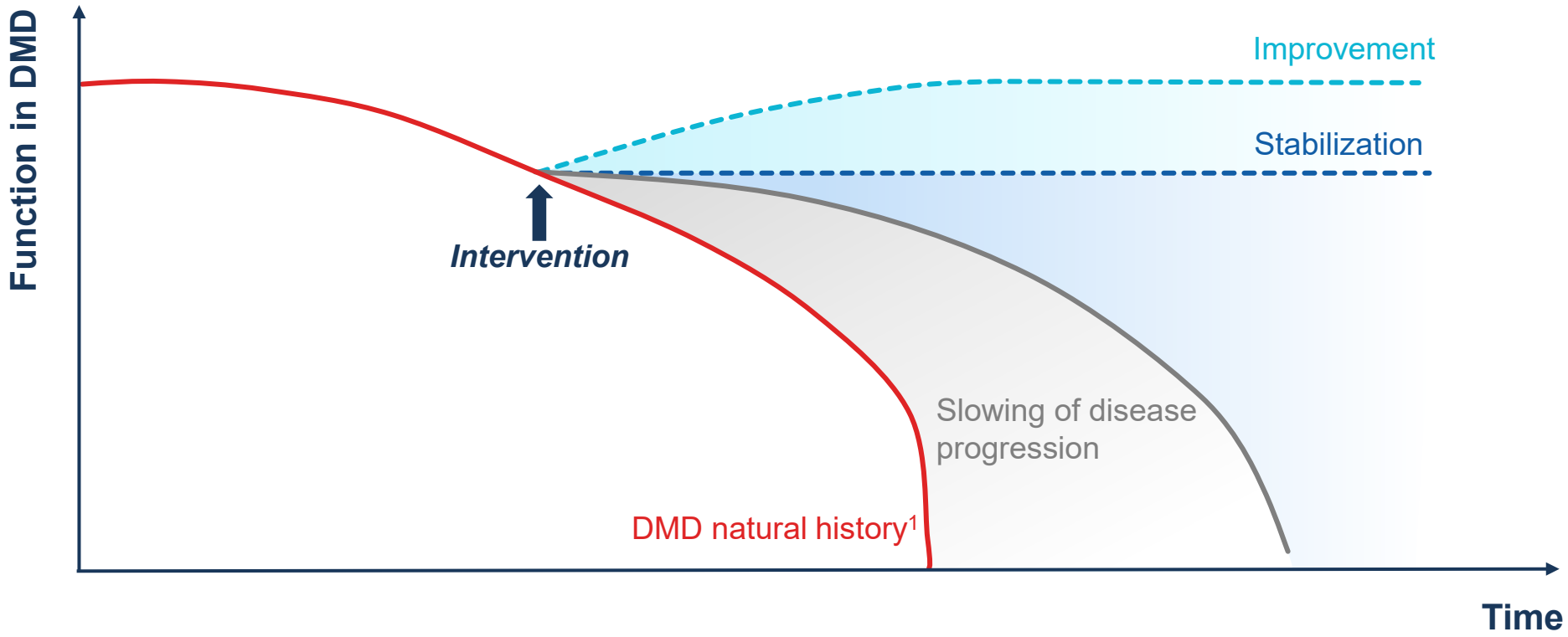
"With Duchenne, there's just so many losses and they are constant, it's like losing a game over and over again but still having to play. This disease has robbed our son of so much – and to be honest it's not even those big things I'm thinking of, like sports, and running around with friends. It's more like losing the things that make a person feel dignified."

Caregiver

CNS, central nervous system; DMD, Duchenne muscular dystrophy; GI, gastrointestinal.

1. Goemans N, et al. *Eur Neurol Rev*. 2014;9:78–82; 2. Asher DR, et al. *Expert Opin Biol Ther*. 2020;20:263–274; 3. Ohlendieck K, Swandulla D. *Pflügers Arch*. 2022;473:1813–1839.

Moving away from progressive decline to a modifiable disease trajectory in DMD



DMD, Duchenne muscular dystrophy.

1. Stimpson G, et al. *J Neuromuscul Dis.* 2024;11:153–166.

THANK YOU

Dyne® THERAPEUTICS