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# Zeleciment Rostudirsen Increased Dystrophin Protein Levels and Led to Functional Improvement in Clinical Measures in the DELIVER Trial

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# Additional data from DELIVER primary analysis

# DELIVER baseline participant characteristics were generally well balanced across cohorts

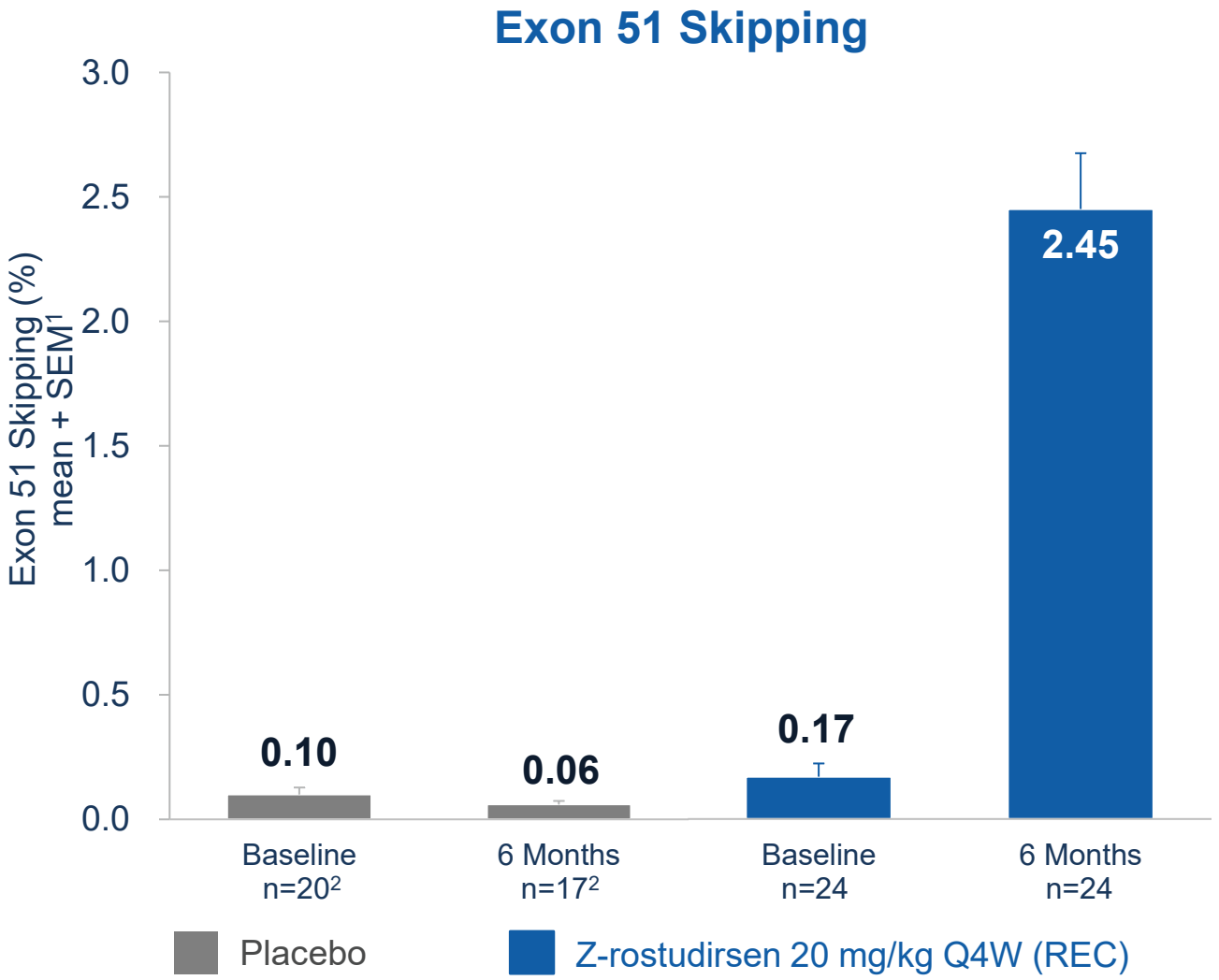
| | | Z-rostudirsen | | | |
|---|---|---|---|---|---|
| | Placebo (MAD+REC) N=24[5] Mean (SD) or n (%) | 20 mg/kg Q4W (REC) N=24 Mean (SD) or n (%) | 10 → 20 mg/kg[6] Q4W (MAD) N=6 Mean (SD) or n (%) | 20 mg/kg Q4W (MAD) N=6 Mean (SD) or n (%) | Overall (MAD+REC) N=86 Mean (SD) or n (%) |
| Age (years) | 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]<br>Daily<br>Other | <br>20 (83.3)<br>4 (16.7) | <br>20 (83.3)<br>4 (16.7) | <br>6 (100)<br>0 | <br>6 (100)<br>0 | <br>73 (84.9)<br>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 (%)<br>Eteplirsen<br>Other | <br>4 (16.7)<br>2 (8.3) | <br>2 (8.3)<br>5 (20.8) | <br>0<br>0 | <br>0<br>2 (33.3) | <br>15 (17.4)<br>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) |

**Zelecimert 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.

DELIVER

# Z-rostudirsen had robust target engagement at 6 months relative to baseline




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1. Biopsies taken approximately 28 days after most recent dose. 2. Not all participant samples could be analyzed at Baseline or Week 25. 6 months = Week 25 for DELIVER; Q4W, every 4 weeks; REC, registrational expansion cohort; SEM, standard error of the mean.

DELIVER

# Baseline characteristics well balanced after propensity score weighting: Ambulant z-rostudirsen vs untreated control

**ActiLiège Next study:**[1] Contemporaneous, ongoing natural history study collecting digital and clinic-based outcome measures

**Inclusion criteria**:

- Age 4–16 years
- Ambulant
- Corticosteroid treatment for ≥12 weeks
- DMD excluding mutations amenable to exon 44 skipping (ActiLiège)

**BL covariates included in propensity score:**[2]

- Age, height, NSAA total score, 10MWR velocity, TTR velocity, and SV95C

| | Untreated control[5,6] N=60 Mean (SD) or n (%) | z-rostudirsen[6] (REC) N=21[7] Mean (SD) or n (%) |
|---|---|---|
| Age (years) | 7.4 (2.8) | 6.7 (5.4) |
| Height (cm) | 117.5 (11.9) | 117.4 (26.0) |
| Time since first symptom (years) | 4.9 (2.8) | 4.9 (5.2) |
| Receiving ongoing corticosteroid treatment | 60 (100) | 21 (100) |
| Duration of corticosteroid treatment (years)[3] | 2.7 (2.3) | 1.7 (3.4) |
| TTR velocity (rise/sec)[4] | 0.22 (0.14) | 0.23 (0.17) |
| 10MWR velocity (m/sec)[4] | 1.9 (0.6) | 1.9 (0.7) |
| NSAA total score (points)[4] | 23.1 (7.3) | 21.8 (7.6) |
| SV95C (m/sec)[4] | 1.6 (0.5) | 1.6 (0.6) |

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1. ActiLiège Next study, ClinicalTrials.gov: NCT05982119 (Sponsor: CHU Liège, CI: Prof. Laurent Servais). 2. 1/PS for z-rostudirsen and 1/(1-PS) for control were used as weight in analysis. 3. Cumulative duration of previous and most recent corticosteroid treatment at the time of randomization. 4. Ambulant participants; out-of-threshold values imputed. 5. Untreated control cohort includes a prespecified analysis of 55 ambulant participants from ActiLiège and five ambulant participants from DELIVER REC placebo. 6. Data shown are after propensity score weighting. 7. Three non-ambulant participants from the z-rostudirsen REC treatment cohort removed from analyses.

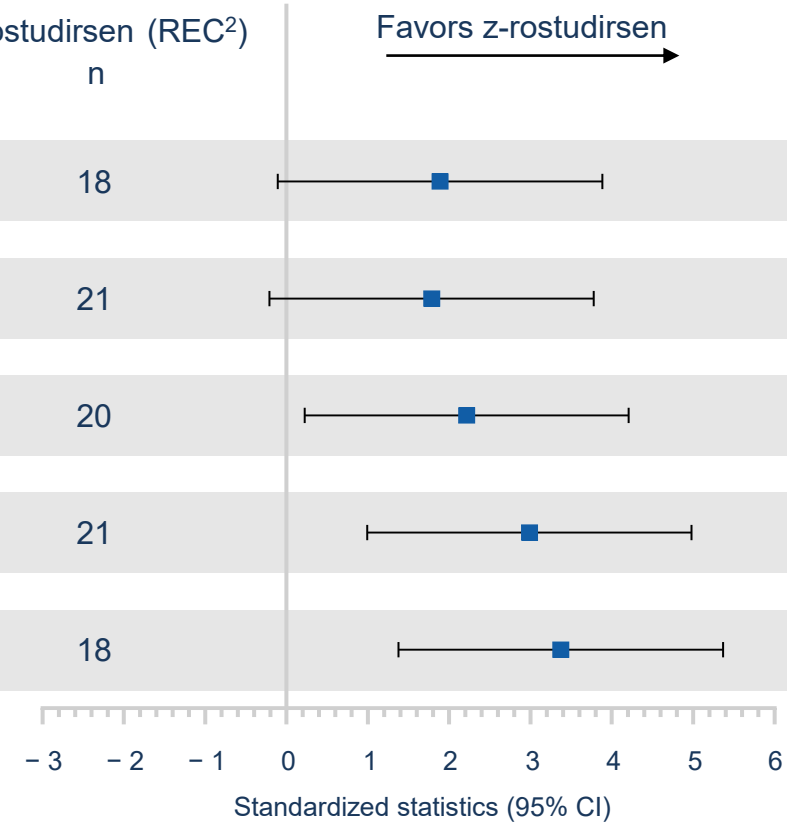
10MWR, 10-meter walk/run; BL, baseline; cm, centimeter; DMD, Duchenne muscular dystrophy; m, meters; MAD, multiple ascending dose; NH, natural history; NSAA, North Star Ambulatory Assessment; REC, registrational expansion cohort; SD, standard deviation; sec, second; SV95C, stride velocity 95th centile; TTR, time to rise.

DELIVER

# Z-rostudirsen showed functional improvement at 6 months compared to a large untreated cohort across multiple clinical measures

## Change from baseline at Month 6

| | Untreated control[1] n | Z-rostudirsen (REC[2]) n | LSM change difference (95% CI) | p-value |
|---|---|---|---|---|
| **TTR velocity** | 56 | 18 | **0.03 rise/sec** (−0.00 to 0.05) | 0.0632 |
| **10MWR velocity** | 59 | 21 | **0.11 m/sec** (−0.01 to 0.23) | 0.0784 |
| **SV95C** | 60 | 20 | **0.09 m/sec** (0.01 to 0.18) | 0.0298 |
| **NSAA** | 59 | 21 | **2.0 points** (0.7 to 3.4) | 0.0038 |
| **Composite score[3]** | 56 | 18 | **0.32** (0.13 to 0.50) | 0.0012 |

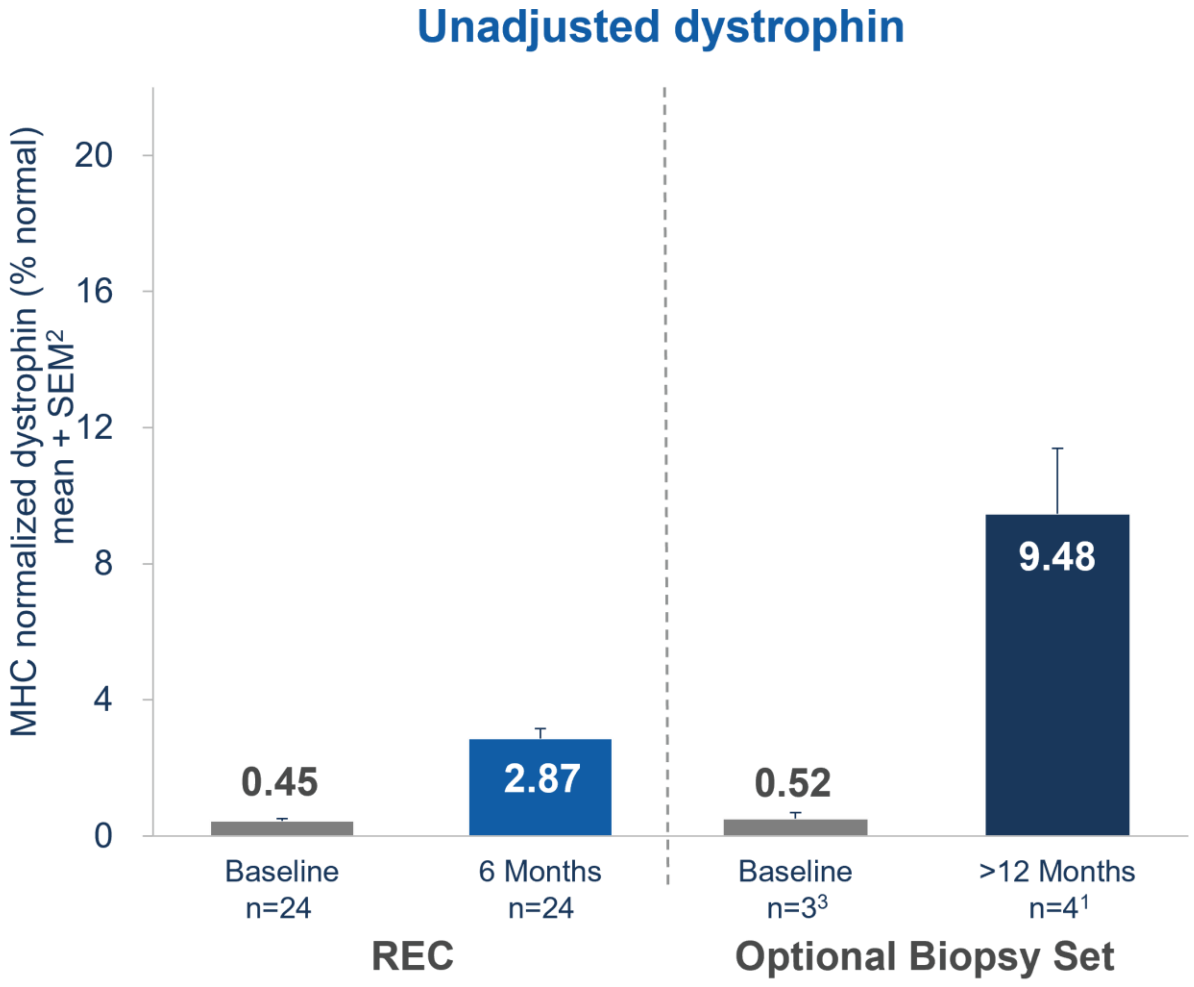


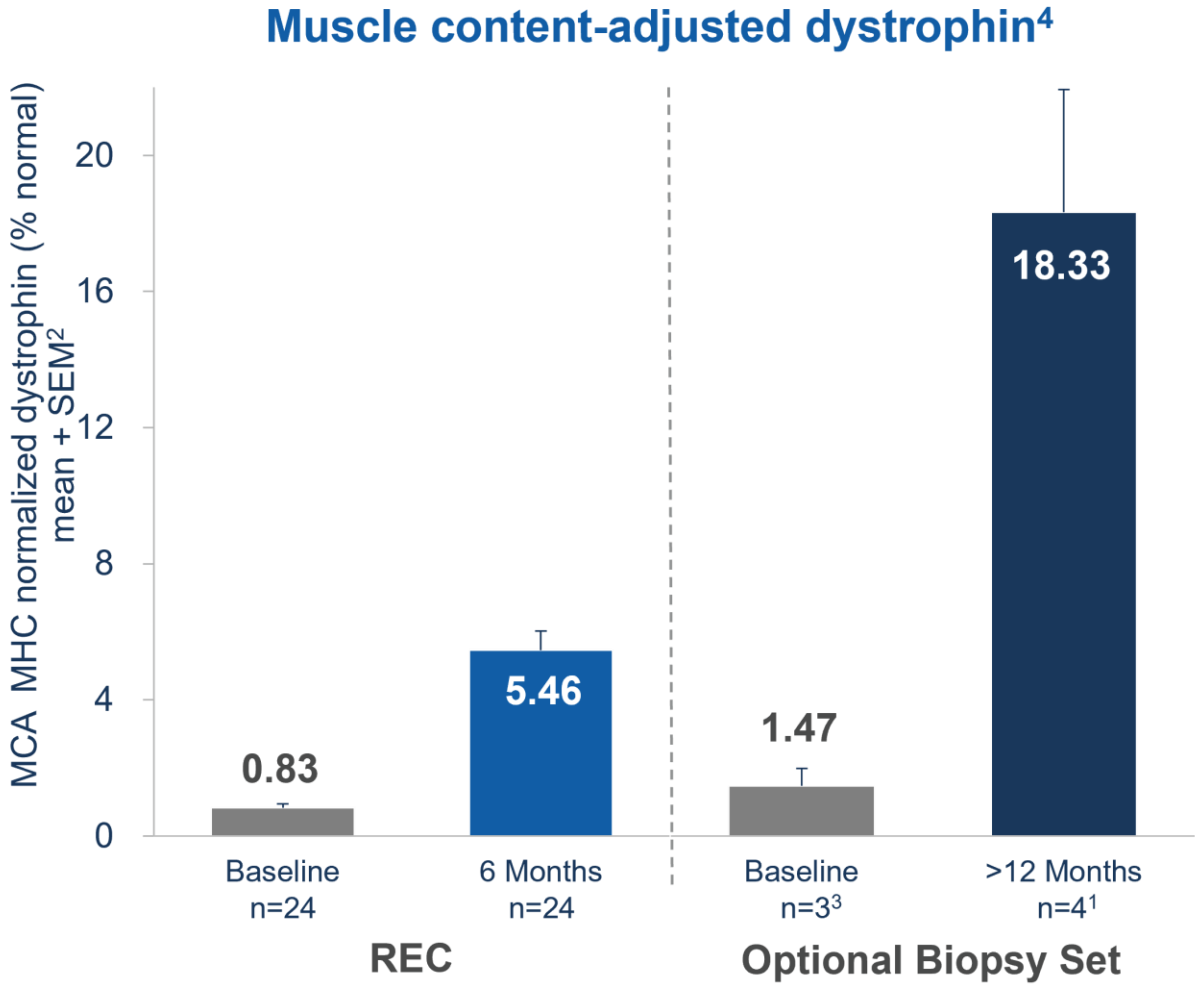

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1. Untreated control cohort includes up to 55 ambulant participants from ActiLiège (Sponsor: CHU Liège, CI: Prof. Laurent Servais) who met analysis inclusion criteria and up to five ambulant participants from DELIVER REC placebo. 2. Ambulant participants treated with z-rostudirsen in the REC. 3. Composite score: a global statistics test derived as the average of SV95C, NSAA, TTR velocity, and 10MWR velocity after standardization for each participant at each visit. 10MWR, 10-meter walk/run; CI, confidence interval; LSM, least-squares mean; m, meters; NSAA, North Star Ambulatory Assessment; REC, registrational expansion cohort; sec, second; SV95C, stride velocity 95th centile; TTR, time to rise.

DELIVER

# Dystrophin levels observed in optional biopsies from participants treated with 20 mg/kg Q4W zeleciment rostudirsen for >12M[1]




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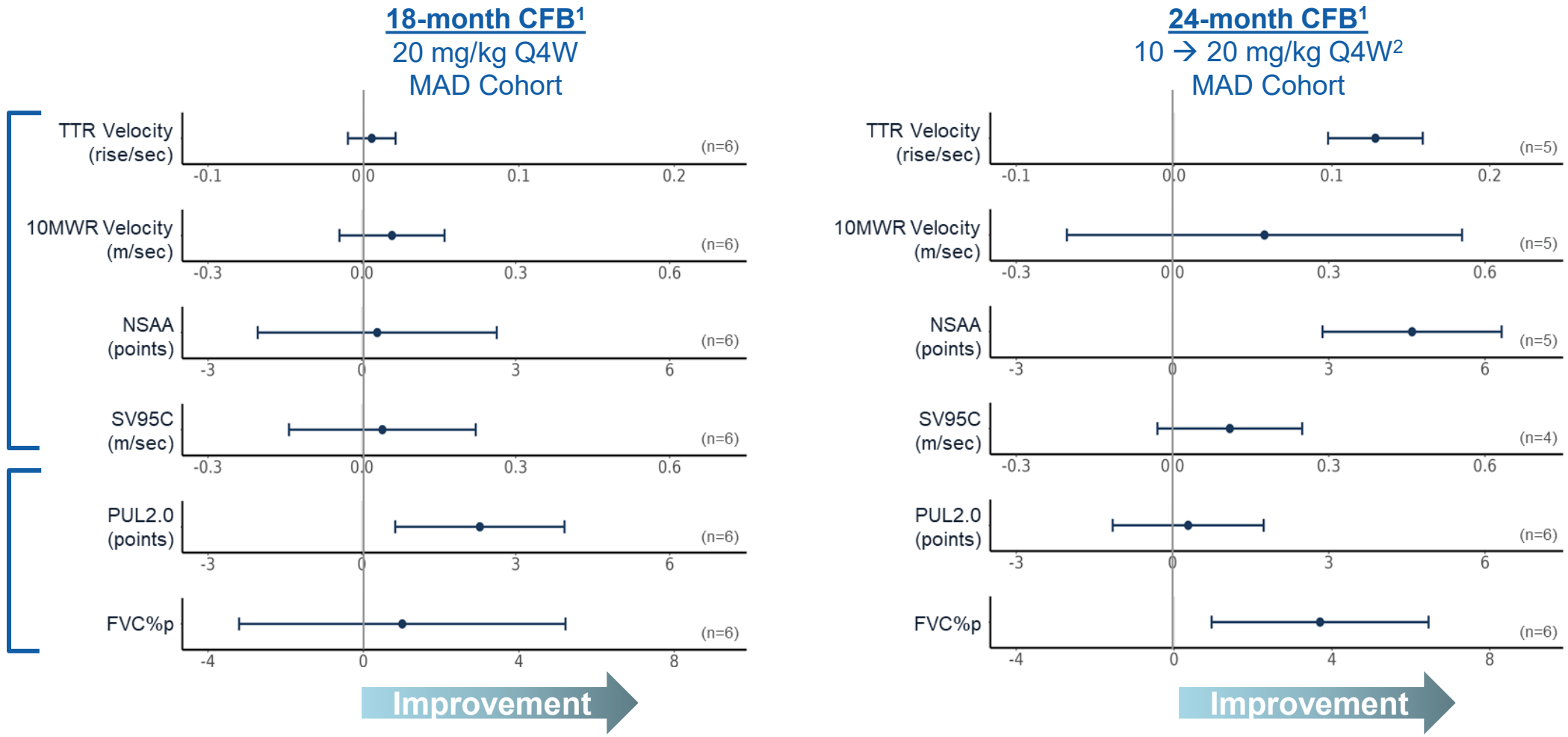
1. >12 month data reflect 4 participants who were dosed with 20 mg/kg Q4W for 67–104 weeks at the time of biopsy. This biopsy was optional per trial protocol in participants who received at least 48 weeks of 20 mg.kg Q4W z-rostudirsen treatment. The sample reported here reflects all optional biopsies collected. 2. Biopsies in REC taken approximately 28 days after most recent dose; optional biopsies taken after at least 48 weeks of 20 mg/kg Q4W z-rostudirsen treatment. 3. Baseline biopsies are pre-treatment biopsies for 3 participants with >12M optional biopsies. One participant with a >12M optional biopsy did not have a baseline biopsy. 4. Muscle content-adjusted dystrophin = MHC normalized dystrophin / % muscle content. 6 months = Week 25 for DELIVER; >12M = Greater than 48 weeks. REC, registrational expansion cohort; MCA, muscle content-adjusted; MHC, myosin heavy chain; Q4W, every 4 weeks; SEM, standard error of the mean.

DELIVER

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

**Ambulatory participants**

**Ambulatory & non-ambulatory participants**




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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.

DELIVER