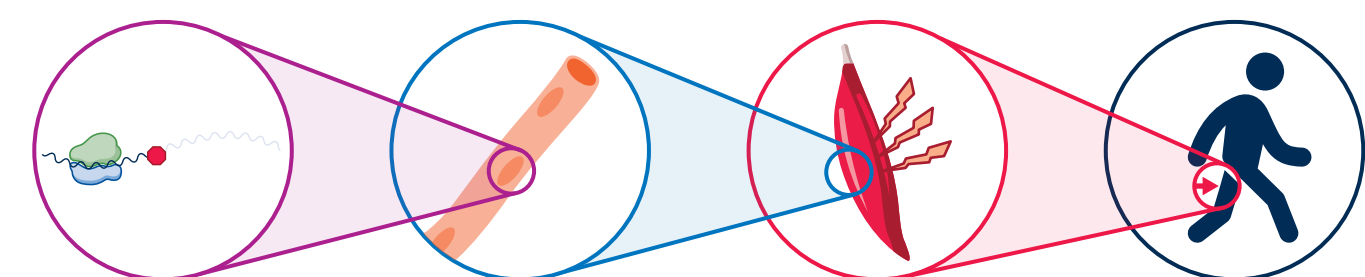


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Introduction

- | Genetic | Protein/cell | Tissue | Function |
|---|--|---|--|
| <p>Variants alter the open reading frame, causing premature truncation of translation^{1,2}</p> | <p>Nonsense-mediated decay reduces transcript abundance,³ and any produced protein is truncated, nonfunctional and unstable⁴</p> | <p>Dystrophin deficiency causes muscle damage, necrosis, inflammation, and fibrosis⁵</p> | <p>Speed, endurance, and quality of movement are negatively impacted⁶</p> |



- ## Objectives

- To present interim findings on the safety and efficacy of nivudirsén from the first 2 cohorts with available muscle biopsies in the 351-201 trial in ambulatory participants with DMD

Results

- The mean $\pm$ standard deviation age of enrolled participants was 7.0 $\pm$ 1.5 years (**Table 1**)

Mean (± SD)	6 mg/kg QW (n = 6)	9 mg/kg QW (n = 6)	12 mg/kg QW (n = 5)	Overall (N = 17)
Age at enrollment, years	7.2 ± 1.3	7.3 ± 1.2	6.4 ± 2.1	7.0 ± 1.5
Weight, kg	21.8 ± 4.0	23.6 ± 1.5	21.7 ± 4.7	22.4 ± 3.5
Height, cm	114.2 ± 6.9	121.4 ± 3.6	113.3 ± 12.0	116.5 ± 8.3
BMI, kg/m ²	16.7 ± 2.2	16.0 ± 0.6	16.8 ± 0.8	16.5 ± 1.4
NSAA total score, points	19.0 ± 7.2	22.3 ± 3.2	20.8 ± 5.7 ^a	20.7 ± 5.4 ^b
6-minute walk distance, m	373.1 ± 79.7	371.6 ± 79.5	270.8 ± 201.1 ^a	346.9 ± 119.9 ^b

- Nivodirsén demonstrated a manageable safety profile (**Table 2**)
- All treatment-related adverse events (AEs) were grade 1 or 2
 - There were 3 unrelated serious AEs (grade 3 influenza, appendicitis, and viral gastroenteritis)
 - No AEs caused permanent dose discontinuation
- The most frequent AEs (≥25%) were
 - Laboratory abnormalities such as cystatin C increased (59%) or glutamate dehydrogenase increased (29%), vomiting (47%), cough (41%), rhinorrhea (35%), diarrhea (35%), and pyrexia (35%)

AE category, n (%)	6 mg/kg QW (n = 6)	9 mg/kg QW (n = 6)	12 mg/kg QW (n = 5)	Overall (N = 17)
Participants with any AE	6 (100.0)	6 (100.0)	3 (60.0)	15 (88.2)
Leading to dose interruption ^a	5 (83.3)	5 (83.3)	1 (20.0)	11 (64.7)
Leading to dose reduction	0	0	0	0
Participants with any TRAE	6 (100.0)	5 (83.3)	3 (60.0)	14 (82.4)
Participants with any SAE	2 (33.3)	1 (16.7)	0	3 (17.6)
Participants with any treatment-related SAE	0	0	0	0
Any AEs leading to death	0	0	0	0
Mean treatment duration, wk	86.3	61.1	13.5	56

- Nivodirsen provided a mean $\pm$ standard error of the mean (SEM) exon skipping of $3.51\% \pm 2.56\%$ ($n = 2$; 6 mg/kg) at week 13 and $3.17\% \pm 1.26\%$ ($n = 4$; 6 mg/kg) and $5.03\% \pm 1.56\%$ ($n = 6$; 9 mg/kg) at week 25 (**Figure 2**)

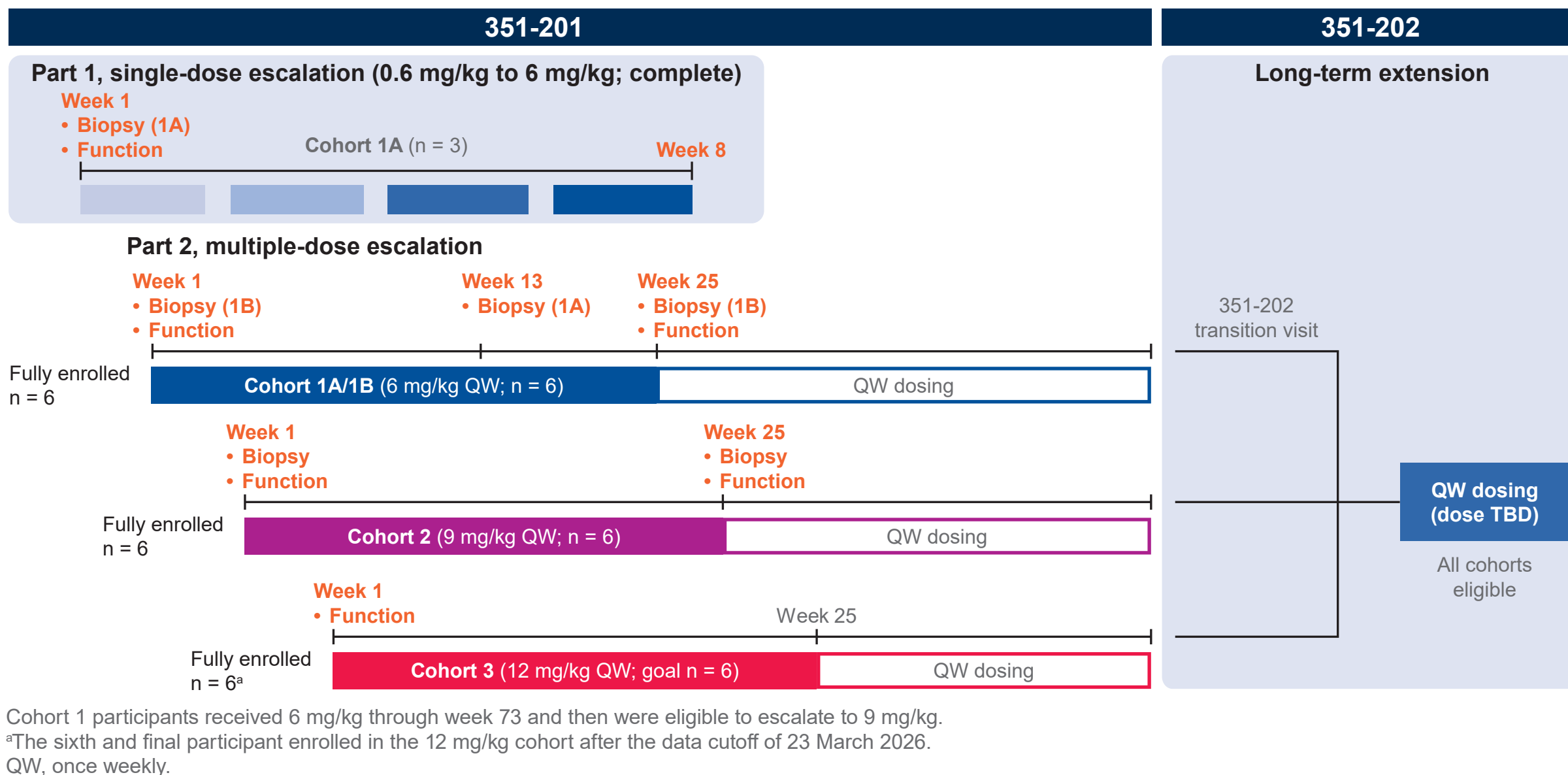
Conclusions

- Most AEs with nivudirsen were generally mild to moderate, and no dose-limiting toxicities were observed, thereby enabling escalation to the 12-mg/kg dose
- Interim analyses of dystrophin up to 25 weeks demonstrated positive changes in boys with DMD receiving nivudirsen ≤ 9 mg/kg
- Clinical biomarkers and transcriptomic profiles suggest improvement in overall muscle health, and exploratory outcomes across multiple functional endpoints suggest benefit that continues to accrue over time
- PD modeling predicts that dystrophin levels with continued nivudirsen treatment will continue to increase toward steady state

Methods

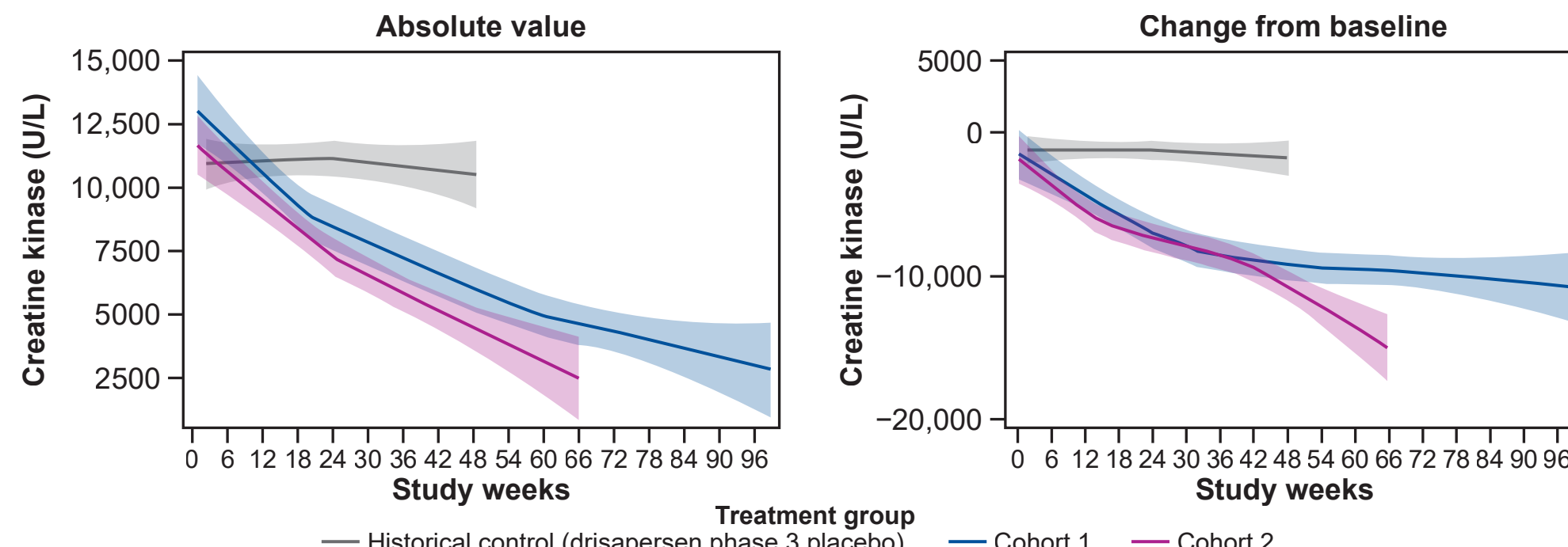
- Cohort 1A (n = 3) received single ascending doses of intravenous nivadirsen (0.6, 1.5, 3, and 6 mg/kg). Then, cohorts 1A and 1B (n = 3 each) received 6 mg/kg once weekly, cohort 2 (n = 6) received 9 mg/kg once weekly, and cohort 3 (n = 6) received 12 mg/kg once weekly (**Figure 1**)

Figure 1. 351-201 study design



- Absolute values and the change from baseline for creatine kinase suggest there is decreased muscle damage following nivudirsen treatment (**Figure 5**)
 - Similar trends were observed for lactate dehydrogenase

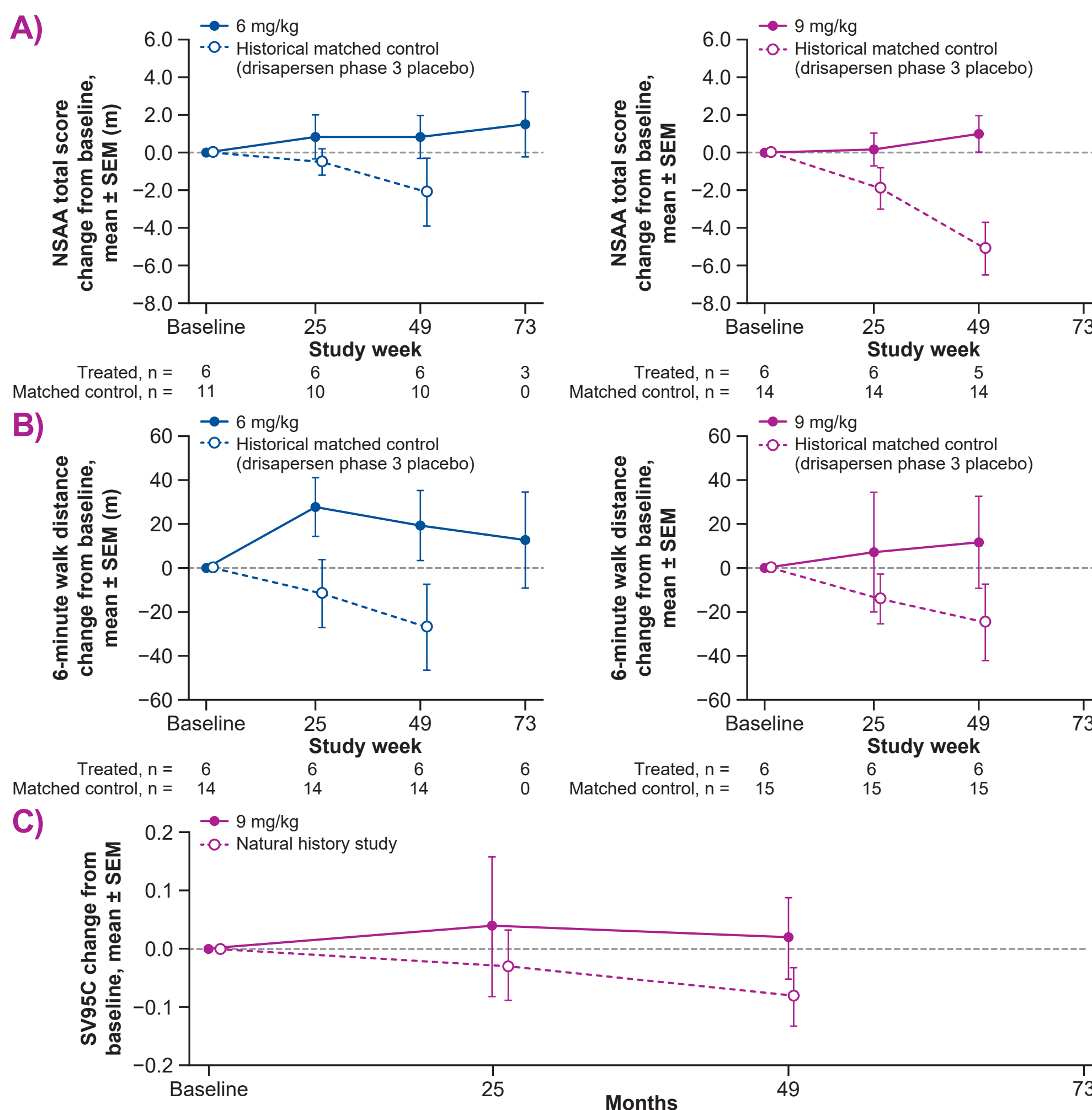
Figure 5. Clinical biomarkers suggest decreased muscle damage following nivudirsen treatment compared to historical placebo



Historical controls plotted from participants in the placebo arm of the disapersen phase 3 trial (NCT01254019; n = 61 participants; age range, 5–16 years). Cohort 1 participants received 6 mg/kg through week 73 and then were eligible to escalate to 9 mg/kg. Data cutoff: 23 March 2026. Lines represent locally estimated scatterplot smoothing (LOESS) estimates, and shaded areas represent 95% point-wise confidence intervals.

- Nivodirsen 6 mg/kg and 9 mg/kg prevented functional deterioration when compared to historical matched controls. The disease stability was retained beyond the 1-year-controlled time point at 6 mg/kg and will continue to be monitored up to 1.5 years as part of the ongoing study. Functional readouts at both doses will continue to be measured as part of the long-term extension study (**Figure 6**)

Figure 6. Nivudirsen prevented functional deterioration compared with matched natural history comparators for A) NSAA total score, B) 6MWD, and C) SV95C



Historical controls for NSAA and 6MWD were participants in the placebo arm of the drisapersen phase 3 trial, and the placebo control data were matched based on participant age and baseline function of each assessment. For SV95C, no baseline data are available for the 6 mg/kg cohort and the control data are from a natural history study of individuals with DMD and matched based on participant age and baseline SV95C.

Data cutoff: 23 March 2026.

6MWD, 6-minute walk distance; DMD, Duchenne muscular dystrophy; NSAA, NorthStar Ambulatory Assessment; SEM, standard error of the mean; SV95C, Stride Velocity 95th Centile.

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