Delpacibart zotadirsen (*Del-zota*) Showed Trends for Functional Improvement in the Phase 1/2 EXPLORE44® Study with Continued Trends After 1-Year of Treatment Compared to DMD44 Natural History

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Disclosure

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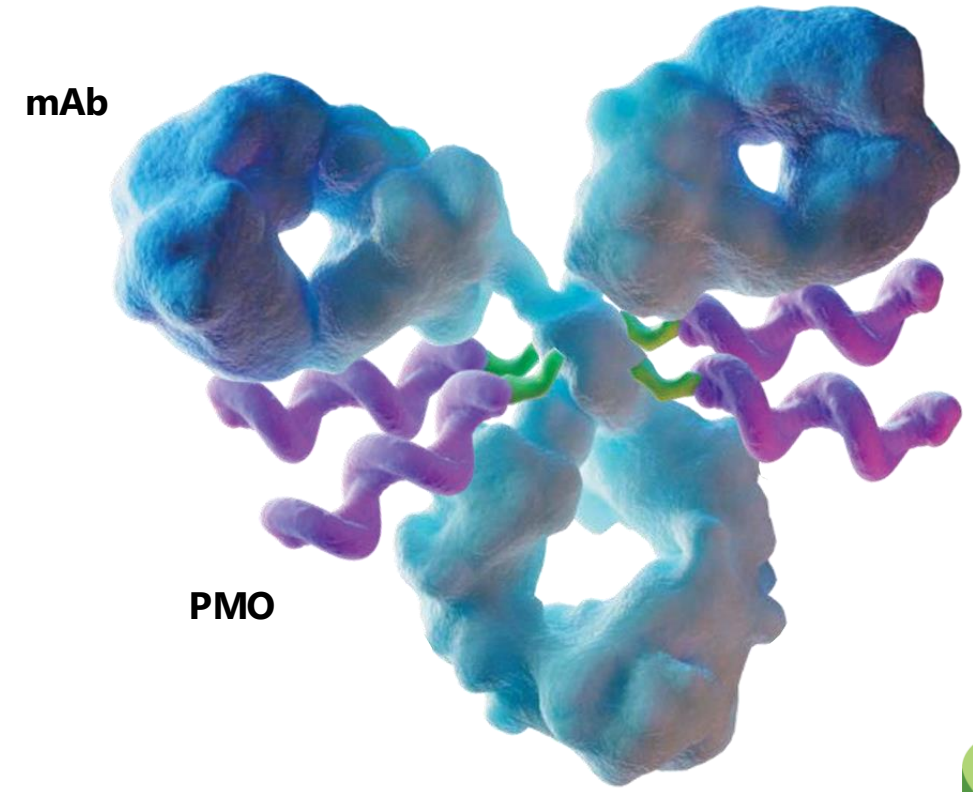
DMD is a severe, progressive neuromuscular disorder caused by mutations in the dystrophin gene, leading to muscle degeneration and early mortality[1-4]

- **~6–7%** of individuals with DMD have mutations amenable to exon 44 skipping (**DMD44**), yet there are currently **no exon skipping therapies available** for DMD44[5, 6]
- As such, there is a **high unmet need** for exon skipping therapies to treat DMD44, particularly those that can benefit a broad range of disease severities[7]
- ***Del-zota*** is an AOC™ designed to deliver a phosphorodiamidate morpholino oligonucleotide (PMO44) targeting dystrophin's exon 44 to muscle cells
  - *Del-zota* induces exon 44 skipping and restores the dystrophin reading frame, enabling the production of a **near full-length dystrophin** that is expected to **restore muscle cell integrity** and **protect against damage**
- The completed Phase 1/2 EXPLORE44® trial is the **first clinical study** to evaluate *del-zota*

Delpacibart zotadirsen abbreviation: *del-zota* (formerly known as AOC 1044)



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AOC, antibody oligonucleotide conjugate; DMD, Duchenne muscular dystrophy; DMD44, Duchenne muscular dystrophy with mutations amenable to exon 44 skipping; mAb, monoclonal antibody.

1. Crisafulli S et al. Orphanet J Rare Dis. 2020;15(1):141. 2. Mah JK et al. Neuromuscul Disord. 2014;24(6):482-491. 3. Mendell JR et al. Ann Neurol. 2012;71(3):304-313. 4. Moat SJ et al. Eur J Hum Genet. 2013;21(10):1049-1053. 5. Aartsma-Rus A et al. Orphanet J Rare Dis. 2012;7(Suppl 2):A20. 6. Wang RT et al. Hum Mutat. 2018;39(9):1193-1202. 7. Bushby K et al. Lancet Neurol. 2010;9(2):177-189. 8.

Key information across EXPLORE44® and EXPLORE44-OLE™

Together, these trials assess the safety, tolerability, PK, PD, and exploratory efficacy of *del-zota* in individuals with DMD44

EXPLORE44® Key Information

- Randomized, double-blind, placebo controlled
- Two cohorts: 5 mg/kg Q6W and 10 mg/kg Q8W*
- Biopsies in all cohorts
- N=19 *del-zota*, N=7 placebo
- After 3 doses, participants eligible to rollover into EXPLORE44-OLE™

EXPLORE44-OLE™ Key Information

- Open-label extension of EXPLORE44®
- EXPLORE44® cohorts maintained until 5 mg/kg selected as dose; all participants then transitioned to 5 mg/kg Q6W*
- 16 additional participants enrolled at 5 mg/kg Q6W
- No need for biopsies

Participant Characteristics

- N=39 (EXPLORE44-OLE™)
- Ages 7–27 years, mean age 13
- Ambulatory (67%, N=26) and non-ambulatory (33%, N=13)
- 90% on steroids

Today's presentation includes data on functional outcomes in EXPLORE44® (4/5 month data compared to placebo) and in EXPLORE44-OLE™ (1 year data compared to DMD44 natural history)

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*Doses expressed as PMO component. Participants at 10 mg/kg Q8W in EXPLORE44® were transitioned to 5 mg/kg Q6W. DMD44, Duchenne muscular dystrophy with mutations amenable to exon 44 skipping; OLE, open-label extension; PD, pharmacodynamics; PK, pharmacokinetics; Q6W, every 6 weeks; Q8W, every 8 weeks.

Del-zota demonstrated an acceptable safety profile

TEAEs	Placebo N=7	EXPLORE44® *Del-zota* N=19	EXPLORE44-OLE™ *Del-zota* N=39
Any TEAE	6 (86%)	16 (84%)	33 (85%)
Related to study drug	0	6 (32%)	10 (26%)
Serious TEAE	0	1 (5%)	3 (8%)†
Serious TEAE related to study drug	0	1 (5%)	1 (3%)
TEAE leading to treatment discontinuation	0	2 (11%)	1 (3%)
TEAE leading to death	0	0	0

- Most TEAEs were **mild or moderate**
- EXPLORE44®:
  - Most common TEAEs in *del-zota* arms (occurring in ≥ 3 participants): procedural pain and headache
  - 1 participant discontinued due to serious TEAE of anaphylaxis
  - 1 participant discontinued due to moderate IRR
- EXPLORE44-OLE™:
  - Most common TEAEs in *del-zota* arms (occurring in ≥ 3 participants): upper respiratory tract symptoms, diarrhea, fall, back pain, headache
  - 1 participant discontinued due to hypersensitivity

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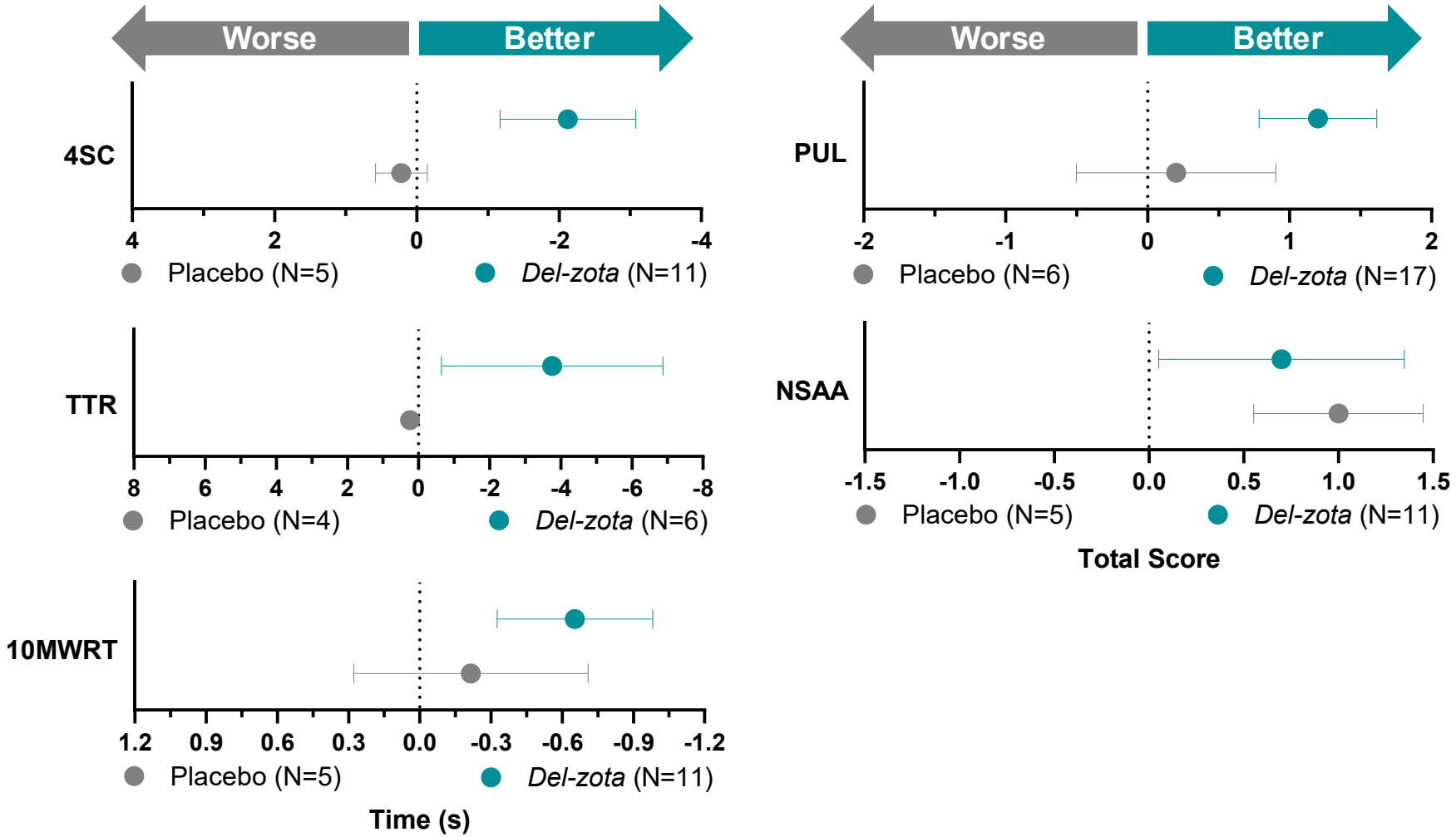
Placebo data are pooled and *del-zota* data are pooled (5 mg/kg and 10 mg/kg). January 2025 data cutoff for EXPLORE44® (final cut) and June 2025 data cutoff for EXPLORE44-OLE™ (interim cut). Safety data represents the number of participants (%) with ≥1 TEAE unless indicated. †SAEs considered unrelated to treatment include femur fracture and suicidal behavior. IRR, infusion-related reaction; OLE, open-label extension; TEAE, treatment-emergent adverse event.

Exploratory analysis: At 4/5 months, *del-zota* was associated with trends toward improvements in functional assessments in participants with DMD44 relative to placebo



January 2025 data cutoff for month 4/5 data. Data are presented as mean change from baseline ± SEM. *Del-zota* data are pooled (5 mg/kg and 10 mg/kg). The *del-zota* group received *del-zota* throughout the EXPLORE44® trial. One participant excluded from ambulatory assessments due to an ankle sprain prior to month 4/5. For TTR, two participants could not complete at baseline, two additional participants could not complete without assistance; these two had baseline TTR >15 seconds. These are exploratory analyses. 10MWRT, 10-meter walk/run test; 4SC, 4-stair climb; DMD44, Duchenne muscular dystrophy with mutations amenable to exon 44 skipping; NSAA, North Star Ambulatory Assessment; PUL, performance of upper limb; TTR, time to rise.

Baseline characteristics: *del-zota* versus DMD44 natural history

PRO-DMD-01 Natural History Study[1]

Data set reflects current standard of care for steroid use

- **Design:** Observational, prospective natural history study (N=269)
- **Population:** Subset of matched DMD44 participants (n=22)
- **Matching criteria**: Exon 44 skip amenable, ambulatory, 7–27 years old, if on steroid stable ≥1 month, weight ≥23 kg
  - 100% on steroids
- **Key assessments:** Clinical outcome assessments (i.e., timed tests, NSAA) progression over time

	PRO-DMD-01 DMD44 (N=22)	EXPLORE44®/ OLE (N=10)*
Age (yrs)	10.6	11.0
4SC (s)	4.3	7.5
10MWRT (s)	5.7	8.1
TTR (s)	7.2	10.2
NSAA (total)	23.6	19.6

Brogna 2023 Natural History Study[2]

Upper Limb Changes in DMD Patients Amenable to Skipping Exons 44, 45, 51 and 53: A 24-Month Study. Children 2023

- **Design:** Observational, prospective natural history study (N=66 unique intervals - DMD44)
- **Population:** utilized subset of generally well matched DMD44 participants (n=27)
- **Matching criteria:** Exon 44 skip amenable; includes ambulatory and non-ambulatory (same population as *del-zota*)
- **Key assessments:** PUL 2.0 (assessed in EXPLORE44®/OLE)

	Brogna DMD44[1] (N=27)†	EXPLORE44®/ OLE (N=17)
Age (yrs)	12.2	13.3
Ambulatory, n (%)	48 (72.7%)	12 (70.6%)
Non-ambulatory, n (%)	18 (27.3%)	5 (29.4%)
PUL (total)	35.6	36.3

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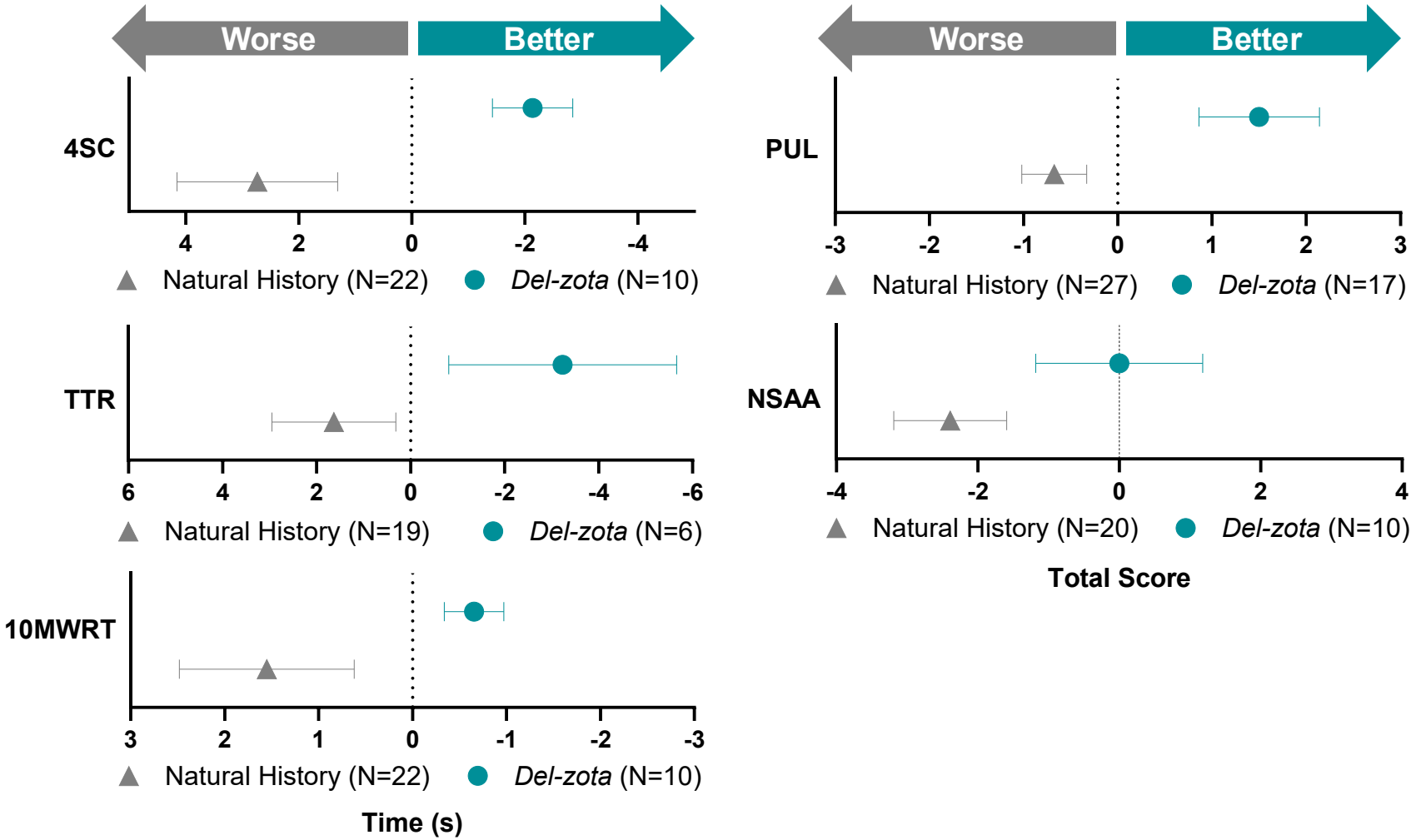
Data are presented as means unless otherwise indicated. *Ambulatory participants only, with one participant excluded due to ankle sprain and one participant unable to complete assessment due to fractured femur. Baseline characteristics shown of participants with functional data at one year. †66 unique intervals. 10MWRT, 10-meter walk/run test; 4SC, 4-stair climb; DMD44, Duchenne muscular dystrophy with mutations amenable to exon 44 skipping; NSAA, North Star Ambulatory Assessment; OLE, open-label extension; PUL, performance of upper limb; TTR, time to rise.

1. CureDuchenne, analyzed by Analysis Group®. 2. Brogna C et al. Children. 2023;10(4):746.

Exploratory analysis: At 1 year, *del-zota* was associated with trends toward improvements in functional assessments in participants with DMD44 relative to matched external DMD44 natural history controls



4SC: Improved from baseline by 2.1 s; natural history group declined by 2.7 s

TTR: Improved by 3.2 s; natural history group declined by 1.6 s

10MWRT: Improved by 0.7 s; natural history group declined by 1.5 s

PUL: Improved by 1.5 points; natural history group declined by 0.7 pts

- PUL improvements were seen in both ambulatory and non-ambulatory participants

NSAA: Remained stable; natural history group declined by 2.4 pts

June 2025 data cutoff for 1 year data. Data are presented as mean change from baseline ± SEM. *Del-zota* data are pooled (5 mg/kg and 10 mg/kg). The *del-zota* group received *del-zota* throughout the EXPLORE44® trial and for another 6 months in EXPLORE44-OLE™. One participant excluded from ambulatory assessments due to an ankle sprain prior to month 4/5 and one participant unable to complete 1 year assessment due to fractured femur. For TTR, two participants could not complete at baseline, two additional participants could not complete without assistance; these two had baseline TTR >15 seconds. These are exploratory analyses. 10MWRT, 10-meter walk/run test; 4SC, 4-stair climb; DMD44, Duchenne muscular dystrophy with mutations amenable to exon 44 skipping; DMD QoL, DMD Quality of Life; NSAA, North Star Ambulatory Assessment; PUL, performance of upper limb; TTR, time to rise.

These findings support continued clinical development of *del-zota* for the treatment of DMD44

Trends Towards Functional Improvement…

Del-zota treatment led to trends towards improvement in functional outcomes compared to placebo at 4/5 months and matched DMD44 natural history controls at 1 year

…Support Continued Clinical Development

These findings, along with a favorable safety profile, support continued clinical development of *del-zota* for the treatment of DMD44

DMD44, Duchenne muscular dystrophy with mutations amenable to exon 44 skipping.

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Authors:

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