

Initial Data from the DELIVER Trial of DYNE-251 in Males with DMD Mutations Amenable to Exon 51 Skipping

Perry Shieh¹, Craig Campbell², Nicolas Deconinck³, Liesbeth De Waele⁴, Kevin Flanigan⁵, Michelle Lorentzos⁶, Han Phan⁷, Chris Mix⁸, Soma Ray⁸, Dazhe Wang⁸, Wildon Farwell⁸, Ashish Dugar⁸, Maria L. Naylor⁸, Michela Guglieri⁹, on behalf of the DELIVER study investigators

¹University of California Los Angeles, Los Angeles, CA, USA; ²London Health Sciences Centre, London, Ontario, Canada; ³Neuromuscular Reference Center UZ Gent, Gent, Belgium; ⁴University Hospitals Leuven, Leuven, Belgium; ⁵Nationwide Children's Hospital, Columbus, OH, USA; ⁶Children's Hospital at Westmead, Westmead, New South Wales, Australia; ⁷Rare Disease Research, LLC, Atlanta, GA, USA; ⁸Dyne Therapeutics, Inc., Waltham, MA, USA; ⁹Royal Victoria Infirmary, Newcastle University, Newcastle-Upon-Tyne, UK



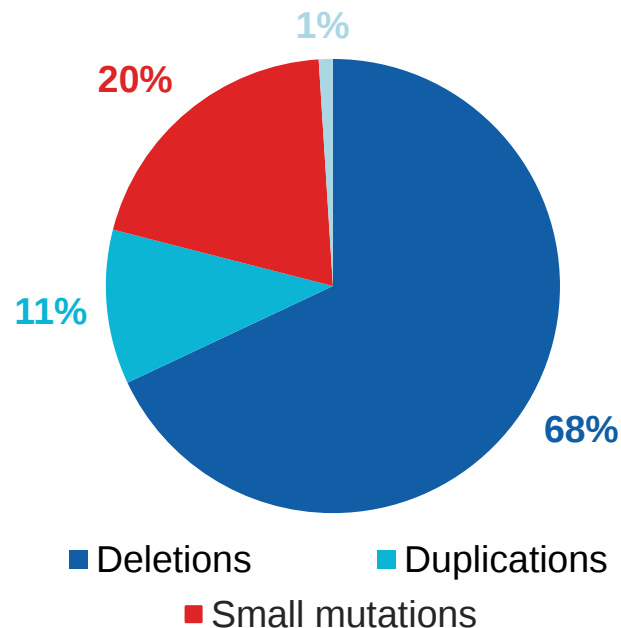
Disclosures

- Consulting: Sarepta, Solid, Dyne, Biogen, Genentech, Novartis, Astellas, Solid, Sanofi, Alexion, Argenx, CSL Behring, Grifols, UCB
- Research Grants: Sarepta, Solid, PTC, Dyne, Biogen, Genentech, Novartis, Astellas, Avidity, AMO Pharma, Abcuro, Sanofi
- DYNE-251 is an investigational medicine being evaluated in the ongoing DELIVER trial and has not received approval by FDA, EMA, or any other regulatory authorities.

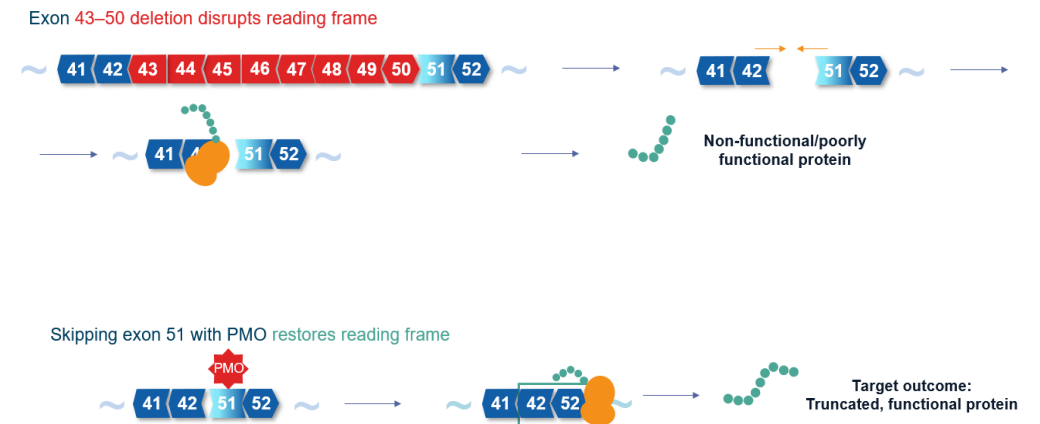
DMD Is Caused by Mutations in the *DMD* Gene

- Duchenne muscular dystrophy (DMD) is caused by mutations in the *DMD* gene which results in greatly reduced production of dystrophin protein, essential for muscle structure, function, and preservation¹⁻⁵

Deletions Account for More Than Two-Thirds of DMD Cases⁶



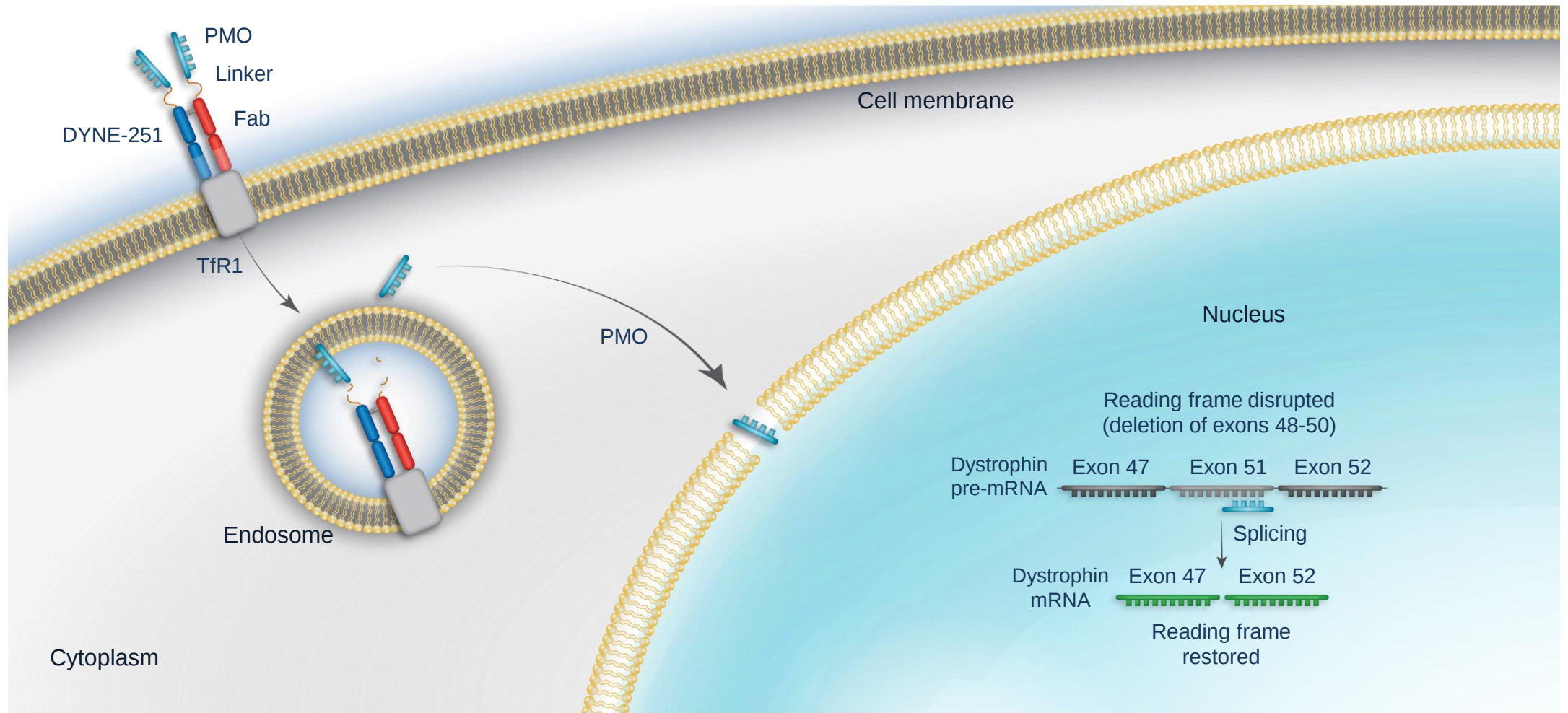
- 80% of deletions occur in two hot spot regions⁷:
 - Exons 45 to 55 (70%)
 - Exons 2 to 20 (14%)
- PMO-induced exon skipping restores the *DMD* mRNA reading frame leading to the production of truncated, functional dystrophin protein⁸



DMD, Duchenne muscular dystrophy.

1. Claflin DR, Brooks SV. *Am J Physiol Cell Physiol*. 2008;294:C651-C658. 2. Ervasti JM, Campbell KP. *J Cell Biol*. 1993;122:809-823. 3. Hoffman EP, Brown RH, Jr, Kunkel LM. *Cell*. 1987;51:919-928. 4. de Feraudy Y, et al. *Ann Neurol*. 2021;89:280-292. 5. Ohlendieck K, et al. *Neurology*. 1993;43:795-800. 6. Bladen CL, et al. *Hum Mutat*. 2015;36:395-402. 8. Niks EH, Aartsma-Rus A. *Expert Opin Biol Ther*. 2017;17:225-236.

DYNE-251 Is Designed to Leverage TfR1 to Deliver Exon 51-Skipping PMO to Affected Muscle in DMD

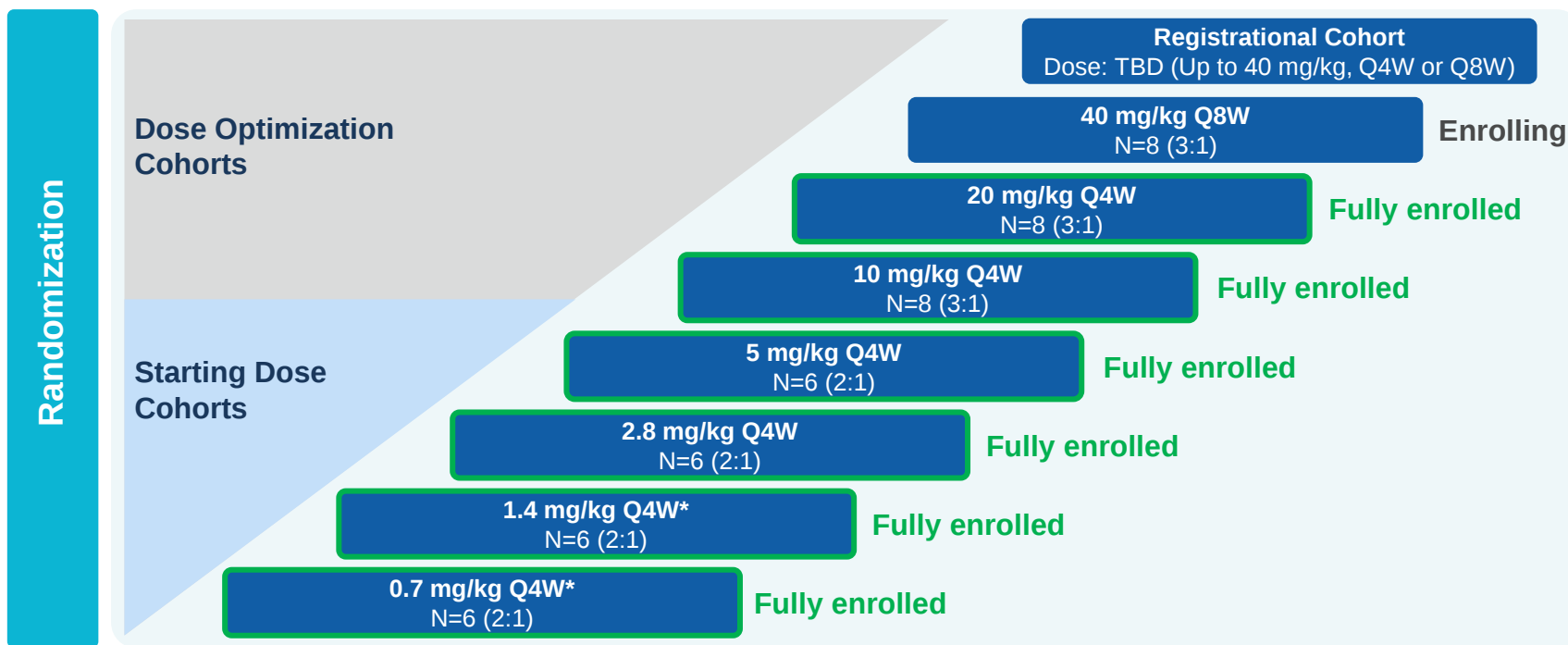


Goal of Treatment: Increase Dystrophin Expression and Enable Effective Delivery to Muscle to Improve Function

DMD, Duchenne muscular dystrophy; Fab, antigen-binding fragment; PMO, phosphorodiamidate morpholino oligomer; TfR1, transferrin receptor 1
Image depicts intended mechanism of action of DYNE-251. Applicable to all *DMD* mutations amenable to skipping of exon 51.

DELIVER: Phase 1/2 Clinical Trial to Evaluate DYNE-251 in Patients with DMD

Global, Randomized, Placebo-Controlled Trial Evaluating DYNE-251 in Ambulant and Non-Ambulant Male DMD Patients (4-16 Years) with Mutations Amenable to Exon 51 Skipping Therapy



Primary Endpoints

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

MAD Study Details

- IV administration of DYNE-251 or placebo every 4 weeks or every 8 weeks
- Muscle biopsies: Baseline and 24 weeks in 2.8 mg/kg and higher cohorts*
- Patients in MAD study escalated to highest tolerable dose in OLE and LTE

Global Trial Designed to be Registrational and to Enable Rapid Achievement of Predicted Pharmacologically Active Dose Levels

DMD, Duchenne muscular dystrophy; LTE, long-term extension; MAD, multiple ascending dose; OLE, open-label extension.

Doses provided refer to PMO component of DYNE-251. Cohorts randomized to active arm or placebo. Study protocol allows for dosing up to 40 mg/kg.

*Muscle biopsies taken at baseline and 24 weeks in 2.8 mg/kg Q4W cohort to 20 mg/kg Q4W cohort; muscle biopsies taken at baseline and 48 weeks in 40 mg/kg Q8W cohort; biopsies not taken in 0.7 mg/kg and 1.4 mg/kg cohorts.

For more information visit the DELIVER clinical trial posting on [ClinicalTrials.gov](https://clinicaltrials.gov) Identifier: NCT05524883 or clinicaltrialsregister.eu EudraCT Number: 2021-005478-24

DYNE-251 Safety Profile Is Favorable to Date

Summary of Treatment Emergent Adverse Events (TEAEs) – Placebo-Controlled Period ¹

TEAE Category	Participants with ≥1 TEAE – n (%)						
	0.7mg/kg Q4W n=6	1.4mg/kg Q4W n=6	2.8mg/kg Q4W n=6	5mg/kg Q4W n=6	10mg/kg Q4W n=8	20mg/kg Q4W n=5	Overall* N=37
Any TEAE	4 (67%)	6 (100%)	3 (50%)	4 (67%)	6 (75%)	1 (20%)	24 (65%)
Any related TEAE	1 (17%)	2 (33%)	0	3 (50%)	1 (13%)	0	7 (19%)
Any serious TEAE	0	0	0	0	0	1 (20%)	1 (3%)
Any serious related TEAE	0	0	0	0	0	0	0
Any TEAE leading to withdrawal from study drug	0	0	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0	0	0

Most TEAEs Were Mild or Moderate

- 1 serious TEAE unrelated to study drug
 - Dehydration due to gastroenteritis
- Most common TEAEs (≥10% participant incidence)*
 - Headache (16%)
 - Nasopharyngitis (16%)
 - Vomiting (14%)
 - Infusion related reaction (11%)**
 - Fall (11%)
 - Cough (11%)

Additional Safety Data

- No participants have demonstrated anemia or thrombocytopenia²
- No participants have demonstrated kidney injury³
- No participants have demonstrated clinically meaningful changes in electrolytes, including magnesium

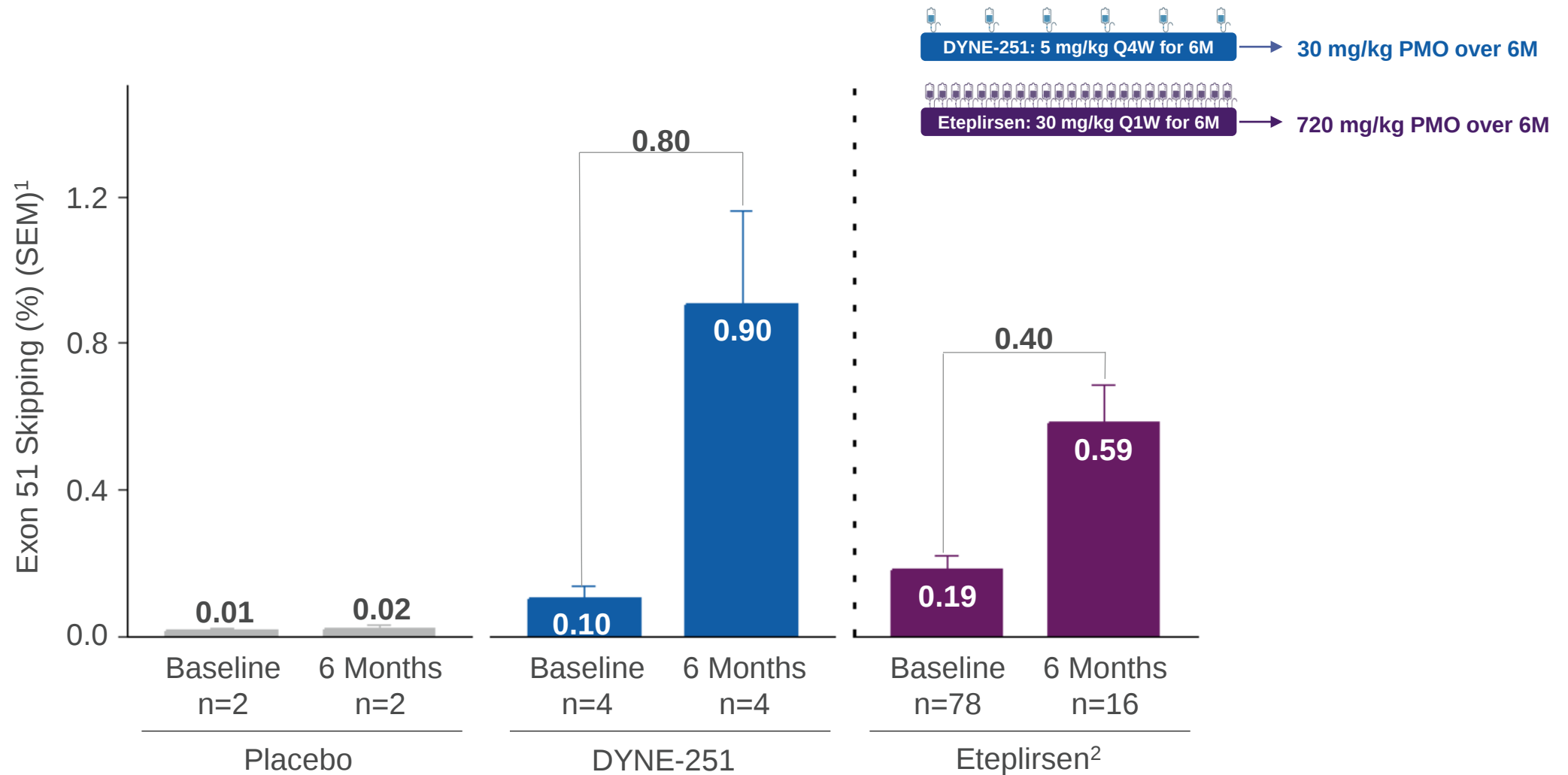
AE, adverse event; Q4W, every 4 weeks dosing; Q8W, every 8 weeks dosing; TEAE, treatment-emergent adverse event.

* All cohorts combined. ** All infusion-related reactions have been mild or moderate in intensity; dosing has continued in all participants.

1. Data as of December 6, 2023; 2. Treatment emergent HGB or PLT persistently below LLN or reported AE. 3. Treatment emergent and persistently abnormal renal parameters or reported AE.

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DYNE-251, Dosed Monthly, Showed Increase in Percent Exon Skipping at 6 Months

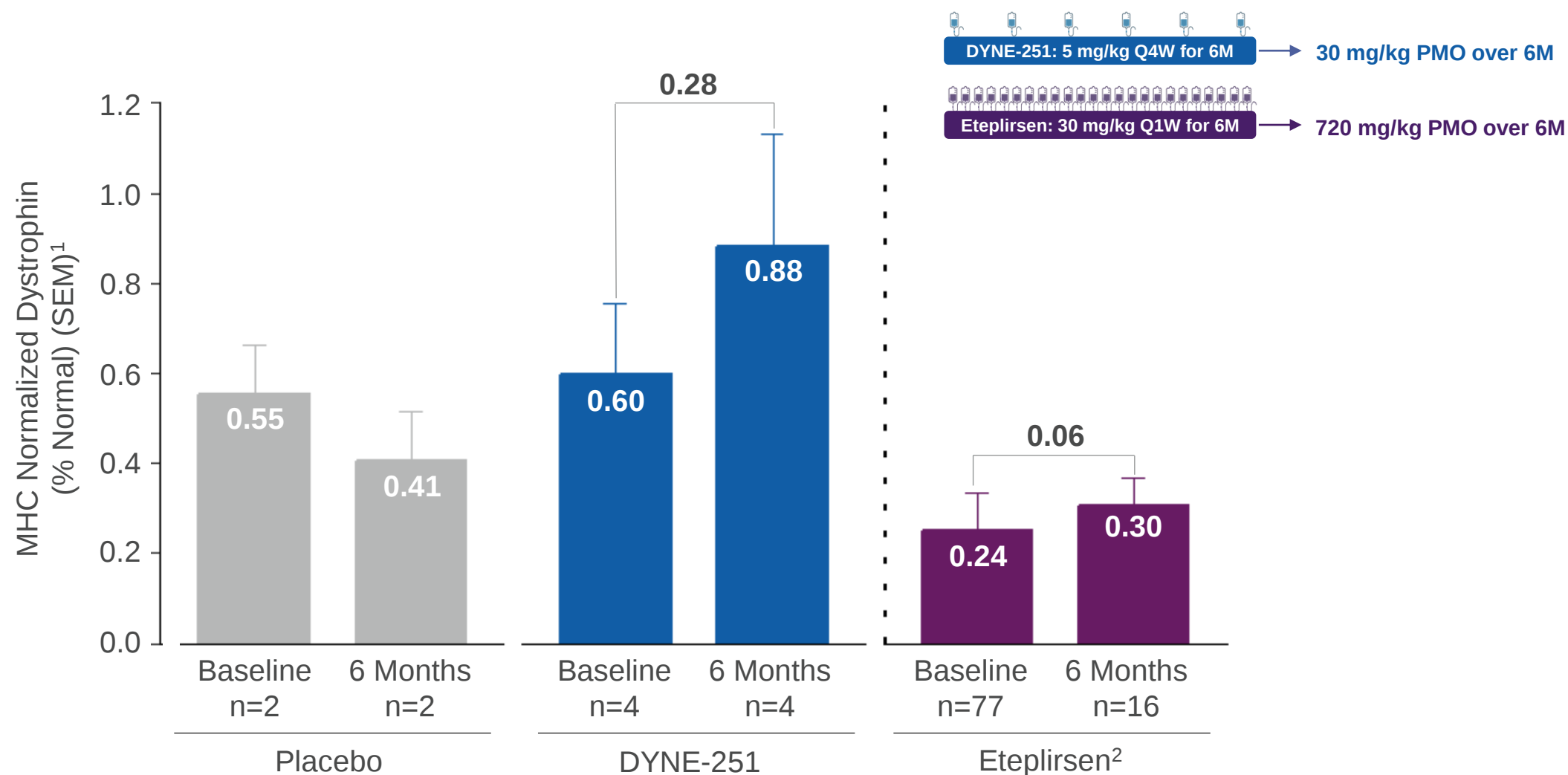


PMO, phosphorodiamidate morpholino oligomer; Q4W, every 4 weeks dosing; SEM, standard error of the mean.

1. DELIVER biopsy taken approximately 28 days after most recent dose; 6 months = Week 25 for DELIVER and Week 24 for eteplirsen data; 2. No head-to-head trials have been conducted comparing DYNE-251 to eteplirsen. Eteplirsen data may not be directly comparable due to differences in trial protocols, dosing regimens and patient populations. Accordingly, these cross-trial comparisons may not be reliable. Eteplirsen data from McDonald CM, et al. *J Neuromuscul Dis* 2021;8:989–1001.

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DYNE-251, Dosed Monthly, Showed Increase in Percent Dystrophin At 6 Months



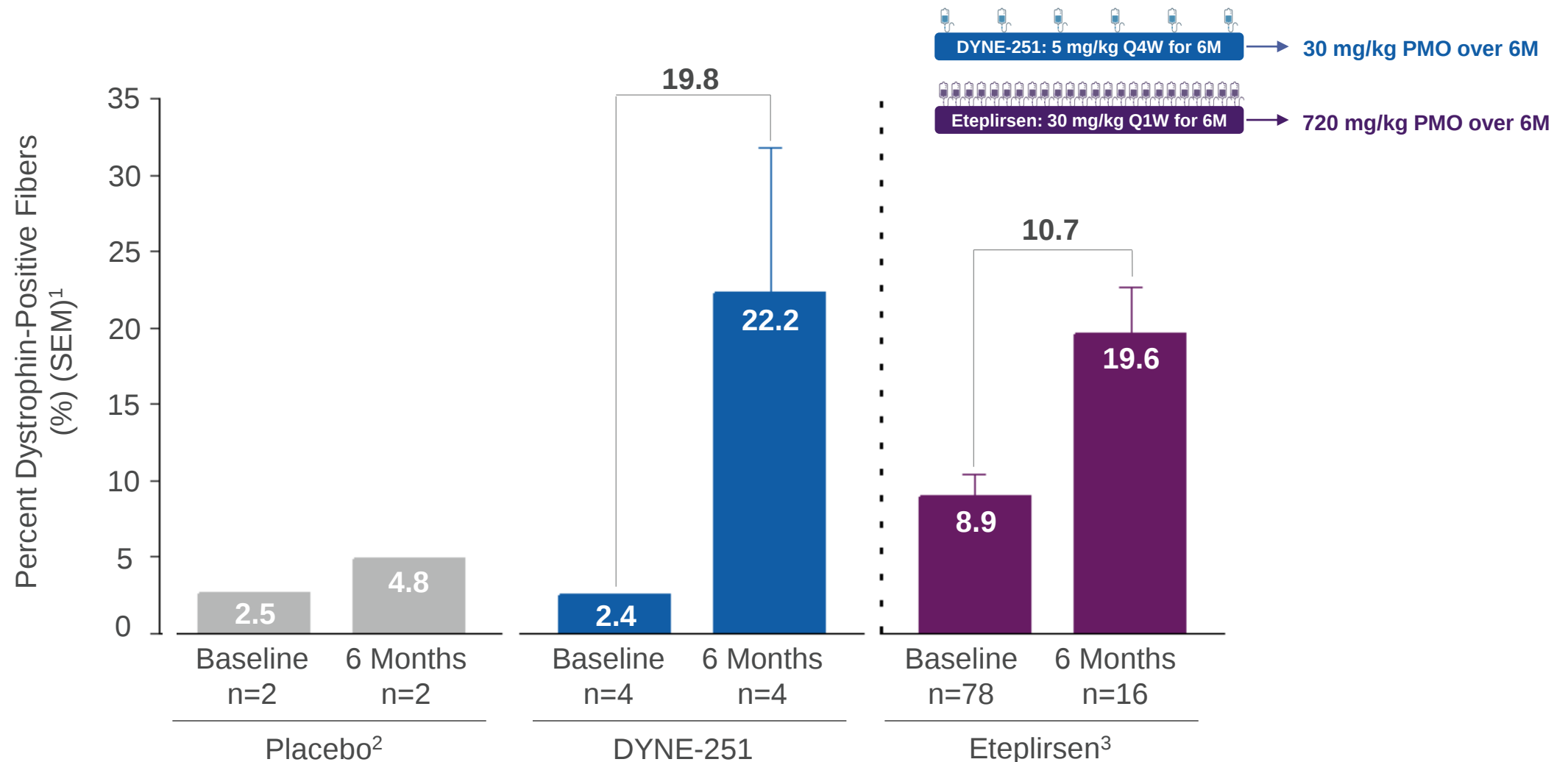
MHC, myosin heavy chain; PMO, phosphorodiamidate morpholino oligomer; Q4W, every 4 weeks dosing; SEM, standard error of the mean.

1. DELIVER biopsy taken approximately 28 days after most recent dose; 6 months = Week 25 for DELIVER and Week 24 for eteplirsens data; 2. No head-to-head trials have been conducted comparing DYNE-251 to eteplirsens. Eteplirsens data may not be directly comparable due to differences in trial protocols, dosing regimens and patient populations.

Accordingly, these cross-trial comparisons may not be reliable. Eteplirsens data from McDonald CM, et al. *J Neuromuscul Dis* 2021;8:989–1001.

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DYNE-251, Dosed Monthly, Showed Increase in Percent Dystrophin Positive Fibers (PDPF) At 6 Months



PDPF, percent dystrophin-positive fiber; PMO, phosphorodiamidate morpholino oligomer; Q4W, every 4 weeks dosing; SEM, standard error of the mean.

1. DELIVER biopsy taken approximately 28 days after most recent dose; 6 months = Week 25 for DELIVER and Week 24 for eteplirsen data. 2. PDPF data not available for 1 patient from placebo group; 3. No head-to-head trials have been conducted comparing DYNE-251 to eteplirsen. Eteplirsen data may not be directly comparable due to differences in trial protocols, dosing regimens and patient populations. Accordingly, these cross-trial comparisons may not be reliable. Eteplirsen data from McDonald CM, et al. *J Neuromuscul Dis* 2021;8:989–1001.

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Summary

- DYNE-251 consists of an exon 51-skipping PMO conjugated to a TfR1-targeting Fab designed to deliver increased levels of PMO to muscles.
 - DYNE-251 leverages TfR1 biology to enable receptor-mediated muscle delivery.
- DELIVER is an ongoing, randomized, placebo-controlled global trial of DYNE-251 in ambulant and non-ambulant male DMD patients with mutations amenable to exon 51 skipping therapy.
- The safety profile of DYNE-251 is favorable to date¹, with the majority of TEAEs reported as mild or moderate.
 - The trial is fully enrolled through the 20 mg/kg cohort and favorable safety profile has supported dosing up to 40 mg/kg.
- In participants treated with 5 mg/kg (PMO equivalent) DYNE-251, initial data show levels of exon skipping, dystrophin, and PDPF increased at 6 months vs. baseline.
- These initial data support the continued clinical development of DYNE-251 for the treatment of DMD.

DMD, Duchenne muscular dystrophy; MAD, multiple ascending dose; PDPF, percent dystrophin-positive fiber; PMO, phosphorodiamidate morpholino oligomer; TfR1, transferrin receptor 1.

1. Data as of December 6, 2023.

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USA

Chamindra Laverty
University of California, San Diego

Perry Shieh
University of California, Los Angeles

Susan Apkon
Children's Hospital Colorado

Han Phan
Rare Disease Research, LLC

Brenda Wong
UMass Memorial Medical Center

Kevin Flanigan
Nationwide Children's Hospital

Erika Finanger
Shriners Hospitals for Children Portland

Richard Finkel
St Jude Children's Research Hospital

Russell Butterfield
University of Utah - PPDS

Amy Harper
Virginia Commonwealth University

CANADA

Craig Campbell
London Health Sciences Centre

Hugh McMillan
Children's Hospital of Eastern Ontario

UNITED KINGDOM

Rajesh Karuvattil
Alder Hey Children's Hospital

Michela Guglieri
Royal Victoria Infirmary

Anne-Marie Childs
Leeds Teaching Hospitals NHS Trust

BELGIUM

Nicolas Deconinck
UZ Gent

Liesbeth De Waele
UZ Leuven

SPAIN

Andres Nascimento
Hospital Sant Joan de Déu Universidad de Barcelona

Francina Munell Casadesus
Hospital Universitario Vall d'Hebron - PPDS

ITALY

Marika Pane
Fondazione Policlinico Universitario A Gemelli

Claudio Bruno
Istituto G Gaslini Ospedale Pediatrico IRCCS - INCIPIT - PIN

Valeria Sansone
NeMO Clinical Research Center

Stefano Previtali
Ospedale San Raffaele S.r.l. - PPDS

AUSTRALIA

Michelle Lorentzos
Children's Hospital at Westmead

