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

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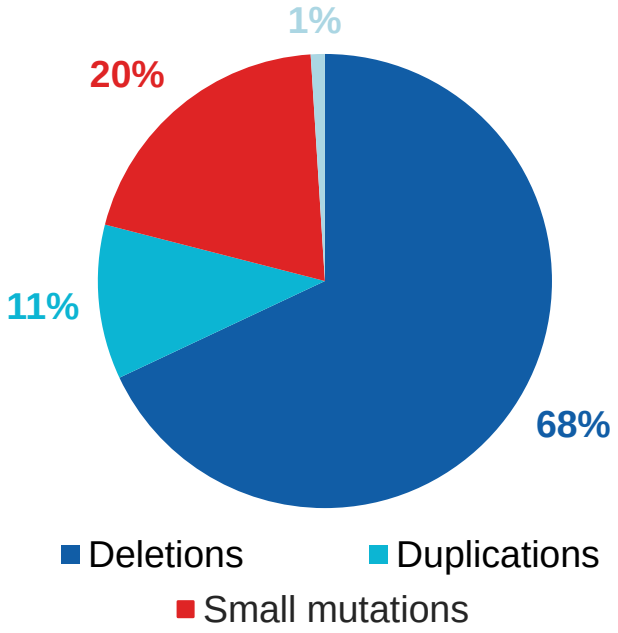
Disclosures

- 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.

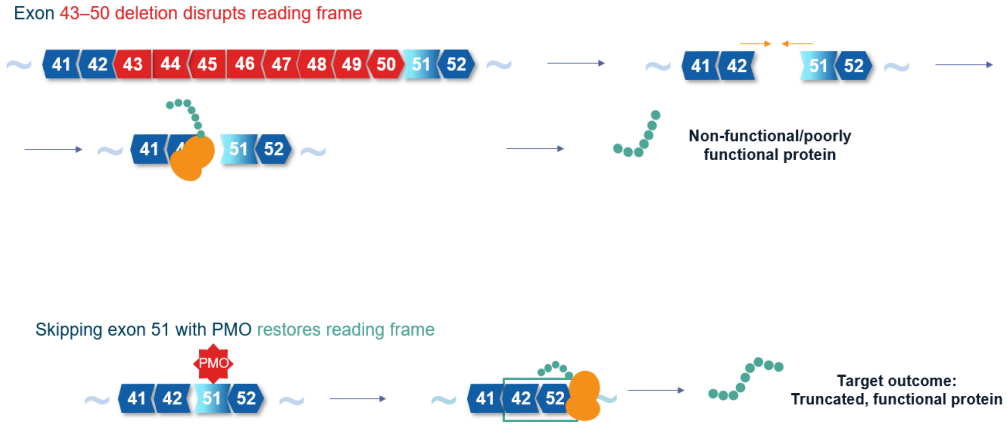
DMD Is Caused by Mutations in the *DMD* Gene

- 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 preservation[1-5]

Deletions Account for More Than Two-Thirds of DMD Cases[6]



- 80% of deletions occur in two hot spot regions[7]:
  - 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 protein[8]



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.

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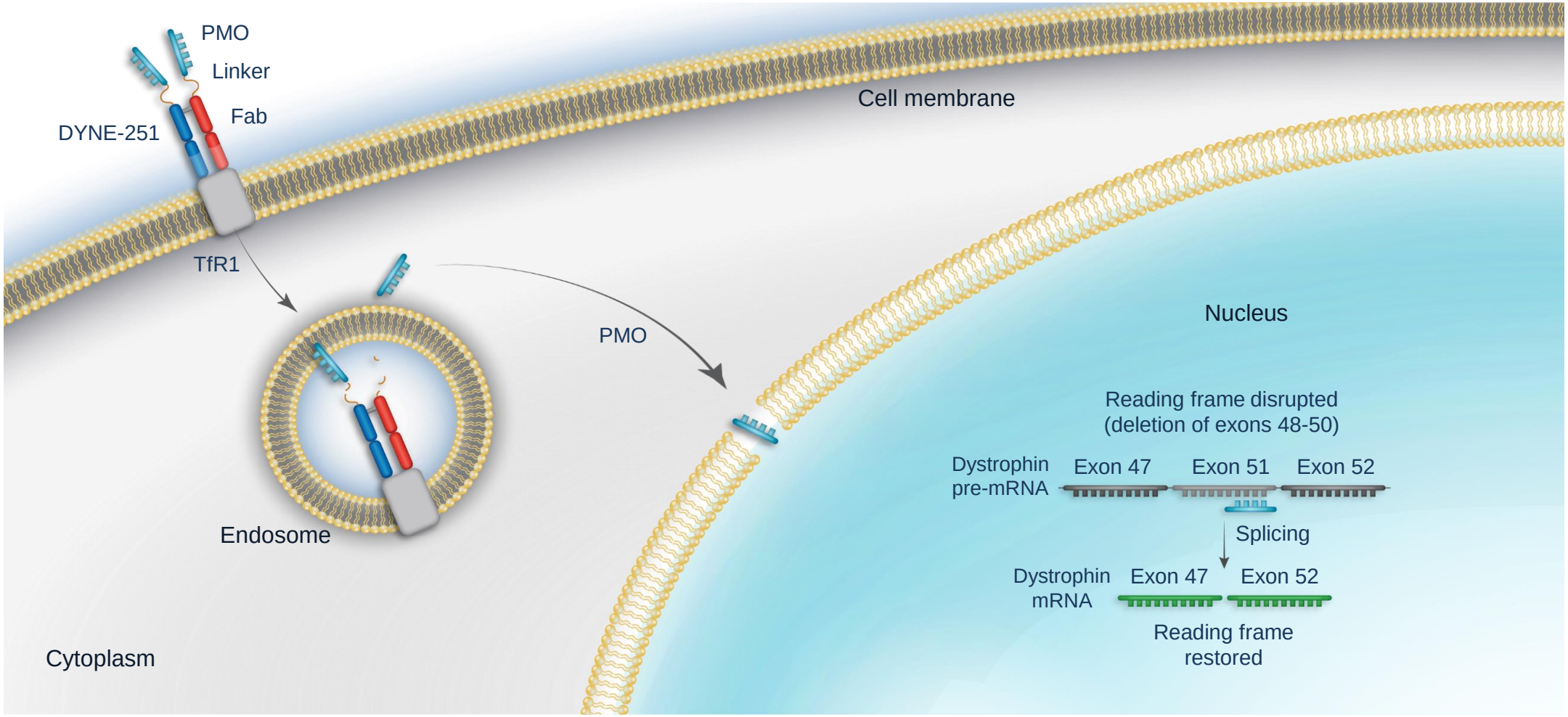
DYNE-251 Is Designed to Leverage TfR1 to Deliver Exon 51-Skipping PMO to Affected Muscle in DMD



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.

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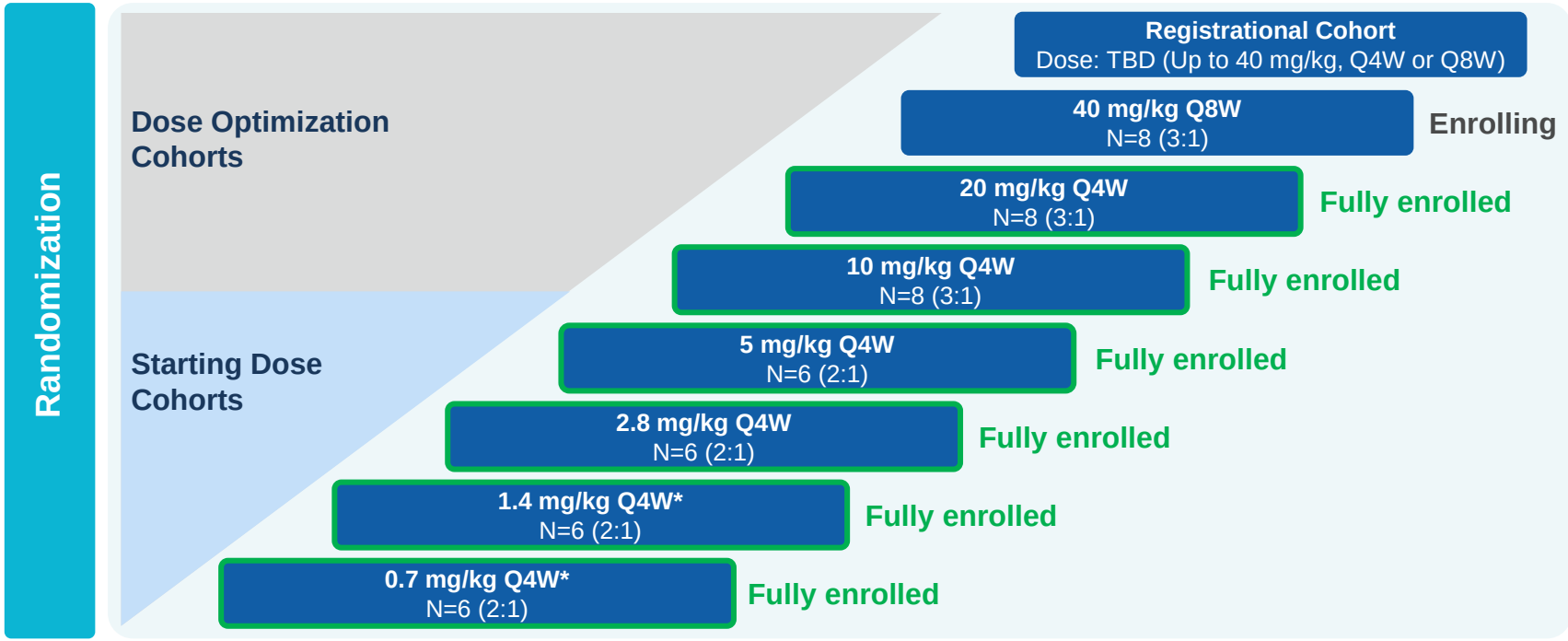
DELIVER: Phase 1/2 Clinical Trial to Evaluate DYNE-251 in Patients with DMD

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 ClinicalTrials.gov Identifier: NCT05524883 or clinicaltrialsregister.eu EudraCT Number: 2021-005478-24

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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 thrombocytopenia [2]
- No participants have demonstrated kidney injury[3]
- 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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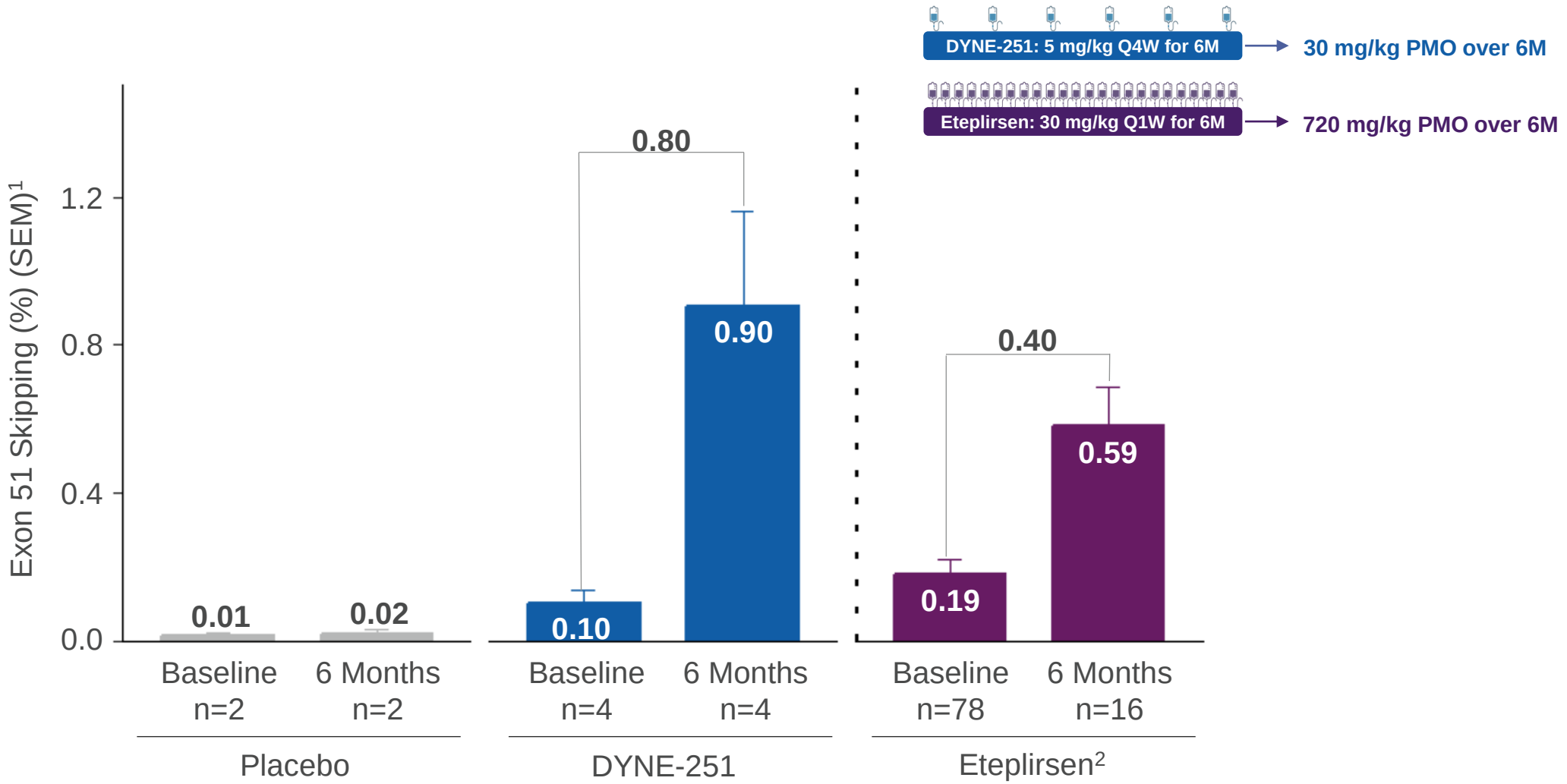
DYNE-251, Dosed Monthly, Showed Increase in Percent Exon Skipping at 6 Months



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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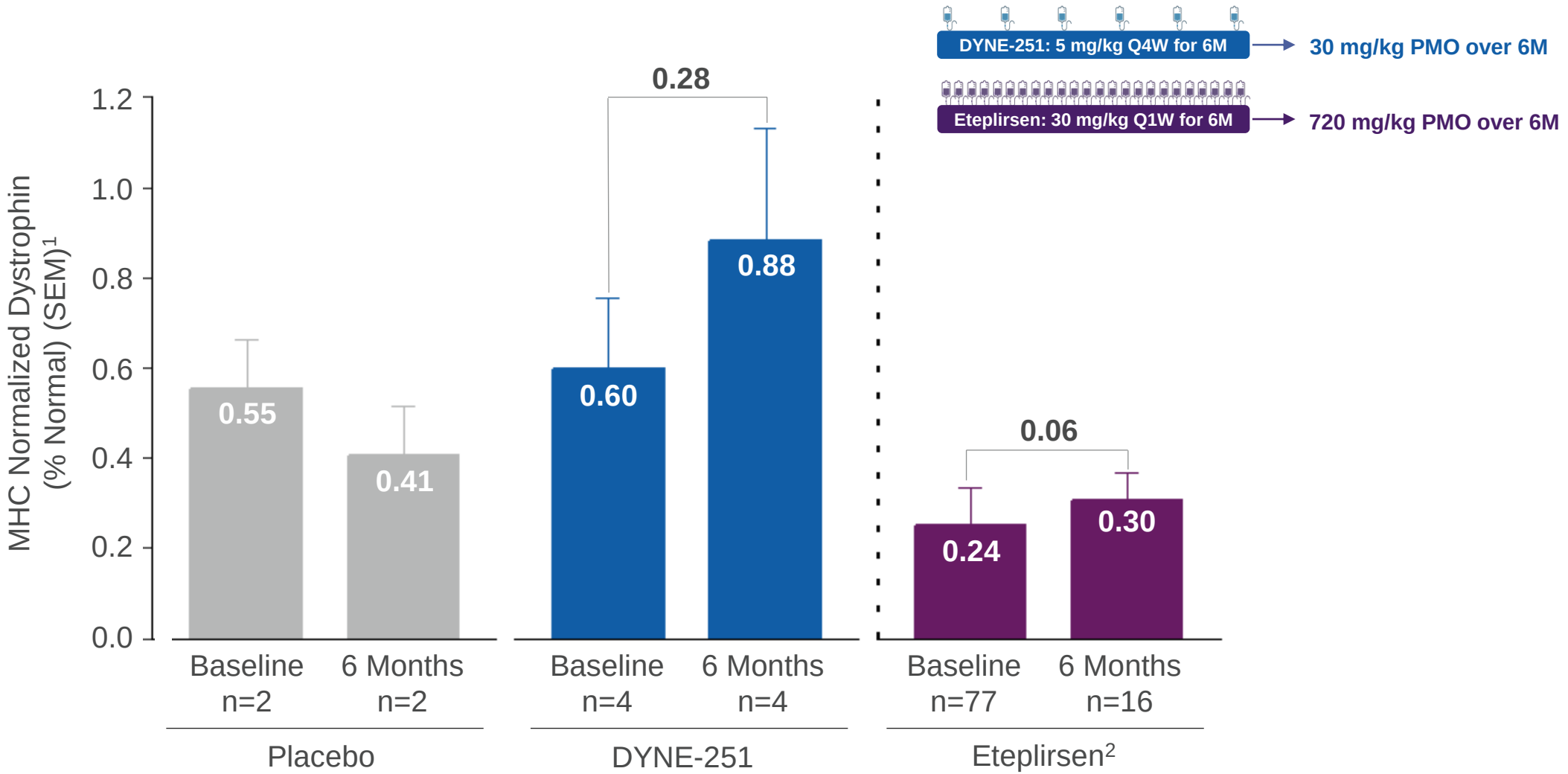
DELIVER

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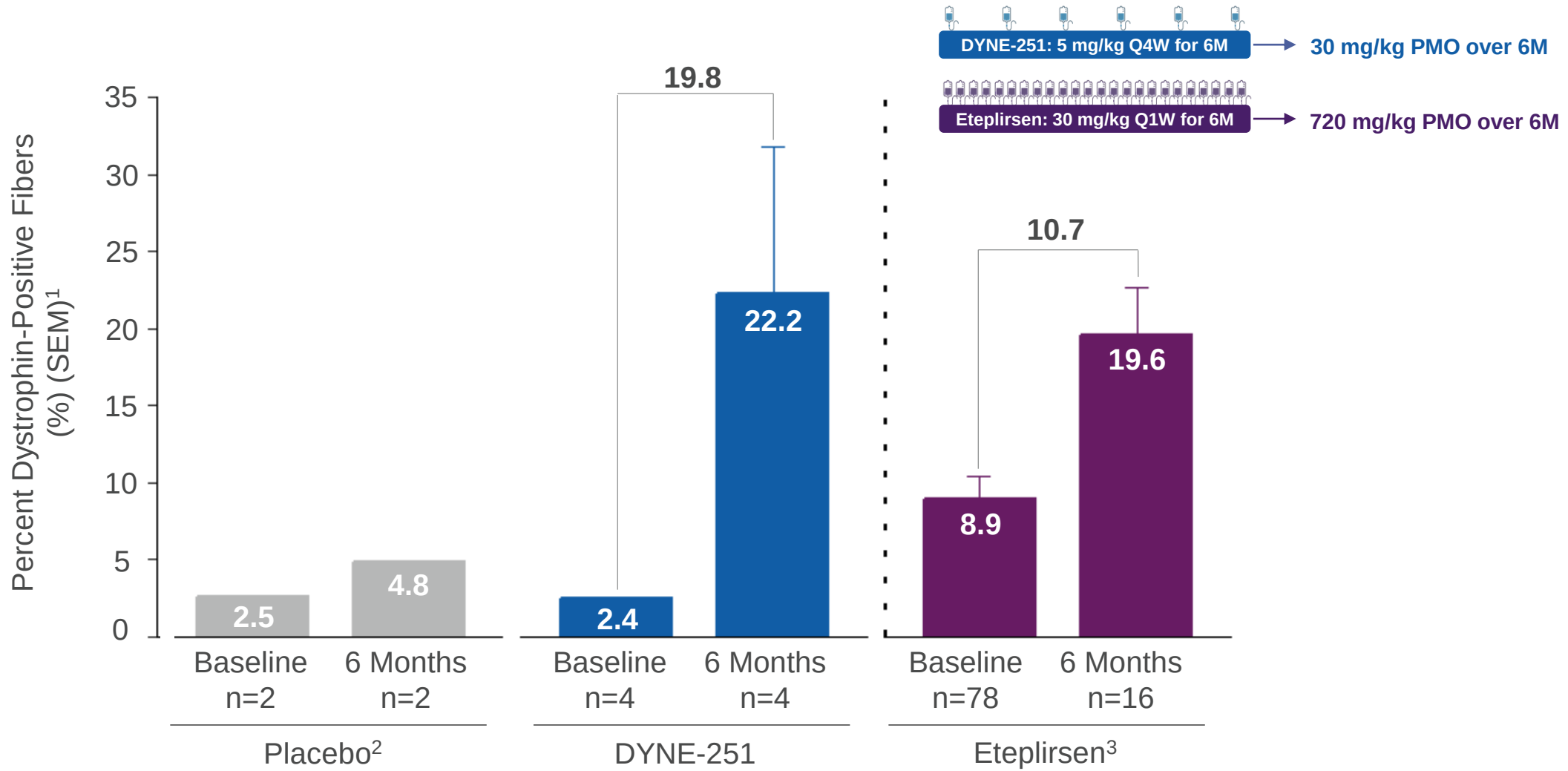
DYNE-251, Dosed Monthly, Showed Increase in Percent Dystrophin Positive Fibers (PDPF) At 6 Months



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 date[1], 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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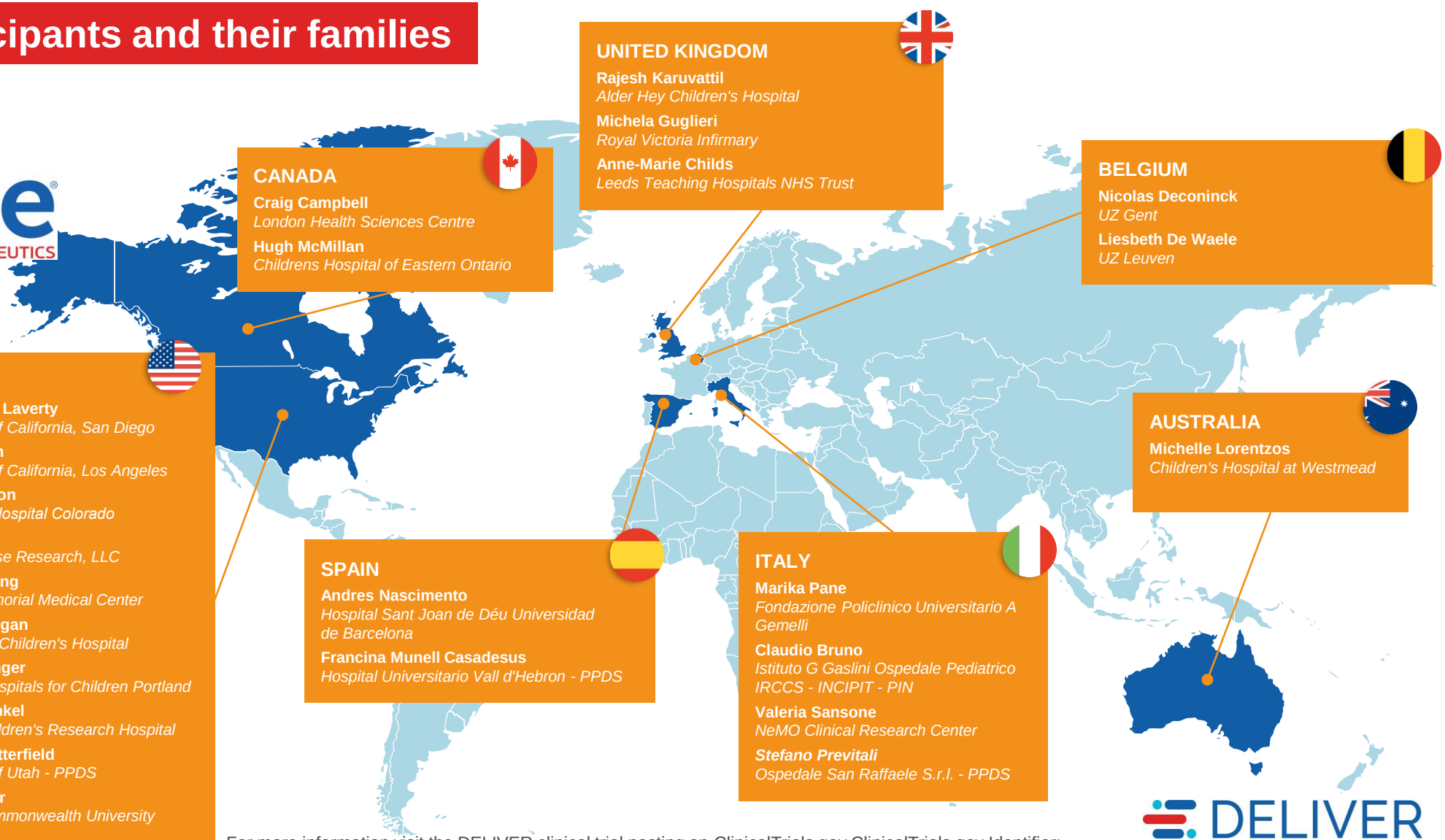
Acknowledgements

DELIVER participants and their families



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For more information visit the DELIVER clinical trial posting on ClinicalTrials.gov ClinicalTrials.gov Identifier: NCT05524883 or clinicaltrialsregister.eu EudraCT Number: 2021-005478-24