DELIVER, a Randomized, Double-blind, Placebo-Controlled, Multiple Ascending Dose Study of DYNE-251 in Boys With DMD Amenable to Exon 51 Skipping

Marc L. Blaylock, Che-Hsien Lin, Sangeeta Haik, Arthur Wagner
Dyne Therapeutics, Inc., Waltham, MA, USA

BACKGROUND

- Duchenne muscular dystrophy (DMD) is characterized by progressive loss of muscle function leading to premature death.1
- Dyne developed the FORCE™ platform, which harnesses the natural expression of transferrin receptor 1 (TfR1) on muscle cells for targeted delivery of oligonucleotides (Figure 1).1,2
- The therapeutic potential of approved, unconjugated phosphorodiamidate morpholino oligomer (PMO) therapeutics for DMD is limited by poor delivery to muscle, especially cardiac muscle, modest production of dystrophin, and frequent dosing.3,4
- DYNE-251 is an exon 51–skipping PMO conjugated to an antigen-binding fragment (Fab) targeting TfR1 (Figure 2).

Figure 1. Dyne FORCE™ Platform: Modern Oligo Therapeutics for Muscle Diseases

Figure 2. DYNE-251s Designed to Target the Genetic Basis of DMD in Patients Amenable to Exon 51 Skipping

METHODS

TRIAL DESIGN AND PATIENT POPULATION

- DELIVER is a Phase 1/2, randomized, double-blind, placebo-controlled, multiple ascending dose (MAD) trial which includes a MAD/placebo-controlled period (24 weeks), an open-label extension period (OLE, 24 weeks), and a long-term extension (LTE) period (96 weeks; Figure 3).
- Approximately 46 patients globally will be enrolled into 7 cohorts: 0.7, 1.4, 2.8, 5, 10, 20, and 40 mg/kg of DYNE-251 (doses refer to PMO component of DYNE-251).
- Participants will be randomized in a 2:1 or in a 3:1 DYNE-251–to–placebo ratio, administered intravenously every 4 weeks during the MAD/placebo-controlled period.
- All patients will be escalated to the highest safe and tolerable dose of DYNE-251 during the OLE and LTE periods.

CONCLUSIONS

- In preclinical studies in mdx mice, FORCE-M23D demonstrated exon skipping and dystrophin expression in skeletal and cardiac muscle and functional improvement.6 In NHPs, DYNE-251 led to pronounced exon 51 skipping in cardiac and skeletal muscle and demonstrated a favorable safety profile.5
- The preclinical data on the use of the FORCE platform supported initiation of clinical development of DYNE-251. The Phase 1/2 DELIVER trial will inform further development of DYNE-251 for the treatment of DMD.

ACKNOWLEDGMENTS: Medical editing and editorial support were provided by Symbiotix, LLC, and funded by Dyne Therapeutics, Inc. DISCLAIMER INFORMATION: All authors are employees of Dyne Therapeutics, Inc. and may hold Dyne stock and/or stock options.

REFERENCES