XXIII CONGRESSO NAZIONALE
Associazione Italiana di Miologia

Robust Preclinical Data Support Development of DYNE-251 as a Potential Treatment for Individuals with DMD Mutations Amenable to Exon 51 Skipping

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Forward-Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding Dyne's strategy, future operations, prospects and plans, objectives of management, the potential of the FORCE platform, the anticipated timelines for reporting data for the DYNE-251 trial, the trial design of the DYNE-251 clinical trial, and the sufficiency of Dyne's existing cash resources for the period anticipated, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," or "would," or the negative of these terms, or other comparable terminology are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Dyne may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including: uncertainties inherent in the identification and development of product candidates, including the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical studies and clinical trials; the timing of and Dyne's ability to initiate and enroll patients in clinical trials; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical trials; whether Dyne's cash resources will be sufficient to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; as well as the risks and uncertainties identified in Dyne's filings with the Securities and Exchange Commission (SEC), including the Company's most recent Form 10-Q and in subsequent filings Dyne may make with the SEC. In addition, the forward-looking statements included in this presentation represent Dyne's views as of the date of this presentation. Dyne anticipates that subsequent events and developments will cause its views to change. However, while Dyne may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Dyne's views as of any date subsequent to the date of this presentation.

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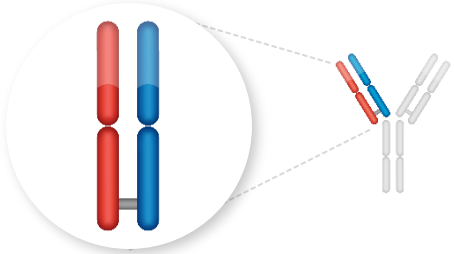
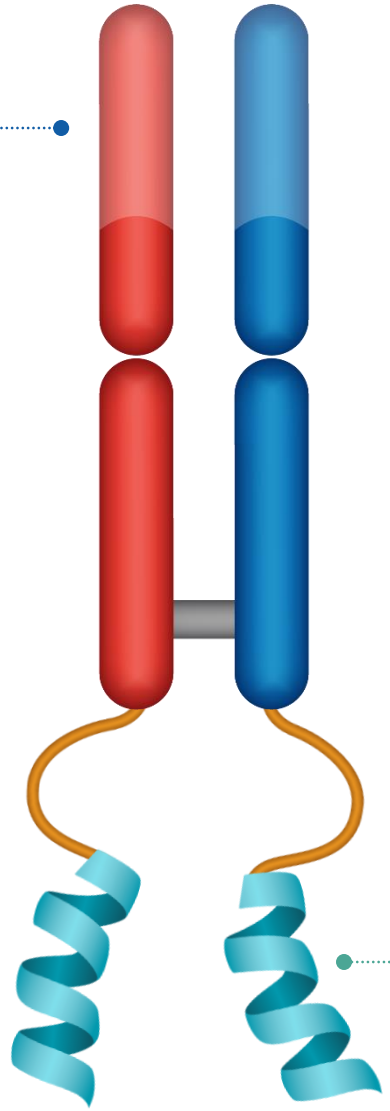
The FORCE platform, FORCE-M23D, and DYNE-251 are investigational or otherwise in development and have not been approved as safe or effective by the FDA or any other regulatory authority.

Dyne FORCE™ Platform: Modern Oligo Therapeutics for Muscle Diseases

ANTIBODY

Proprietary Fab targets TfR1 to enable muscle delivery



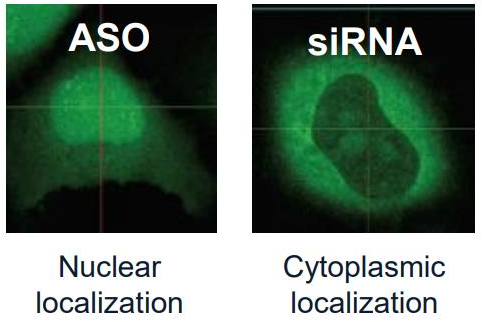


LINKER

Clinically validated, enables precise conjugation of multiple payloads to a single Fab

PAYLOAD

Modularity enables rational selection of payload to target the genetic basis of disease

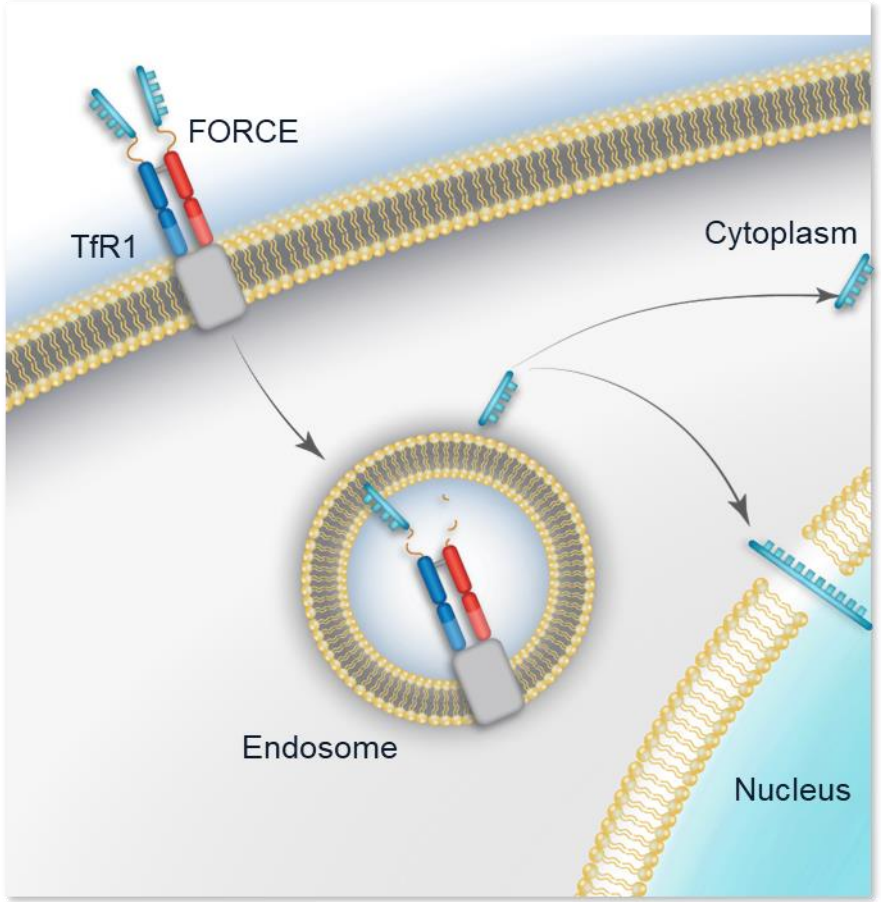


Nuclear localization

Cytoplasmic localization

ASO, antisense oligonucleotide; Fab, antigen biding fragment; siRNA, small interfering ribonucleic acid.
Adapted from Ohrt T., et al. *Nucleic Acids Res* 2006;34:1369.

FORCE™ Platform Harnesses Cell Biology to Modify Disease



- Harnesses natural mechanism of TfR1 receptor-mediated delivery to transport therapeutics across the cell membrane
- Achieves endosomal escape without any membrane-destabilizing agents
- Distinctive pharmacokinetic profile creates opportunity for durable target engagement and wide therapeutic index

TfR1, transferrin receptor 1.

Desjardins CA, et al. Nucleic Acids Res. 2022;50(20):11401-11414.

Building a Global DMD Franchise of Transformative Therapies[1]

Overview

- Mutation in the *DMD* gene that encodes for dystrophin
- Onset in first few years of life
- Life expectancy ~30 years

Clinical Presentation

- Muscle weakness
- Progressive loss of function
- Loss of ambulation
- Respiratory/cardiac failure

Population

- ~12,000 - 15,000 (US)
- ~ 25,000 (Europe)

Current Approved Exon 51 Therapies Only Increased Dystrophin Production[2] <1%

OUR APPROACH

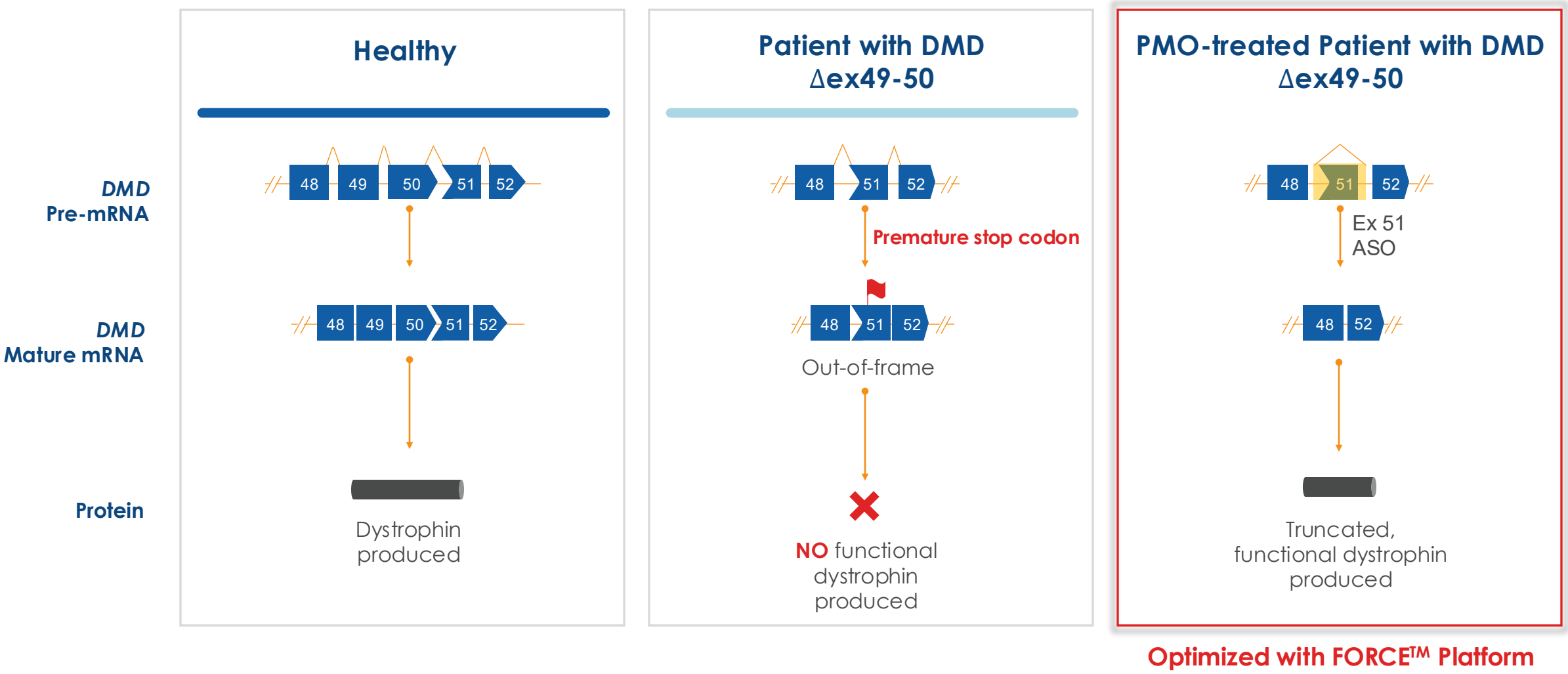
Best-in-class Targeted Exon Skipping

Increase dystrophin expression and enable less frequent dosing to potentially **stop or reverse disease progression**

DMD, Duchenne Muscular Dystrophy.

1. Desjardins CA, et al. Nucleic Acids Res. 2022;50(20):11401-11414.
2. EXONDYS51 - United States Prescribing Information (USPI).

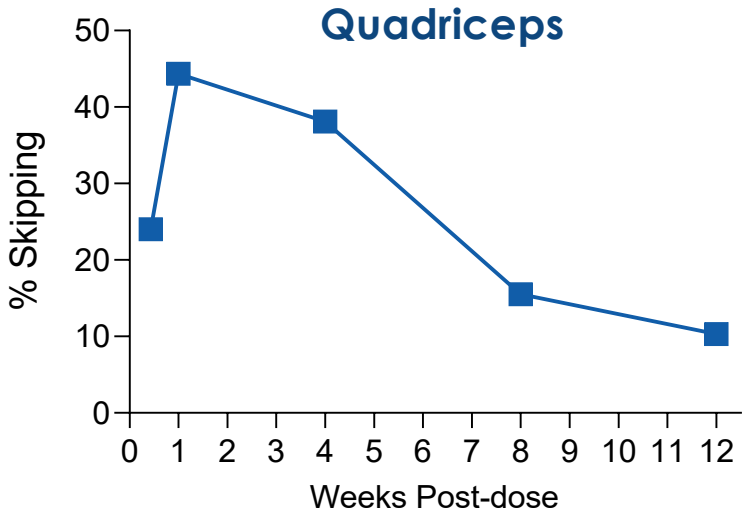
Targeting the Genetic Basis of DMD with a Proven Mechanism

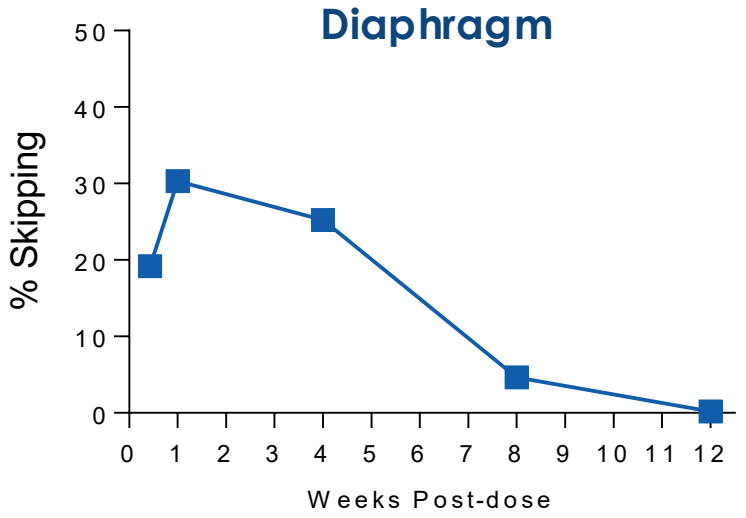


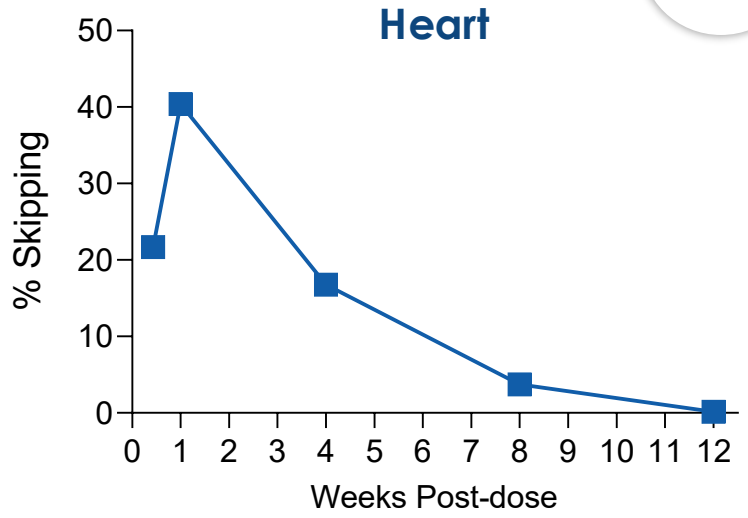
Optimized with FORCE™ Platform

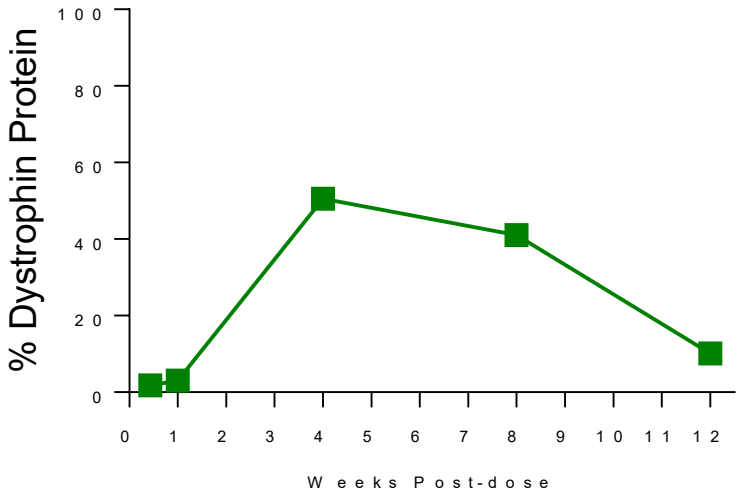
PMO, phosphorodiamidate morpholino oligomer; DMD, Duchenne muscular dystrophy; ex, exon; mRNA, messenger RNA.
Adapted from Lim KRQ., et al. Drug Des Devel Ther 2017;11:533.

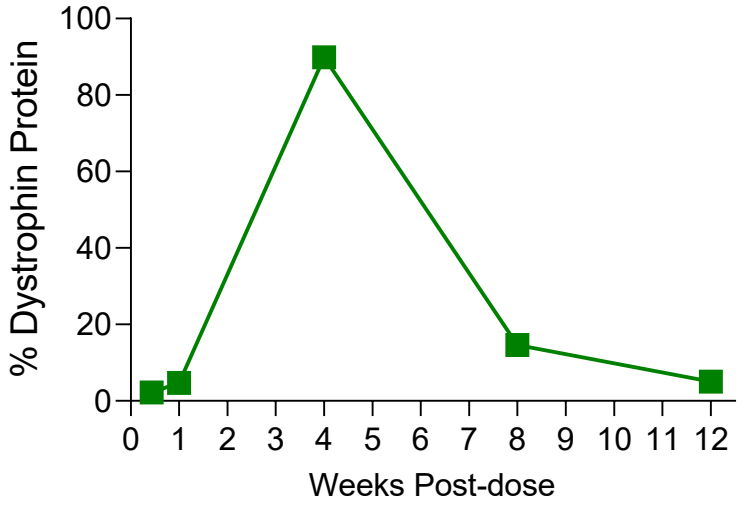
FORCE Achieved Robust and Durable Skipping and Dystrophin Expression in Cardiac and Skeletal Muscle

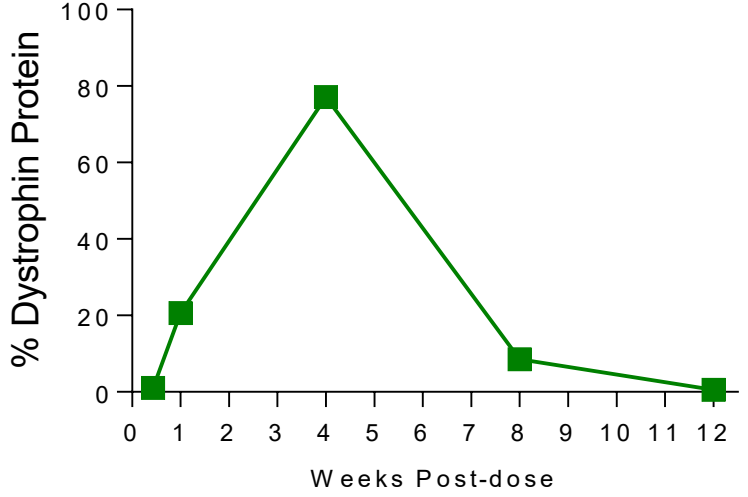












Note: Single IV 30 mg/kg dose of FORCE-M23D in mdx mouse model on day 0; N = 3- 5 per cohort.

Desjardins CA. Nucleic Acids Res 2022;50:11401-11414.

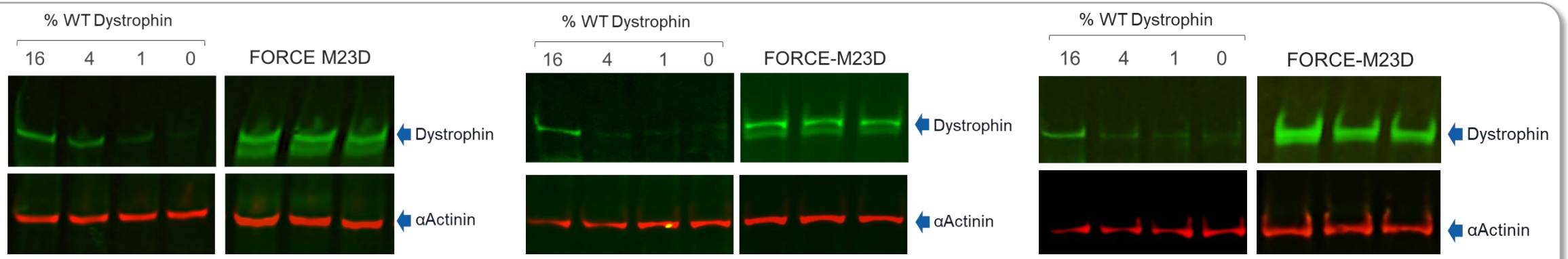
FORCE Achieved Robust and Durable Dystrophin Expression and Sarcolemma Localization in Muscle

Quadriceps

Diaphragm

Heart

Dystrophin expression by WB

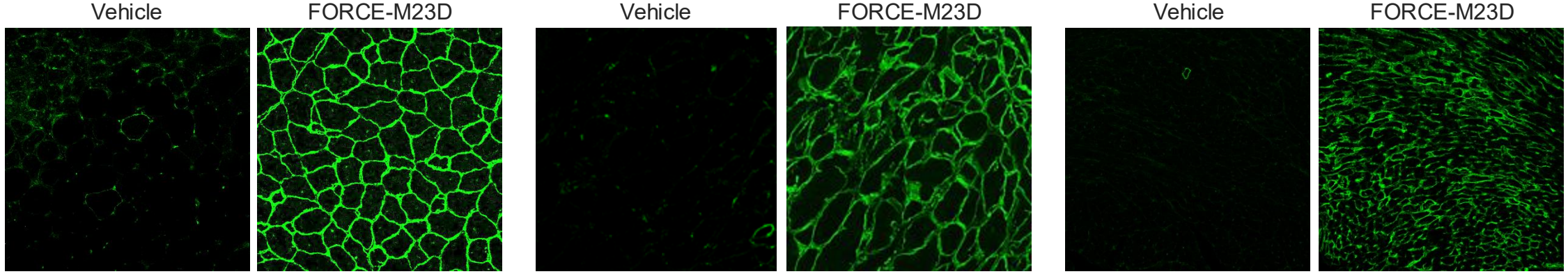


51% of wild-type dystrophin

90% of wild-type dystrophin

77% of wild-type dystrophin

Dystrophin localization to sarcolemma



68% dystrophin-positive fibers

~80% dystrophin-positive fibers

~80% dystrophin-positive fibers

Single 30 mg/kg IV dose of FORCE-M23D in mdx mouse model on day 0; analysis on week 4 for all muscles. N= 3 - 5 per cohort.

Desjardins CA. Nucleic Acids Res 2022;50:11401-11414.

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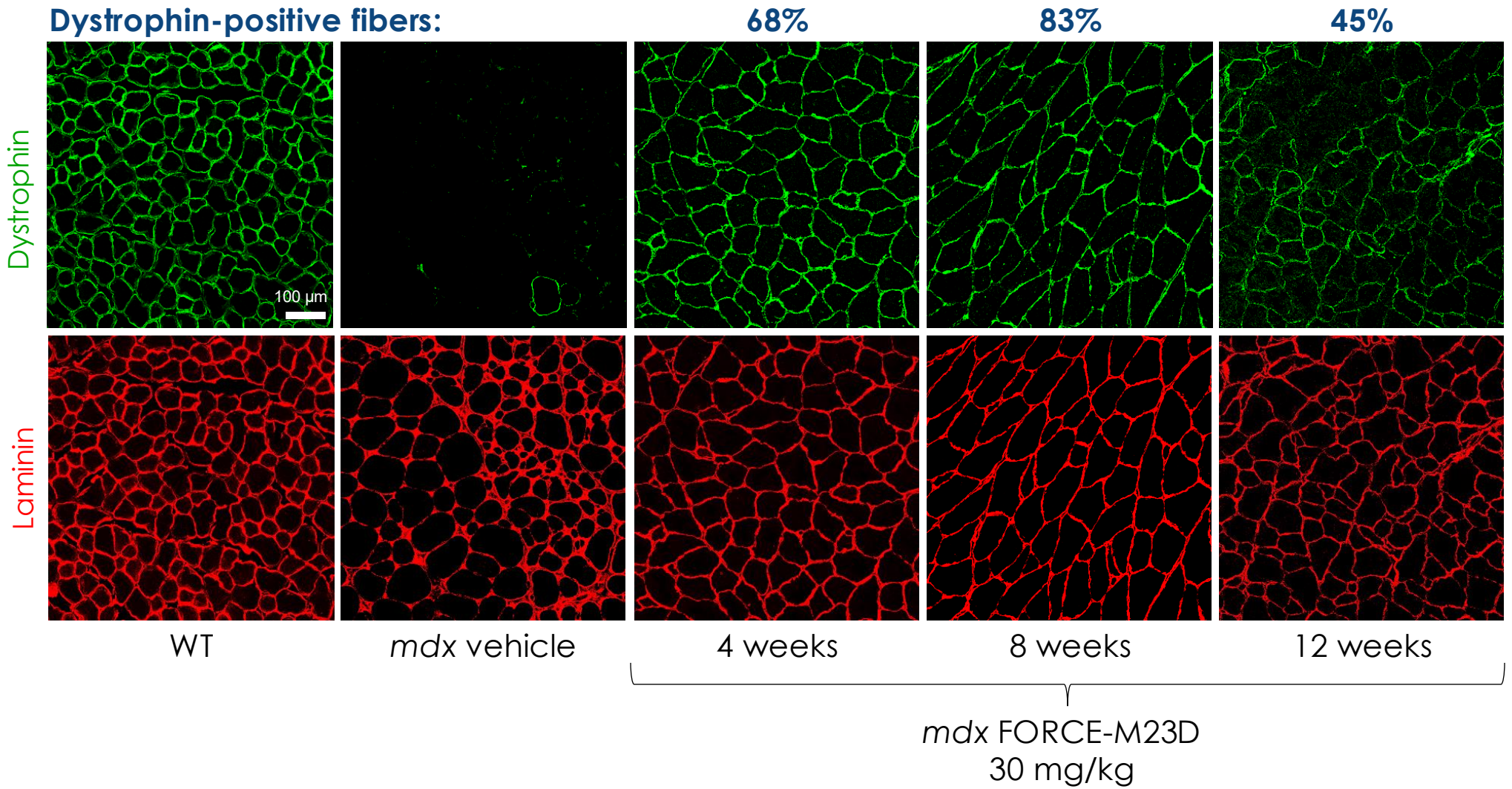
FORCE-M23D Achieved Durable Dystrophin Localization to Sarcolemma in Quadriceps

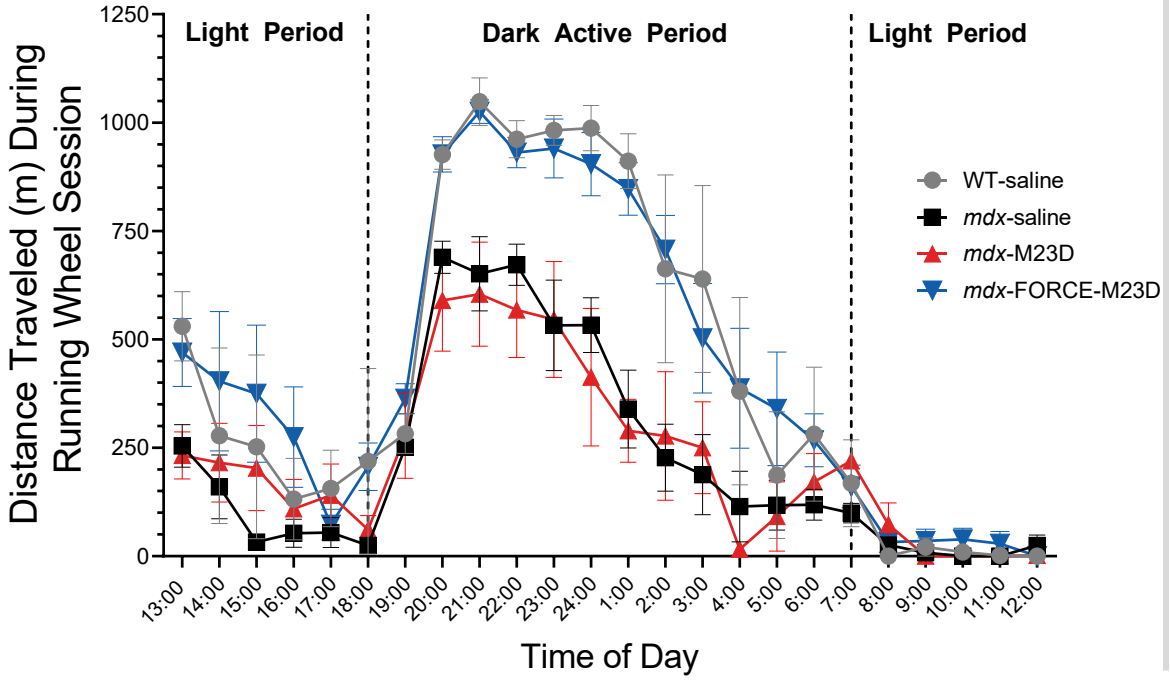


WT, wild-type.
Note: mdx mice injected via tail vein with vehicle or 30 mg/kg PMO-equivalents of FORCE–M23D. .
Desjardins C. et al., Nucleic Acids Res. 2022 Aug 10:gkac641. doi: 10.1093/nar/gkac641.
The FORCE platform, FORCE-M23D, and DYNE-251 are investigational or otherwise in development and have not been approved as safe or effective by the FDA or any other regulatory authority.

FORCE-M23D Demonstrated Functional Benefit in mdx Mice

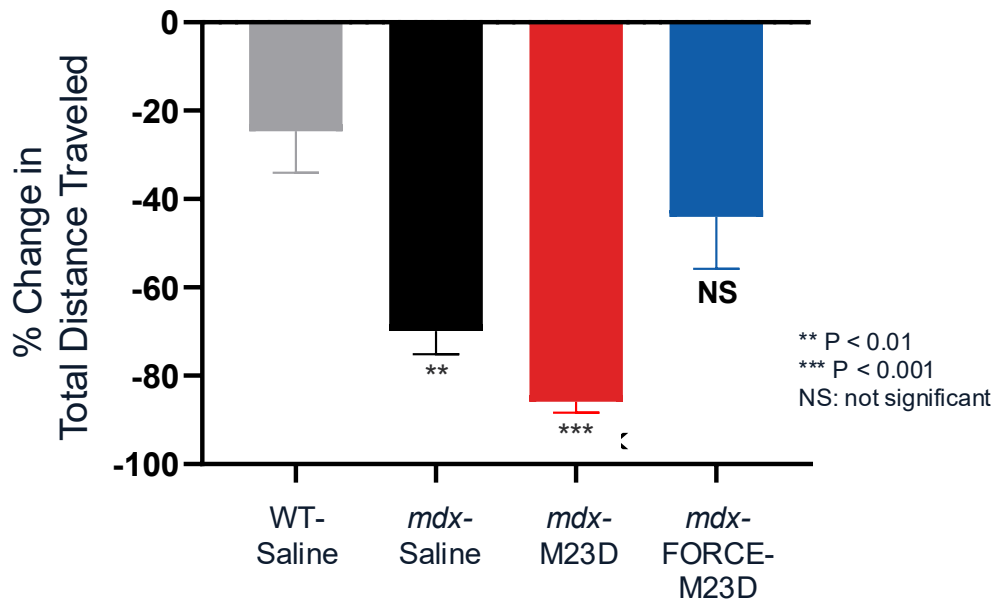
Distance traveled in home cage running wheel

(Assessed 4 weeks after treatment)



Distance traveled in open field following hind limb fatigue challenge

(Assessed 2 weeks after treatment)



WT, wild-type.
Single 30 mg/kg IV dose. Hind limb fatigue challenge test statistical analysis comparison to wild type (WT) group using one-way ANOVA followed by post-hoc Dunnett's test.
Desjardins CA. Nucleic Acids Res 2022;50:11401-11414.
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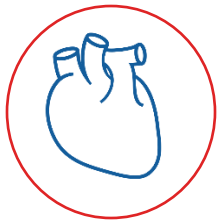
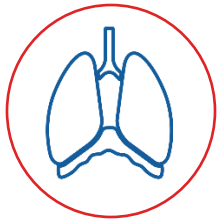
DYNE-251 Demonstrated Robust Exon Skipping & Favorable Safety Profile in NHPs[1,2]

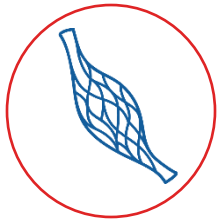
High Level of Exon 51 Skipping Achieved in Key Muscles at 2 Months[a]



43% in heart



52% in diaphragm



18% in quadriceps

GLP Toxicology Studies: 5-Week & 13-Week[b]

- No dose limiting toxicity observed up to a maximally feasible dose
- No changes in cardiac, respiratory, neurologic or ophthalmic endpoints
- No effect on kidney function
- No effect on liver function
- No effect on coagulation
- NOAEL was identified at the highest dose tested

GLP, Good Laboratory Practice; NHPs; non-human primates; NOAEL: No-observed-adverse-effect level.

Notes: a. Based on 5 weekly doses (Week 0 – Week 4) with tissue analysis at 8 weeks. b. Based on conclusions of report from third-party CRO

1. Beskrovnaya O. MSG Annual Meeting 2021. 2. Desjardins CA, et al. Poster presented at: 27th International Hybrid Annual Congress of the World Muscle Society; October 11-15, 2022; Halifax, Canada

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

Population

- Patients with DMD with mutations amenable to exon 51 skipping therapy
- Ages 4 to 16 years
- ~48 male participants
- Ambulant and non-ambulant

Primary Endpoints

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

Key Secondary Endpoints

- Pharmacokinetics
- Change from baseline of:
  - Exon 51 skipping levels
  - Muscle tissue PDPF
  - Multiple assessments of muscle function, including NSAA score and certain timed functional tests

Stages of DELIVER

- Multiple Ascending Dose (MAD): 24 weeks
- Open-Label Extension (OLE): 24 weeks
- Long-Term Extension (LTE): 96 weeks

Initial Safety, Tolerability & Dystrophin Data Expected in H2 2023

DMD, Duchenne Muscular Dystrophy; MAD, multiple ascending dose; NSAA North Star Ambulatory Assessment; OLE, open-label extension; LTE, long-term extension; PDPF, percent dystrophin-positive fibers.

ClinicalTrials.gov,NCT05524883. EudraCT Number: 2021-005478-24

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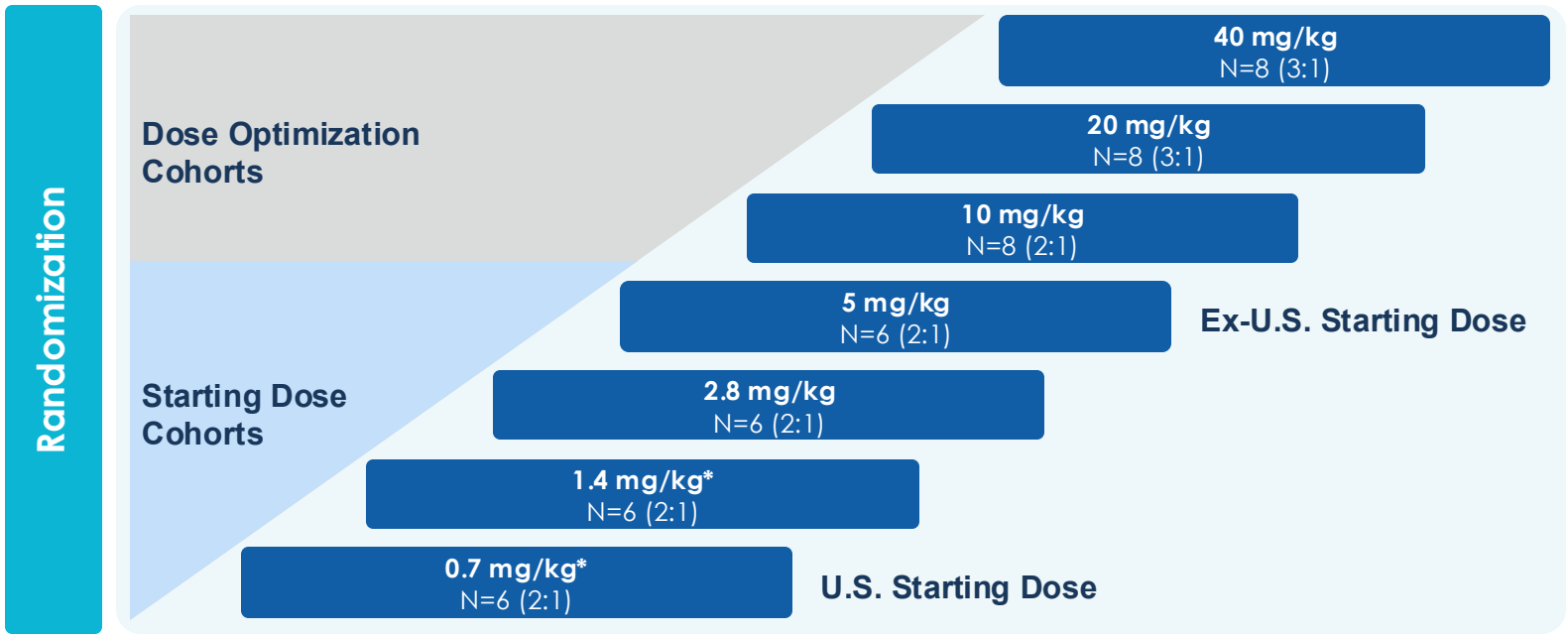
Multiple Ascending Dose Stage of DELIVER

Global, Randomized, Placebo-Controlled Stage Evaluating Once Monthly Administration of DYNE-251 in ~48 Ambulant and Non-Ambulant Male DMD Patients with Mutations Amenable to Exon 51 Skipping Therapy



MAD Study Details

- IV administration of DYNE-251 or placebo every 4 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 Enable Rapid Achievement of Predicted Pharmacologically Active Dose Levels

DMD, Duchenne Muscular Dystrophy; MAD, multiple ascending dose; OLE, open-label extension; LTE, long-term extension.
Patient cohorts will be dosed from 0.7 mg/kg to 40 mg/kg in the U.S. Outside the U.S., patient cohorts will be dosed from 5 mg/kg to 40 mg/kg. Doses provided refer to PMO component of DYNE-251.
Muscle biopsies taken at baseline and 24 weeks in 2.8 mg/kg and higher cohorts; biopsies not taken in 0.7 mg/kg and 1.4 mg/kgcohorts
Dugar A, 2022 NMSG Annual Meeting.
ClinicalTrials.gov,NCT05524883. EudraCT Number: 2021-005478-24
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DELIVER Study: Inclusion and Exclusion Criteria

Inclusion Criteria*

- Age 4 to 16 years inclusive, at the time of informed consent/assent
- Male with a confirmed DMD mutation in the dystrophin gene characterized by exon deletion amenable to exon 51 skipping
- Upper extremity muscle group that is amenable to muscle biopsy
- Brooke Upper Extremity Scale score of 1 or 2
- Ambulatory or non-ambulatory (non-ambulatory participants must have been non-ambulatory for <2 years before enrollment)
- Receiving a stable dosage of glucocorticoids for at least 12 weeks prior to the start of study drug administration
- Left ventricular ejection fraction of ≥50% by echocardiogram or ≥55% by cardiac MRI

Exclusion Criteria*

- Uncontrolled clinical symptoms and signs of CHF
- Any change in prophylaxis/treatment for CHF within 3 months prior to the start of study treatment
- History of major surgical procedure within 12 weeks prior to the start of study drug administration or an expectation of a major surgical procedure during the study
- Requirement of daytime ventilator assistance
- Percent predicted FVC <40% (applies only for participants who are ≥7 years of age)
- Receipt of eteplirsen, or alternative exon-skipping/dystrophin-modifying therapy within 12 weeks of randomization
- Receipt of non-exon skipping investigational drug within 4 months before the start of study drug administration
- Receipt of gene therapy at any time

** Other inclusion and exclusion criteria may apply.*
CHF, congestive heart failure; DMD, Duchenne Muscular Dystrophy; FVC, Forced Vital Capacity; MRI, Magnetic Resonance Imaging.
ClinicalTrials.gov,NCT05524883. EudraCT Number: 2021-005478-24
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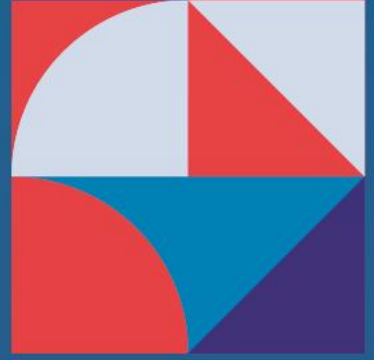
Summary

- The FORCE™ platform was designed to overcome the limitations of oligonucleotide delivery to muscle for the treatment of rare neuromuscular disorders[1]
- In the mdx mouse model of DMD, FORCE-M23D achieved robust and durable exon skipping in skeletal and cardiac muscles, and demonstrated functional benefit[1]
- DYNE-251 demonstrated robust exon 51 skipping and has a favorable safety profile in NHPs[2]
- The safety, tolerability, PK, and PD of DYNE-251 are being investigated in the ongoing Phase 1/2 clinical trial (DELIVER)[3]

DMD, Duchenne Muscular Dystrophy; NHPs, non-human primates, PK, pharmacokinetics, PD, pharmacodynamics.

Acknowledgements

- DELIVER participants and their families
- DELIVER investigators and site staff
- Dyne co-authors : Ester Cotali, Maria L. Naylor, Cody A. Desjardins, Reshmii Venkatesan, Emma O'Donnell, John Hall, Ryan Russo, Sean Spring, Kim Tang, John W. Davis II, Timothy Weeden, Stefano Zanotti, Chris Mix, Baoguang Han, Oxana Beskrovnaya, Ashish Dugar



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