



Building the World's Leading Muscle Disease Company

39TH ANNUAL
J.P. MORGAN HEALTHCARE CONFERENCE
JANUARY 13, 2021

Joachim, living with DM1

Forward-Looking Statements

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OUR MISSION

Life-transforming therapies
for patients with serious muscle diseases

Dyne – Building the Leading Muscle Disease Company

Proprietary FORCE Platform



- Modern oligo therapeutics for muscle diseases
- Overcoming challenge of muscle delivery
- Plug-and-play therapeutics for multiple targets in skeletal, cardiac and smooth muscle diseases

Rare Muscle Disease Focus



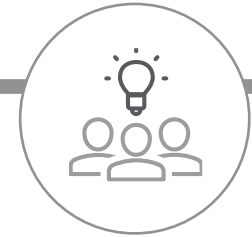
- Robust pipeline: DM1, DMD, and FSHD
- Set standard for evaluating PD in DM1 disease model
- Demonstrated functional benefit in DM1 and DMD models
- Significant market opportunities

Delivering for Patients



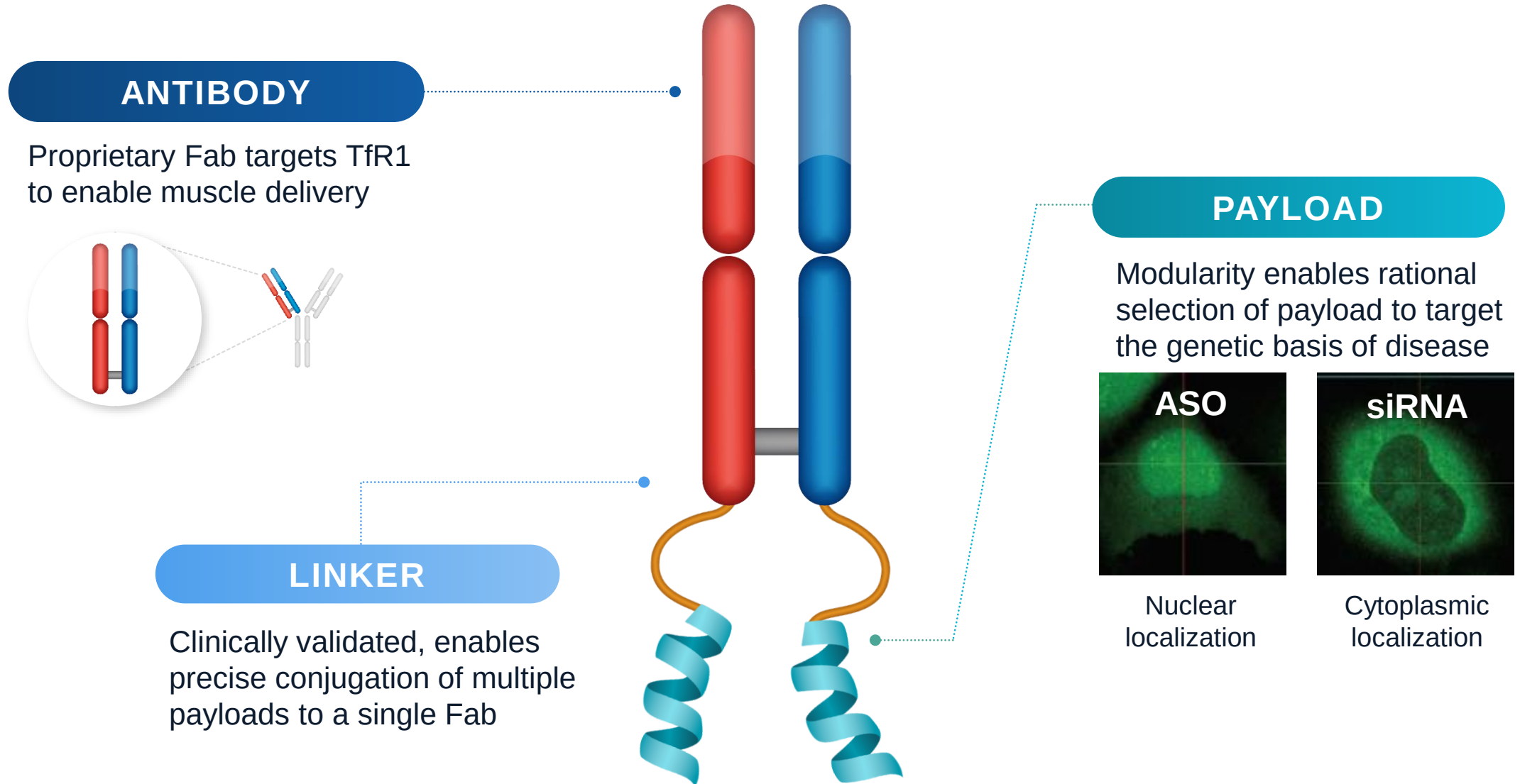
- Developing multiple first-in-class or best-in-class therapies
- Precision medicine strategy
- Three INDs planned between Q4 2021 - Q4 2022

Exceptional Team



- Deep knowledge of muscle diseases and novel therapeutic modalities
- World-class scientific advisory board
- Supported by leading healthcare investors

Dyne FORCE Platform: Modern Oligo Therapeutics for Muscle Diseases

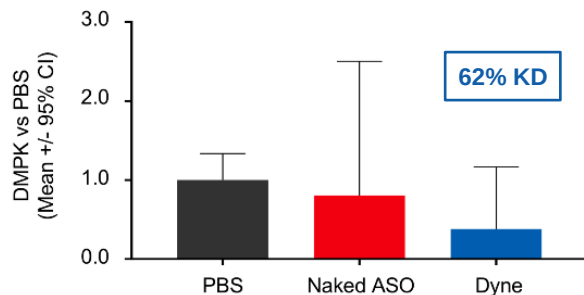


Robust Portfolio Focused on Muscle Diseases

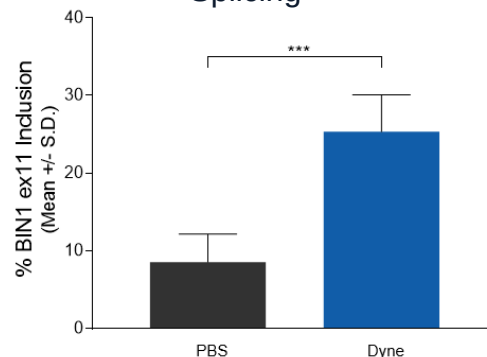
PROGRAM	TARGET	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ESTIMATED PATIENTS
Myotonic Dystrophy (DM1)	DMPK						US: >40,000 Europe: >74,000
Duchenne Muscular Dystrophy (DMD)	Exon 51 Exon 53 Exon 45 Exon 44						US: ~12,000-15,000 Europe: ~25,000
Facioscapulohumeral Muscular Dystrophy (FSHD)	DUX4						US: ~16,000-38,000 Europe: ~35,000
Pipeline Expansion Opportunities							
Rare Skeletal Cardiac Metabolic							

FORCE Demonstrated Functional Benefit Across Multiple Indications and Disease Models

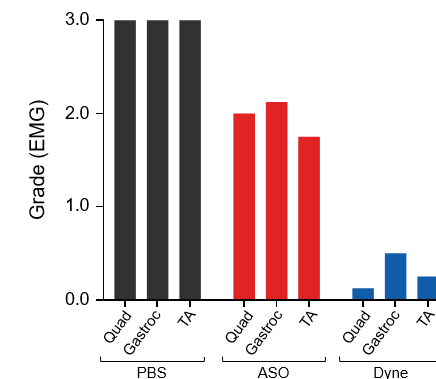
DMPK Knockdown Gastrocnemius



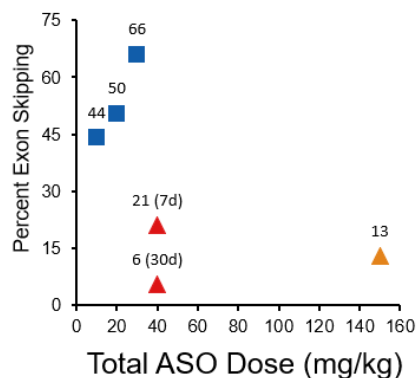
Splicing Changes Splicing



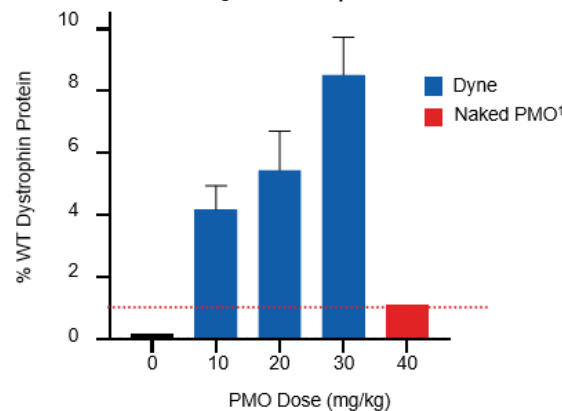
Functional Benefit Myotonia



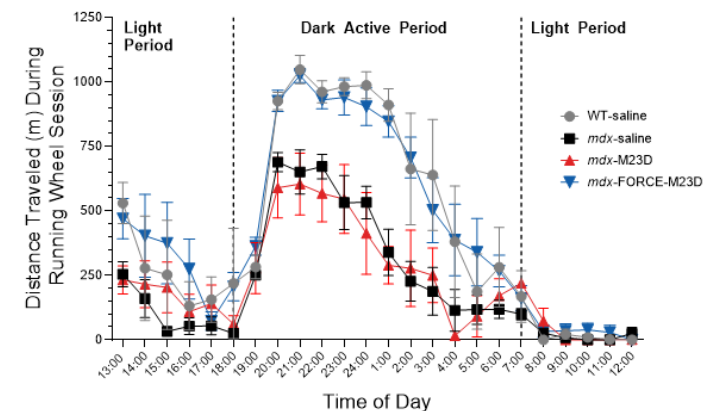
Exon Skipping Quadriceps



Dystrophin Expression Quadriceps



Functional Benefit Home Cage Running Wheel



DM1 Program



Overview

- Mutation in the *DMPK* gene
- Onset at any point, depending on DM1 phenotype
- Life expectancy of 45 - 60 years



Clinical Presentation

- Myotonia
- Muscle weakness
- Cardiac arrhythmia
- Pulmonary abnormalities



Population

- >40,000 (US)
- >74,000 (Europe)



NO
approved
therapies

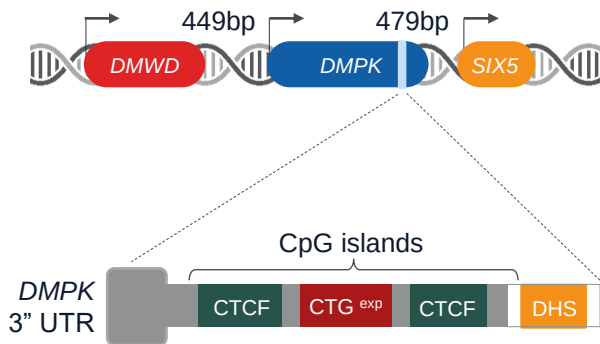
OUR APPROACH

Disease-Modifying Nuclear *DMPK* Knockdown

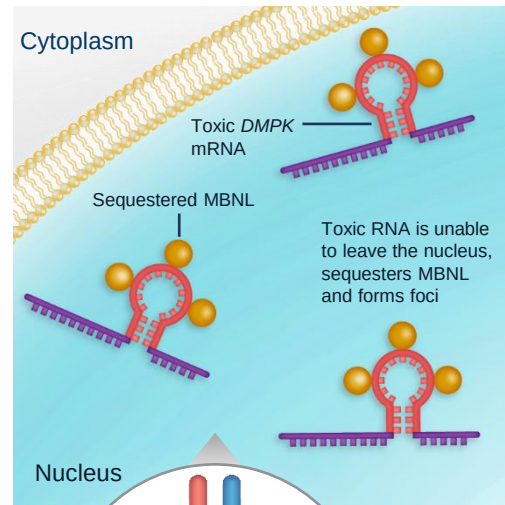
Targeting toxic gain of function *DMPK* RNA to potentially **stop or reverse** disease progression

FORCE Targets the Genetic Basis of DM1

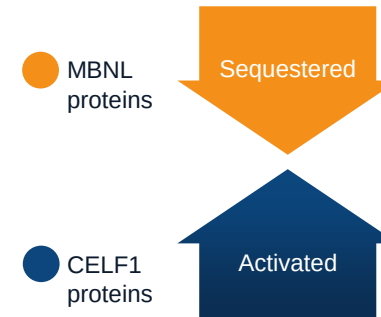
DNA Triplet Repeats



Toxic RNA Forms Foci



RNA Binds Splicing Proteins



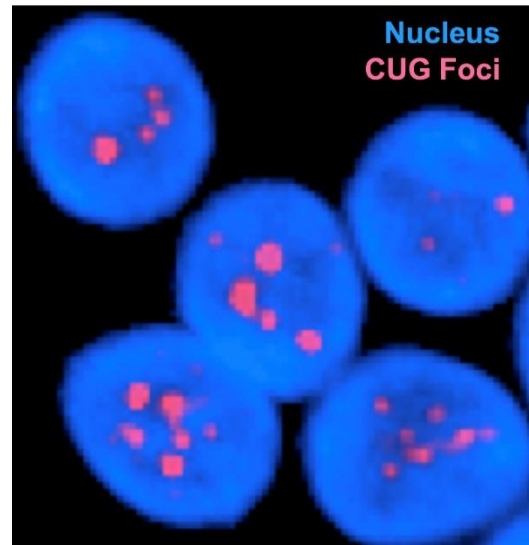
Clinical Presentation

- Myotonia
- Muscle weakness
- Cardiac arrhythmia
- Pulmonary abnormalities

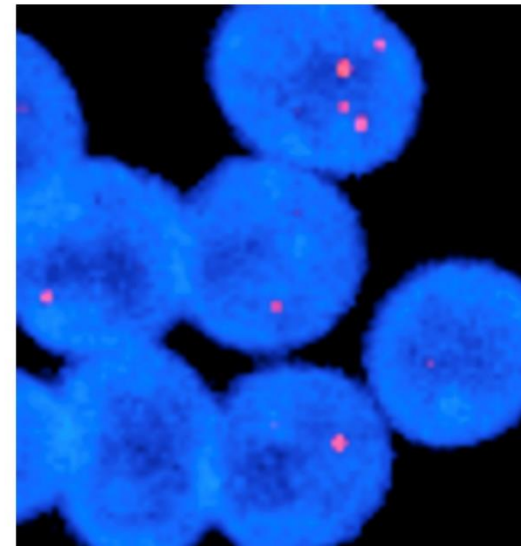
FORCE designed to address the genetic basis of disease by **targeting toxic nuclear *DMPK* RNA**

FORCE Targets Toxic Nuclear *DMPK* RNA and Reduced Nuclear CUG Foci in DM1 Patient Cells

PBS

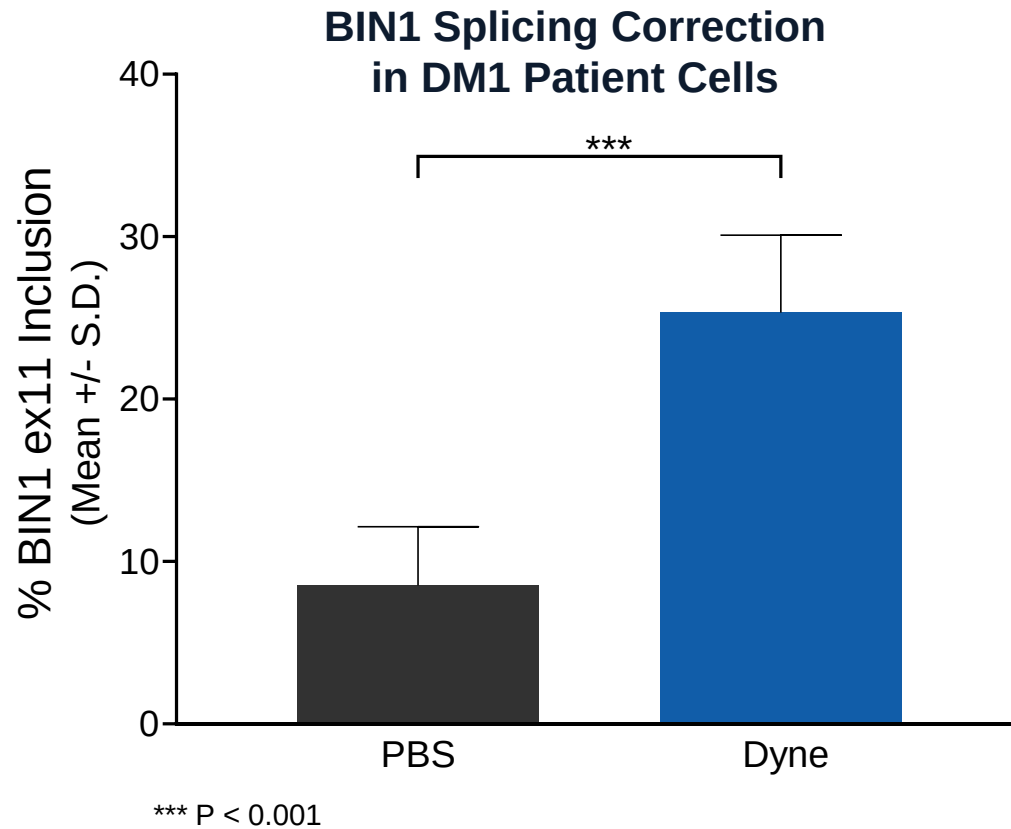


Dyne



Single Dose of FORCE Reduced Nuclear Foci by Approximately 40%

FORCE Targets Toxic Nuclear *DMPK* RNA and Corrected Splicing



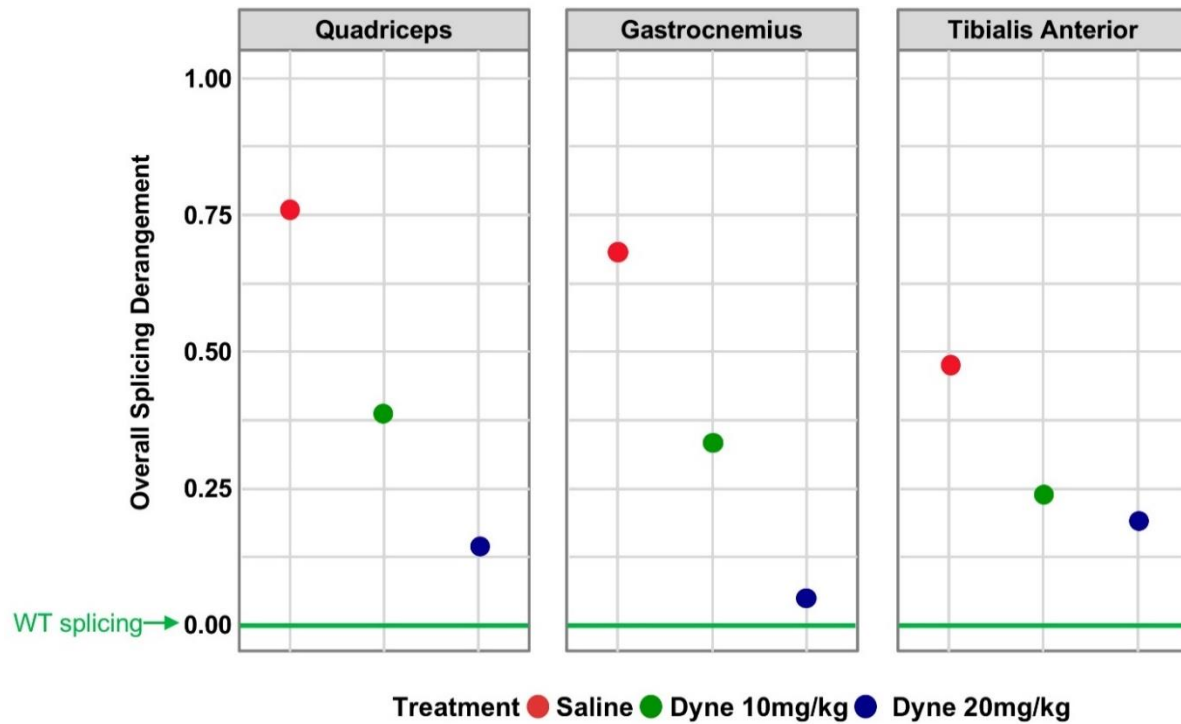
Single Dose of FORCE Fab + linker + oligo

- Targets toxic nuclear *DMPK* RNA
- Released splicing proteins
- Corrected BIN1 splicing as indicated by increased exon 11 inclusion

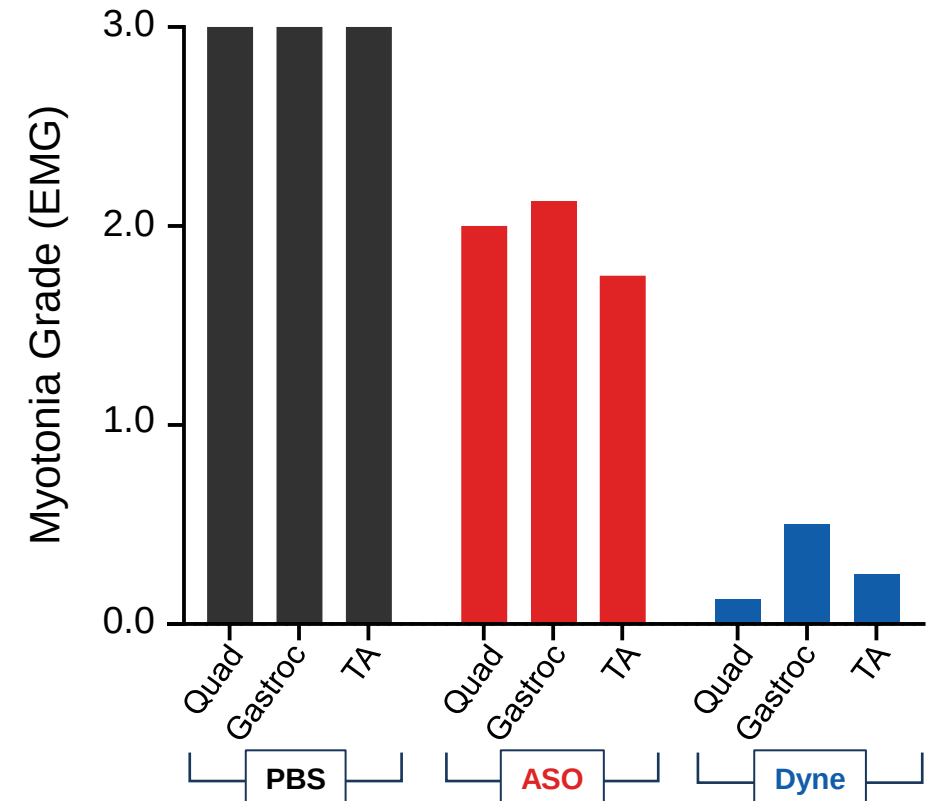
FORCE Nuclear KD of Toxic *DMPK* Corrected Splicing in DM1 Patient Cells

FORCE Dose-Dependently Corrected Splicing and Reversed Myotonia in the HSA^{LR} DM1 Mouse Model

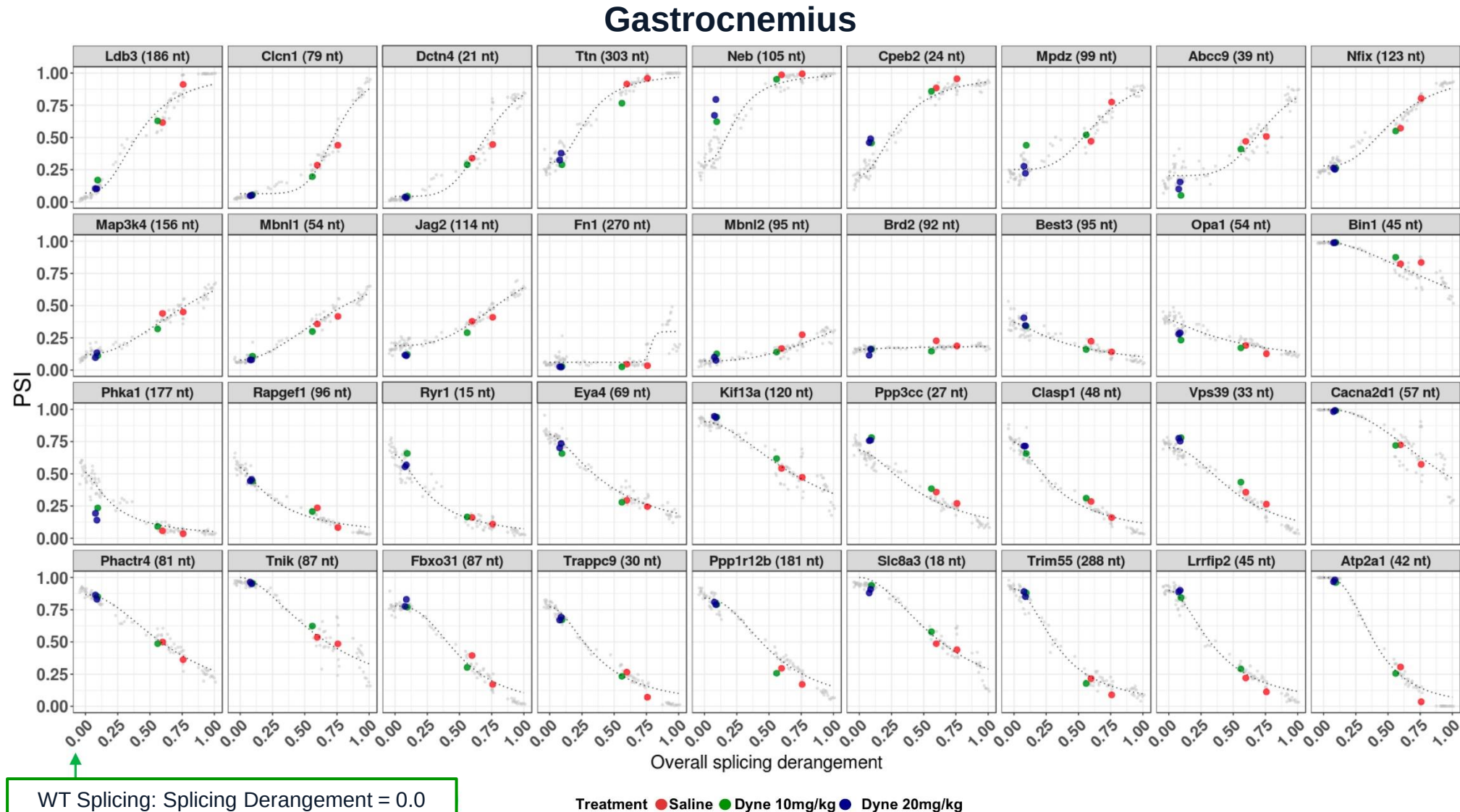
Splicing Correction in Multiple Muscles



Near Complete Myotonia Reversal Within 14 Days After a Single Low Dose

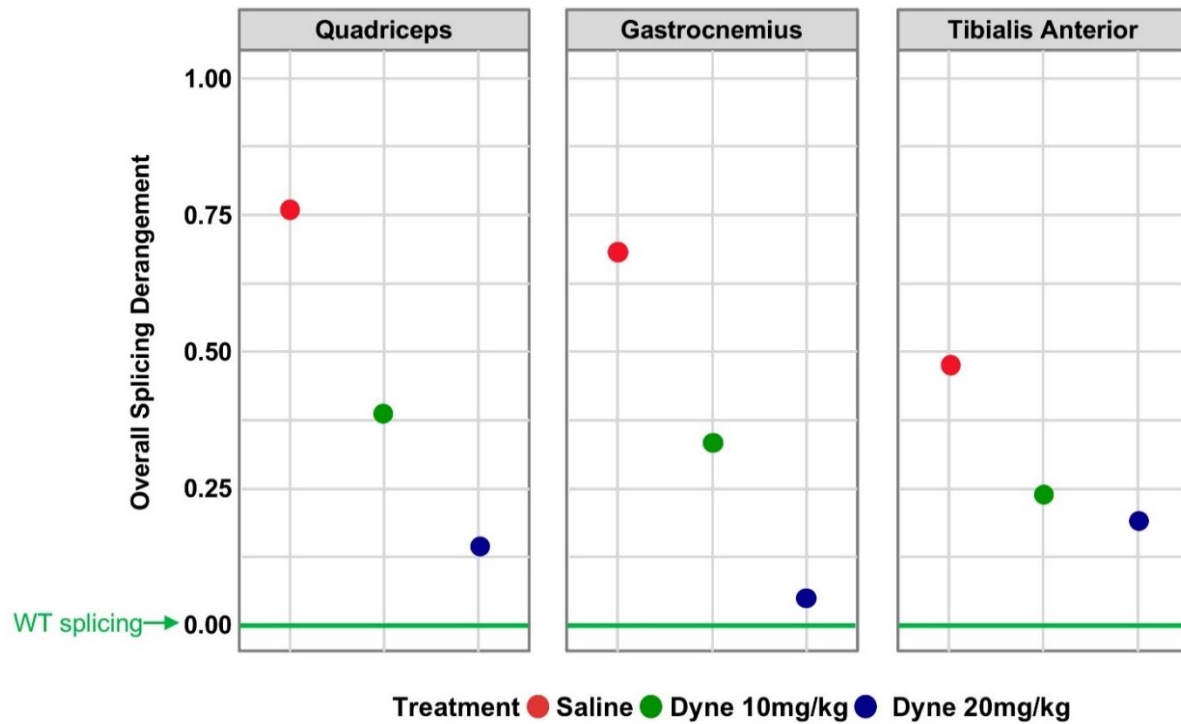


FORCE Dose-Dependently Corrected Splicing in Multiple RNAs in HSA^{LR} DM1 Mouse Model After a Single Dose

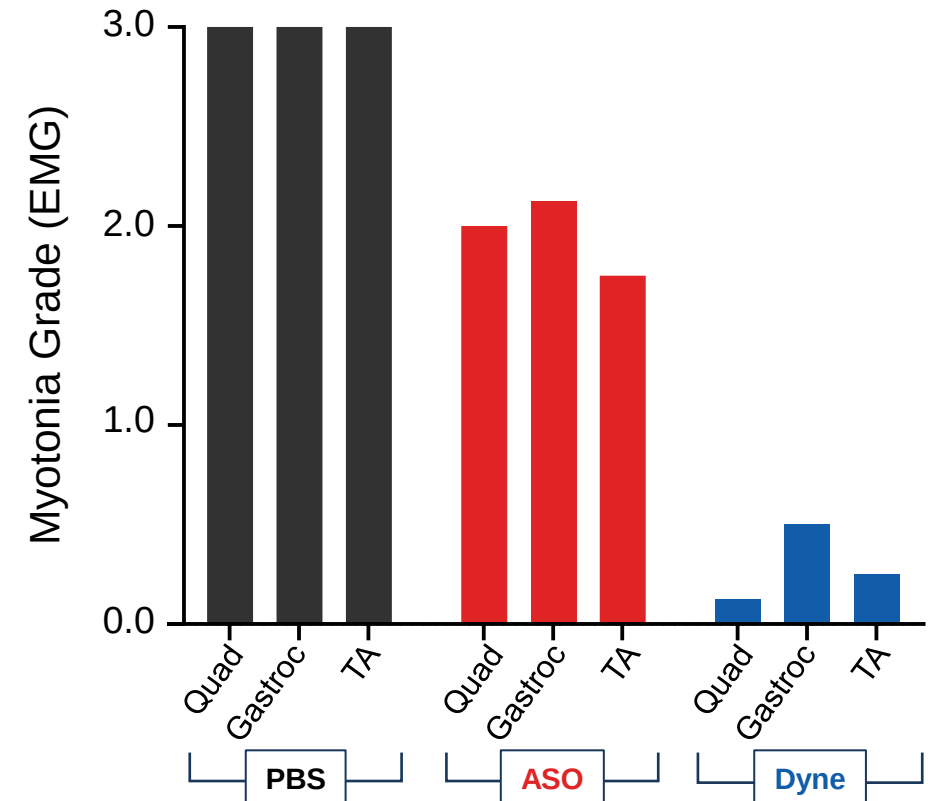


FORCE Dose-Dependently Corrected Splicing and Reversed Myotonia in the HSA^{LR} DM1 Mouse Model

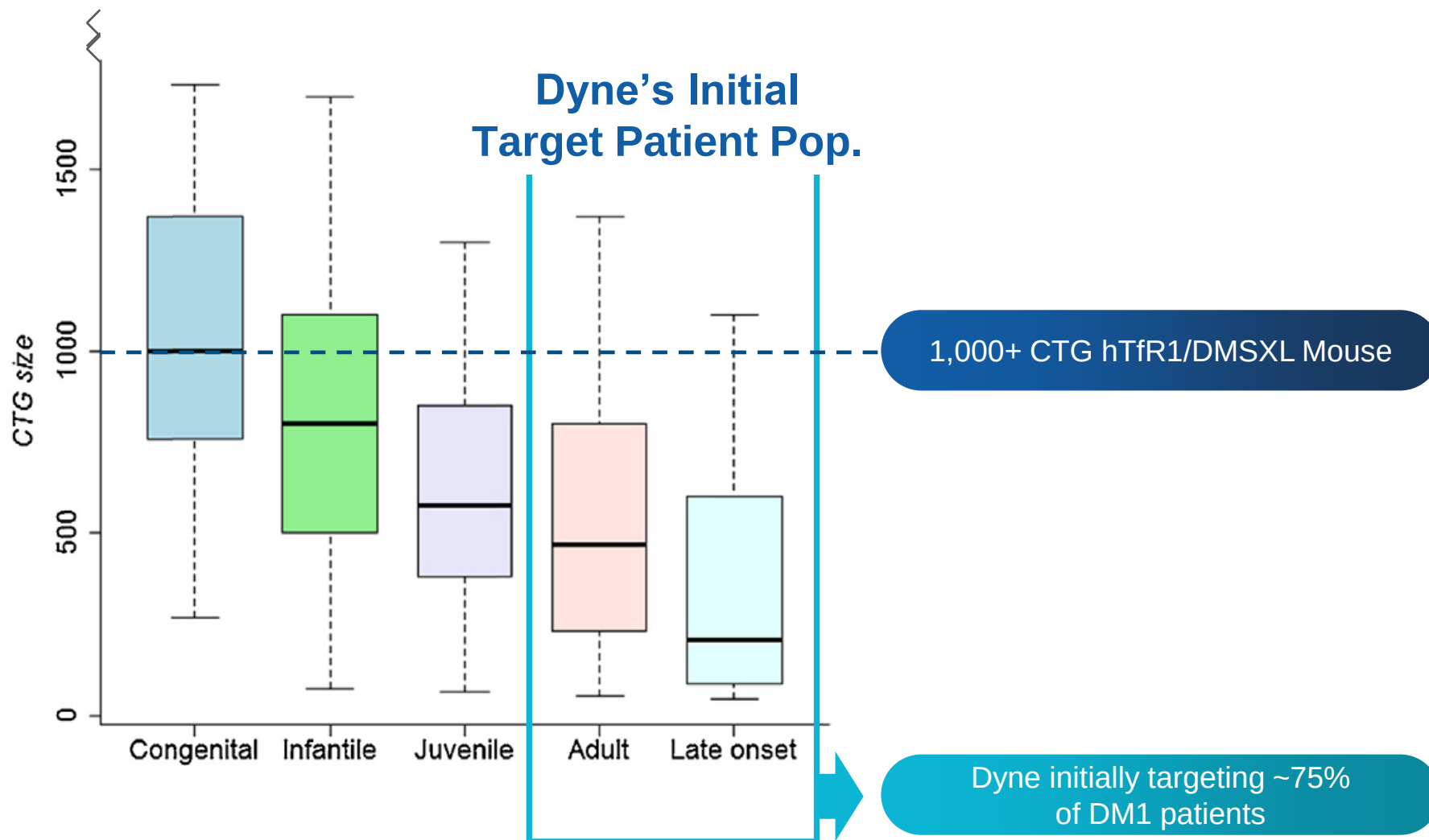
Splicing Correction in Multiple Muscles



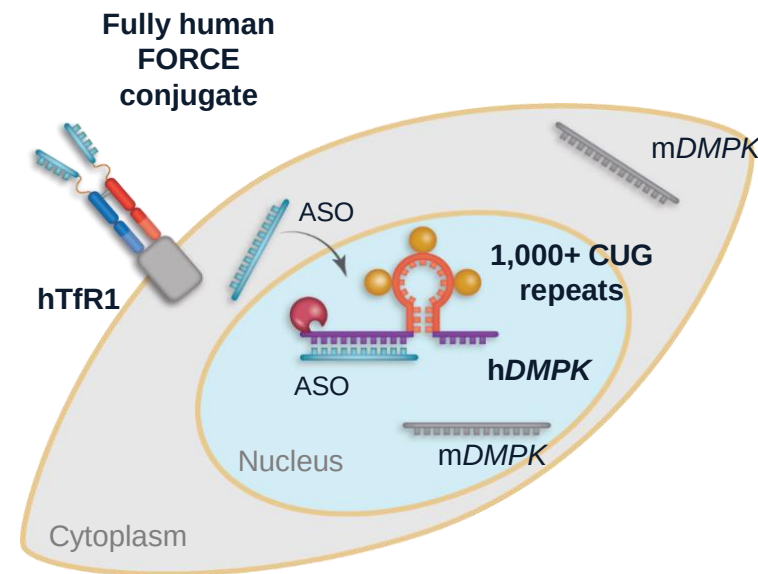
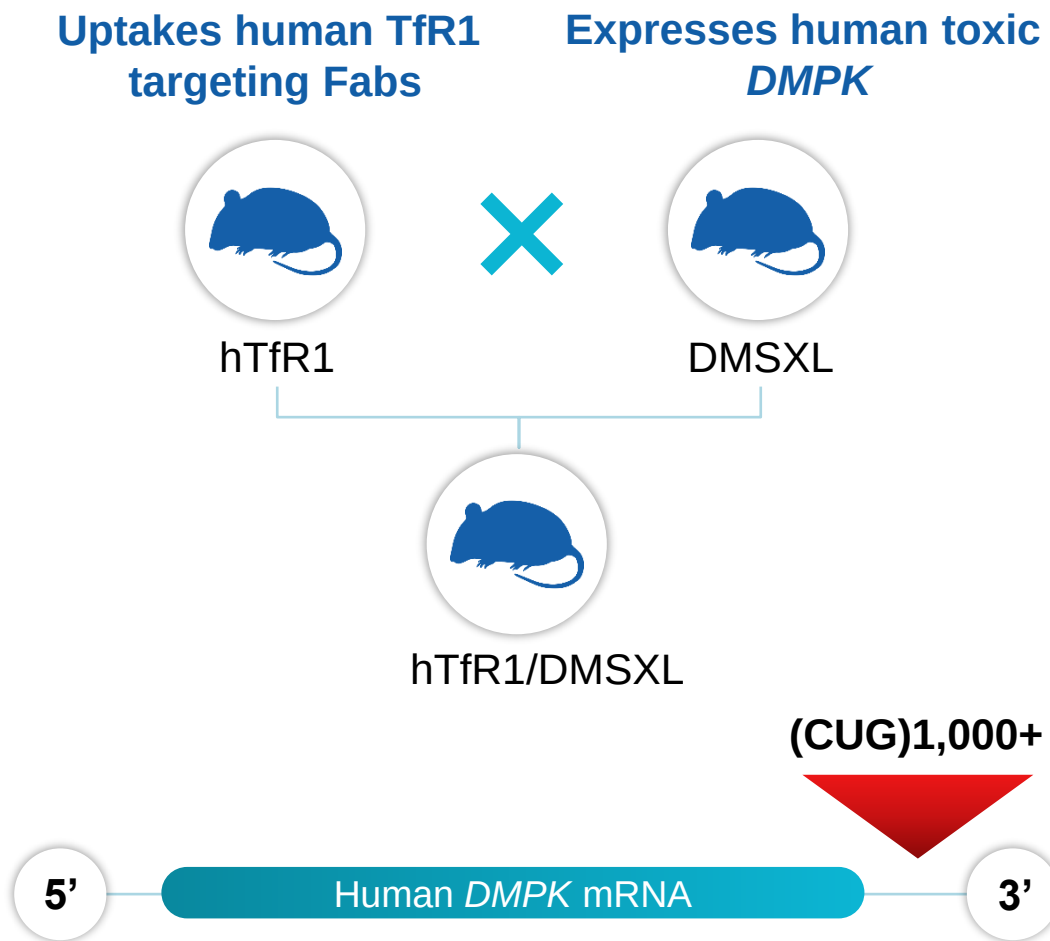
Near Complete Myotonia Reversal Within 14 Days After a Single Low Dose



FORCE Evaluated in hTfR1/DMSXL Mouse Model with 1,000+ CTG Repeat Length Representing Severe DM1 Phenotype

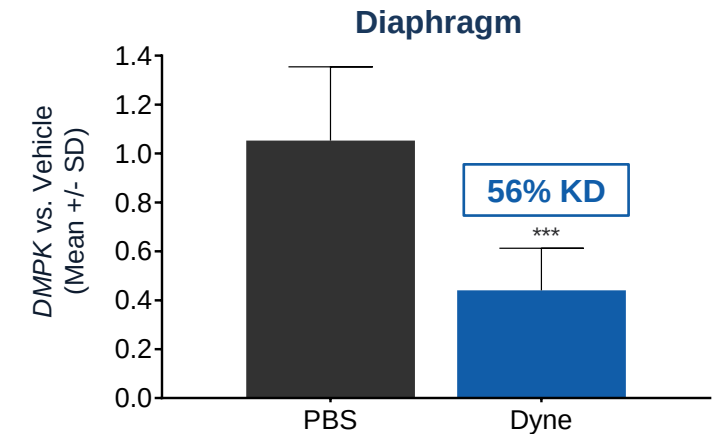
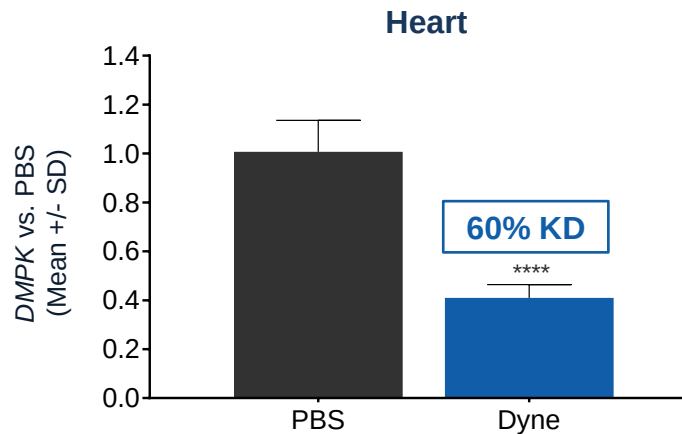
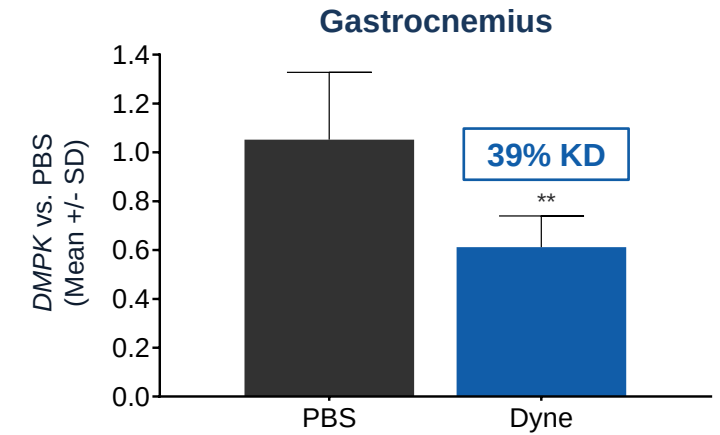
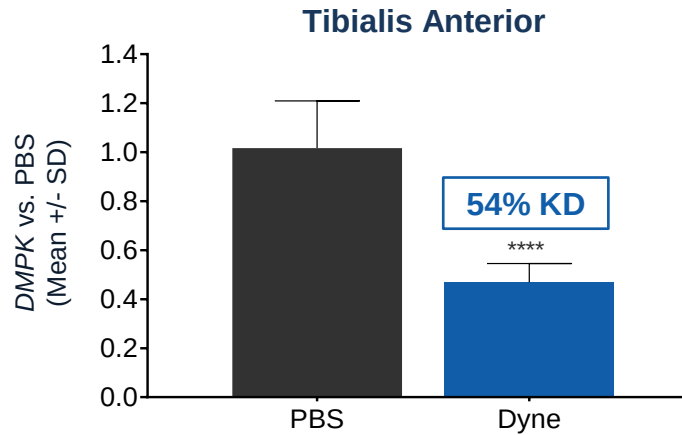
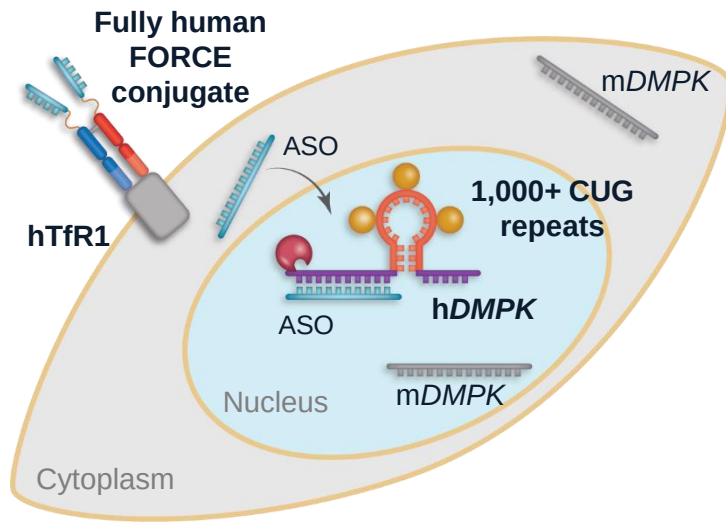


hTfR1/DMSXL: Innovative Model Developed by Dyne to Evaluate PD By Measuring Toxic Human Nuclear *DMPK* KD

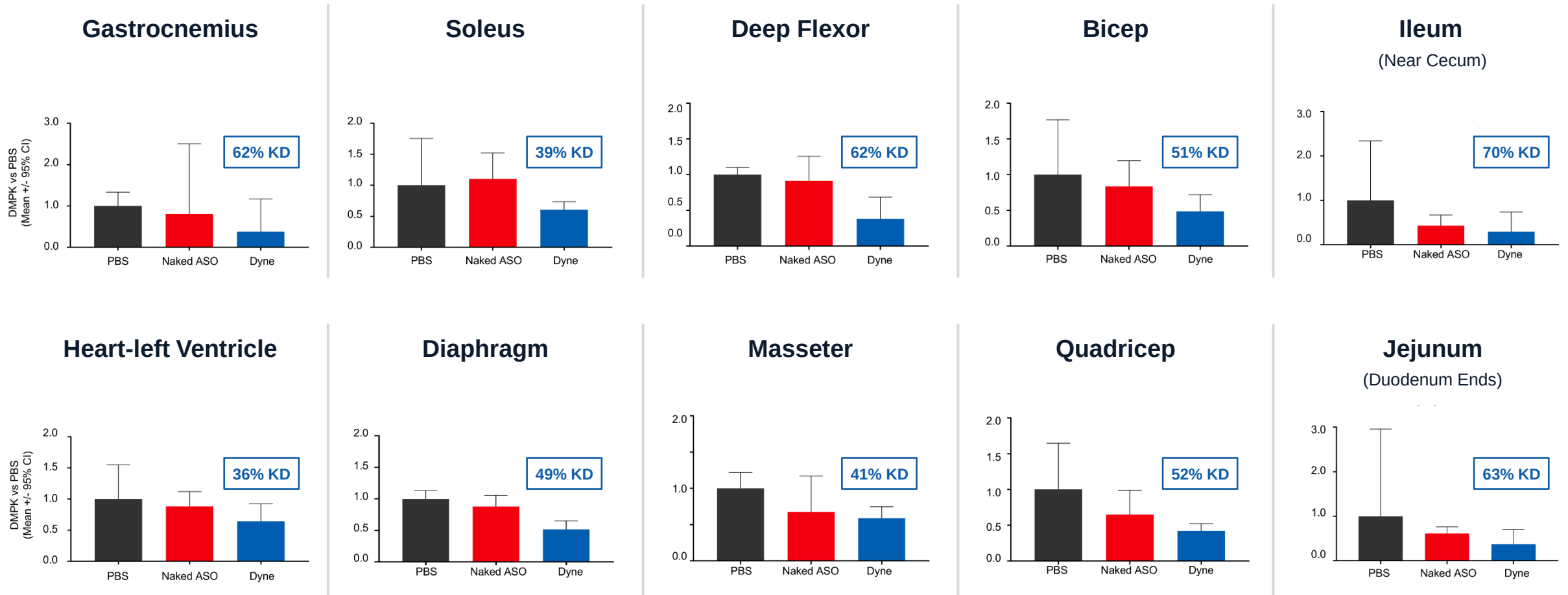


- Expresses human TfR1 receptor, enabling use of human TfR1-targeting Fabs
- Underestimates potency, expressing >10 times less human toxic *DMPK* vs. mouse *DMPK*

Human FORCE Conjugate Demonstrated Robust Toxic Human *DMPK* KD in hTfR1/DMSXL Model



FORCE Achieved Enhanced Distribution and WT *DMPK* KD Across NHP Skeletal, Cardiac and Smooth Muscles



Note: WT NHP with WT *DMPK* expression, n=3 per group, single dose IV at 10mg per kg for ASO, 14-day study.

DM1 Program Summary

Preclinical Summary

- ✓ **Targeted** toxic *DMPK* in the nucleus in patient cells
- ✓ **Robust toxic human *DMPK* KD** in novel hTfR1/DMSXL model
- ✓ **Reduced** nuclear foci
- ✓ **Corrected** splicing changes
- ✓ **Reversed** myotonia after a single dose
- ✓ **Delivered** *DMPK* targeting ASO to mouse and NHP muscle tissues
- ✓ **Enhanced** muscle distribution
- ✓ **Durable** *DMPK* RNA reductions up to 12 weeks

Potential Advantages

- **Tractable development** with rapid path to human PoC
- **Efficient** commercial model, addressable with focused sales force

**One of three INDs planned
between Q4 2021 - Q4 2022**

DMD Program



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)



OUR APPROACH

Building a Best-in-class Targeted Exon Skipping Franchise

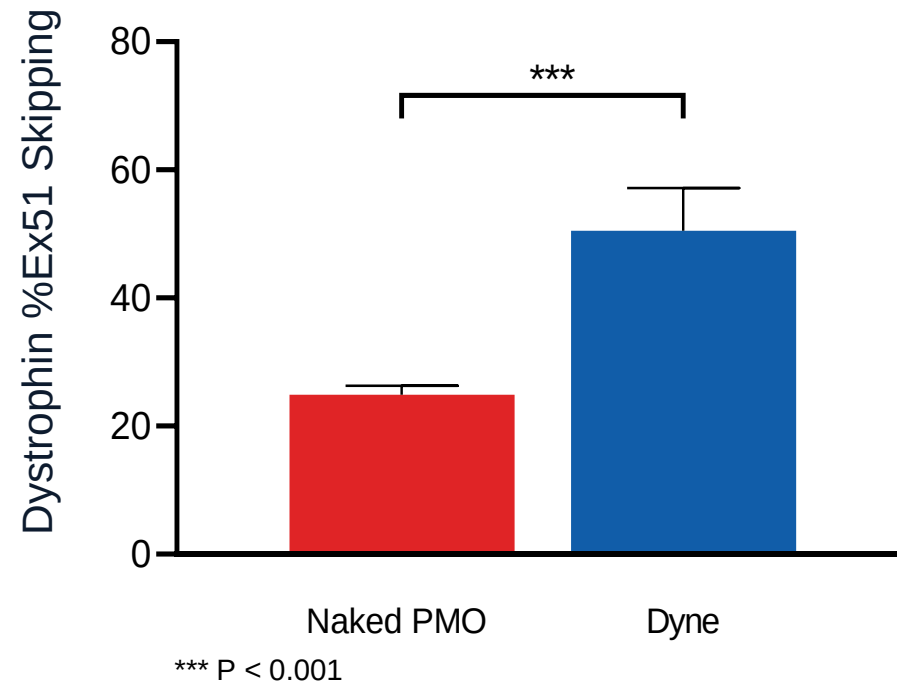
Increase dystrophin expression and enable less frequent dosing to potentially **stop or reverse disease progression**

Current Approved Exon 51 Therapies Only Increased Dystrophin Production

<1%

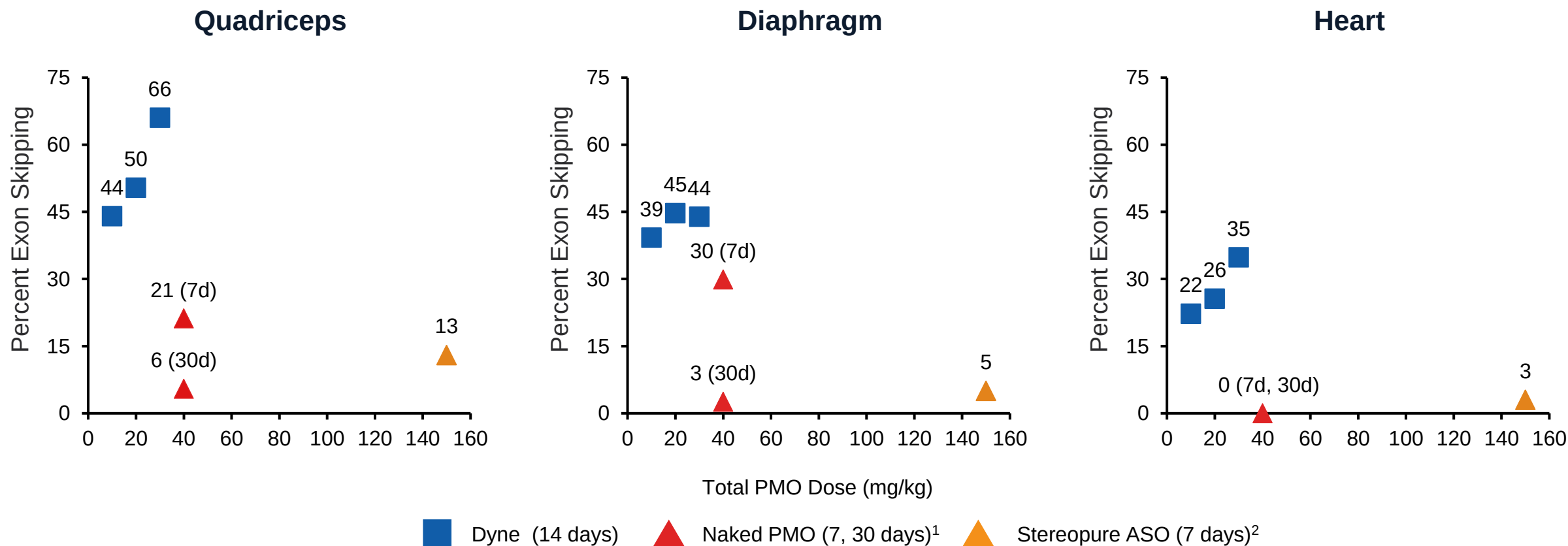
FORCE Achieved Enhanced Exon Skipping Compared to Naked PMO in DMD Patient Myotubes

Exon Skipping in DMD Myotubes with Exon 51 Mutation



FORCE Achieved Effective Exon Skipping in *mdx* Model Greater Than Naked PMO¹ or Stereopure ASO²

In vivo mdx Model Exon Skipping After Single IV Dose

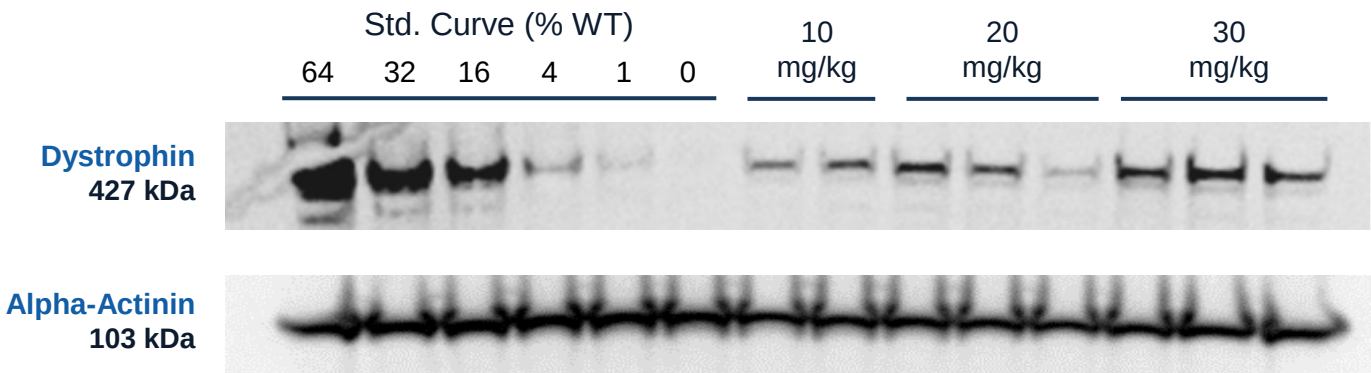


Note: Figures represent average percent exon skipping in *mdx* model after single IV dose. Dyne data based on assessment 14 days after single dose.
1. Naked PMO data consists of Sarepta Therapeutics data disclosed in a patent application filed Dec. 13, 2017 after single IV dose.
2. Stereopure ASO data consists of Wave Life Sciences data disclosed in 2018 WMS presentation with assessment 7 days after single IV dose.

FORCE Dose-Dependently Increased Dystrophin Expression

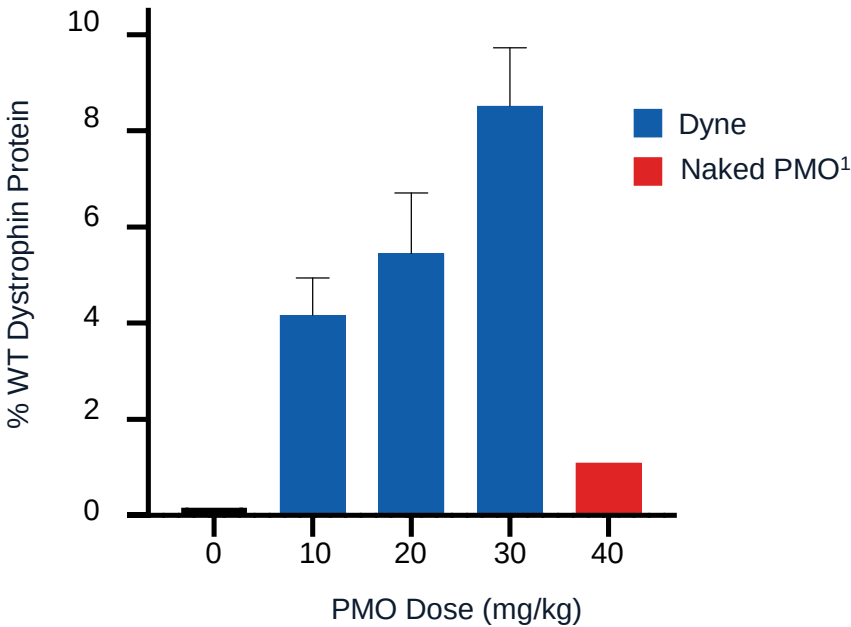
Quadriceps

Dose-Dependent Increase In Dystrophin Expression



Standard curve - Used pooled WT protein and pooled mdx protein, % indicates amt. of WT spiked into sample

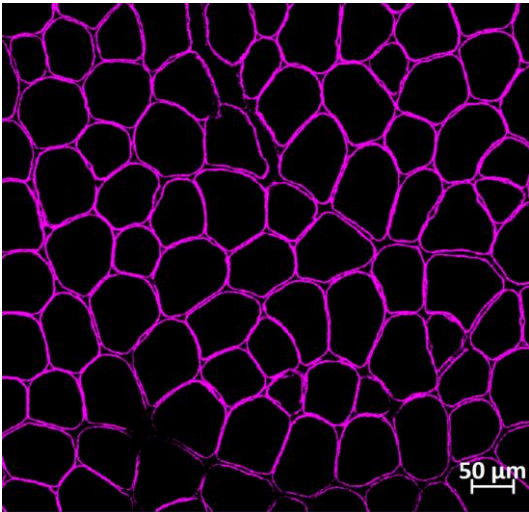
Restored Dystrophin Expression



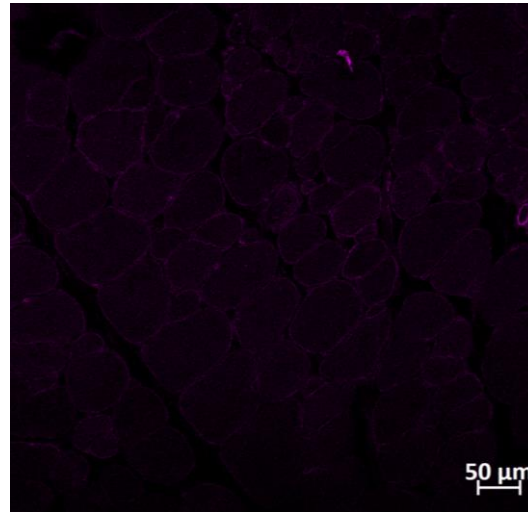
FORCE Restored Dystrophin Expression Based on IHC

Dystrophin Expression in Quadriceps Muscle

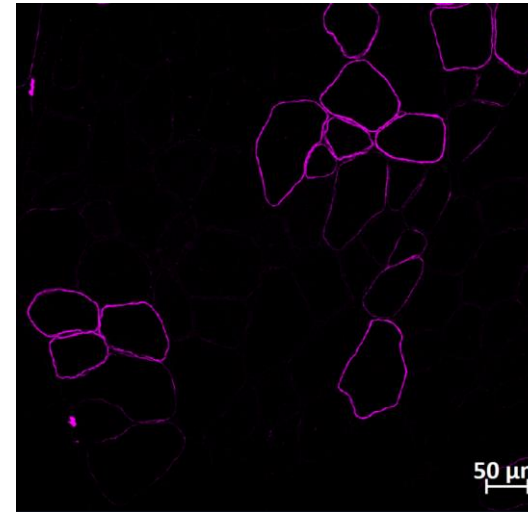
WT-Saline



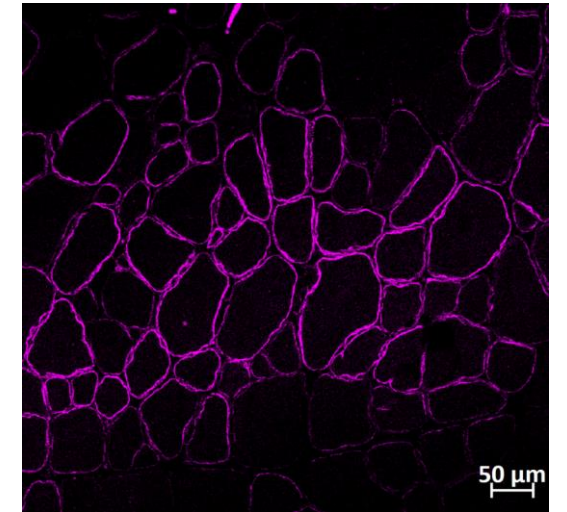
mdx-Saline



mdx-M23D



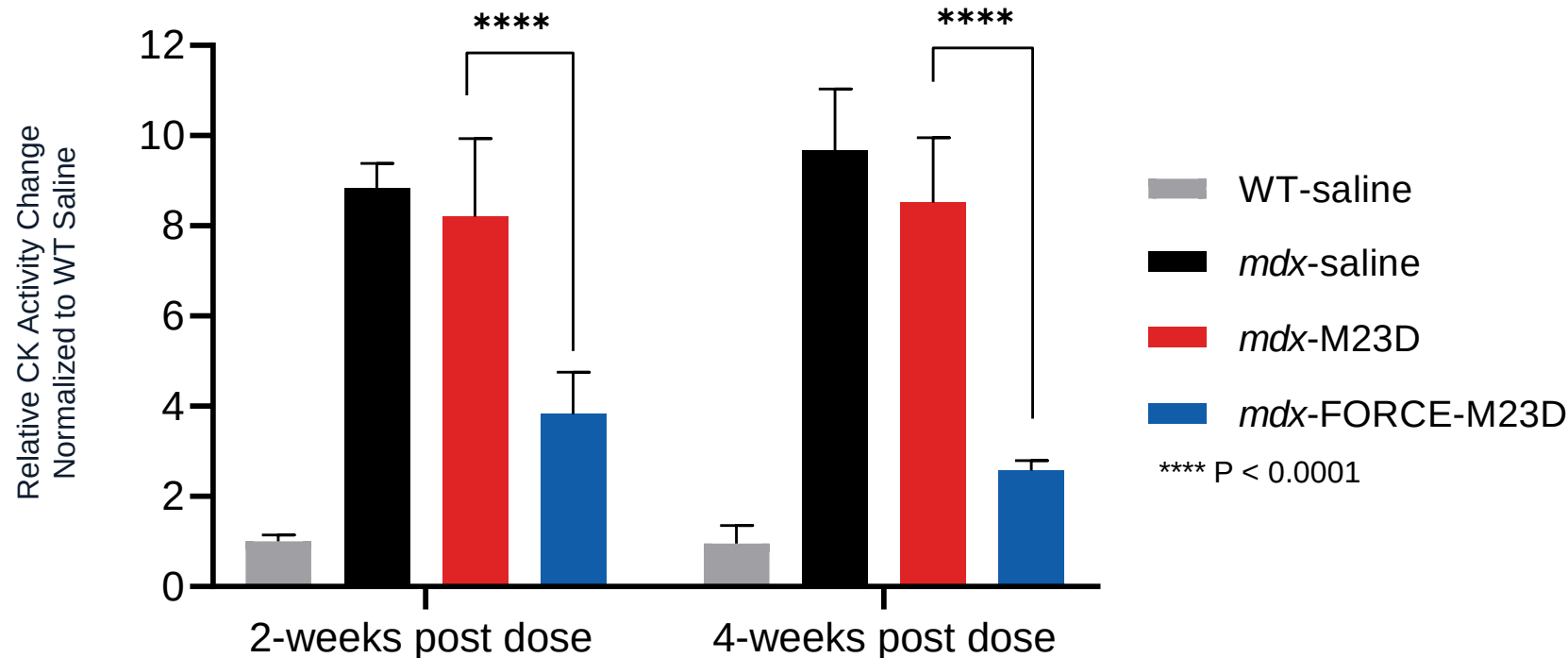
mdx-FORCE-M23D



Increased Dystrophin Expression Restores Muscle Cell Structural Integrity

Single Dose of FORCE Significantly Reduced Serum Creatine Kinase (CK)

CK Levels

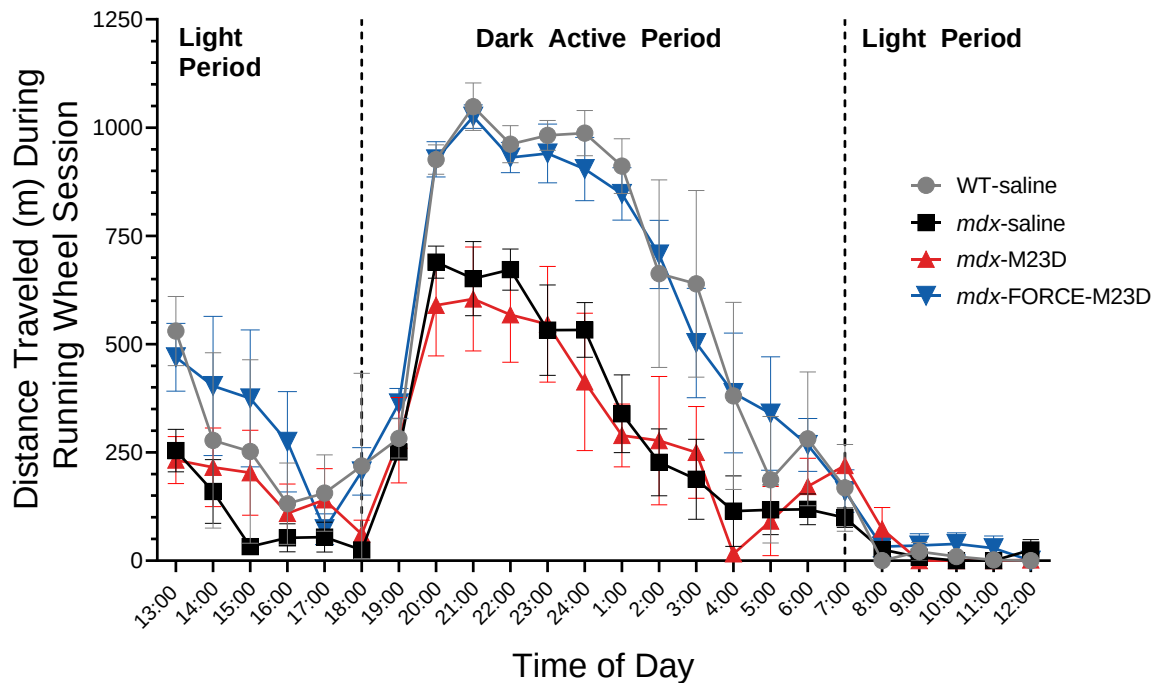


- CK is found inside normal muscle and does not leak into serum
- Serum CK is a clinical biomarker of muscle damage
- FORCE significantly reduced serum CK after a single dose

FORCE Demonstrated Functional Benefit with a Single Dose

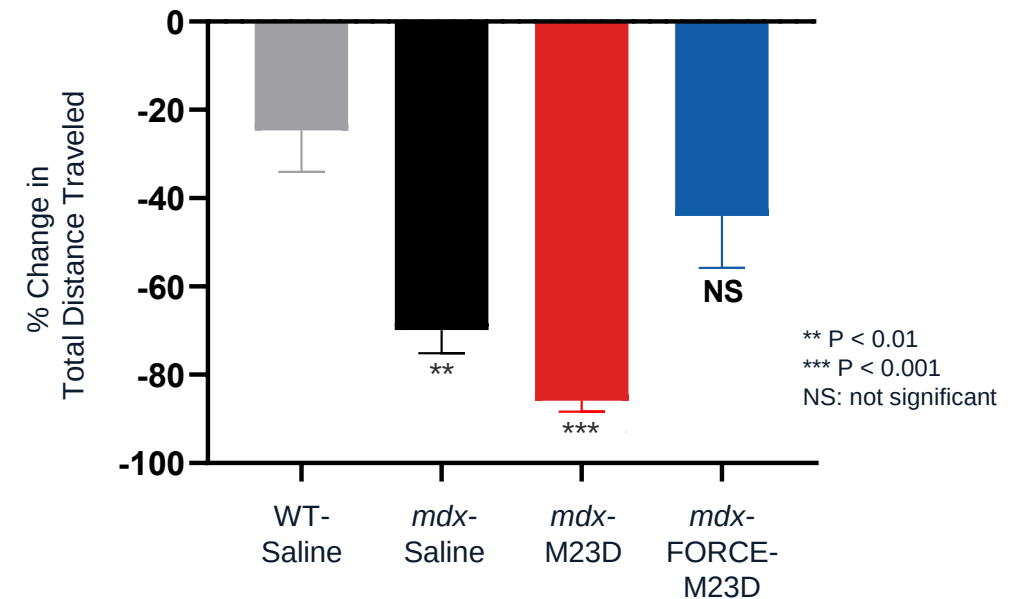
Distance Traveled in Home Cage Running Wheel

(Assessed 4 Weeks After Treatment)



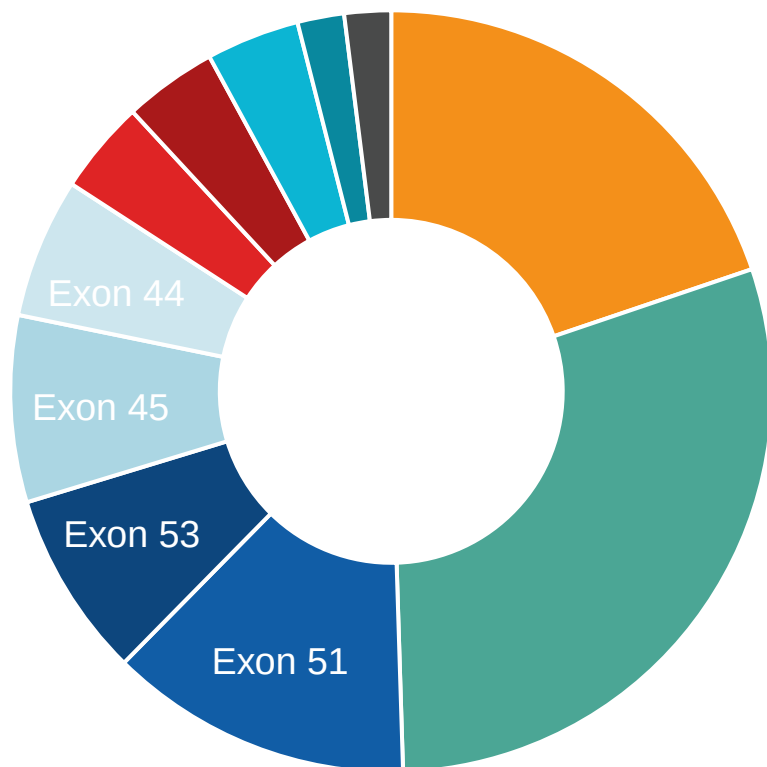
Distance Traveled in Open Field Following Hind Limb Fatigue Challenge

(Assessed 2 Weeks After Treatment)

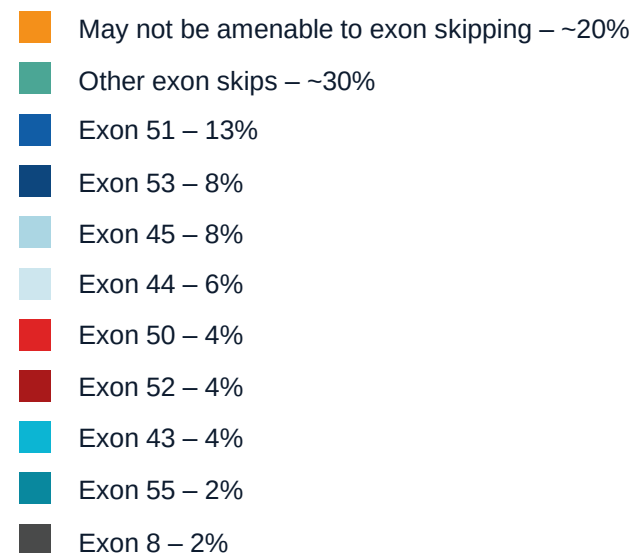


Note: single 30 mg/kg dose in mdx mouse model. Data generated in blinded experiments conducted at third-party CRO. Hind limb fatigue challenge test statistical analysis comparison to wildtype (WT) group using one-way ANOVA followed by post-hoc Dunnett's test.

Dyne Developing Global DMD Franchise to Address Up to ~80% of DMD Population Amenable to Exon Skipping Therapeutics



Approximately
80% of patients
have genotypes amenable to exon skipping



DMD Program Summary

Preclinical Summary

mdx Model

- ✓ **Achieved effective** exon skipping in skeletal and cardiac muscle
- ✓ **Dose-dependently increased dystrophin** expression based on western blot and immunohistochemistry
- ✓ **Reduced serum CK levels**, a clinical biomarker of muscle damage
- ✓ **Demonstrated functional benefit** in multiple standardized assessments

Human DMD Myotubes (Exon 51)

- ✓ **50% increase** in exon skipping, compared to 25% for unconjugated oligo control

Potential Advantages

- **Established** clinical and regulatory path
- **Opportunity to accelerate DMD franchise** expansion (Exon 53, Exon 45, Exon 44) to reach additional patient populations

**One of three INDs planned
between Q4 2021 - Q4 2022**

FSHD Program



Overview

- Aberrant expression of DUX4
- Onset in teen years or young adulthood
- Normal life expectancy



Clinical Presentation

- Progressive wasting and skeletal muscle loss
- Significant physical limitations



Population

- ~16,000 - 38,000 (US)
- ~35,000 (Europe)



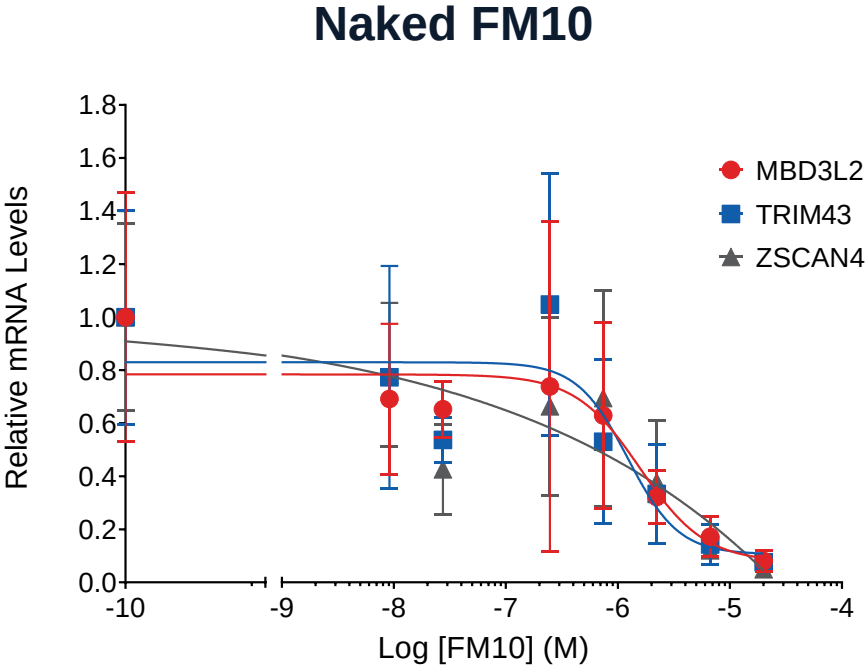
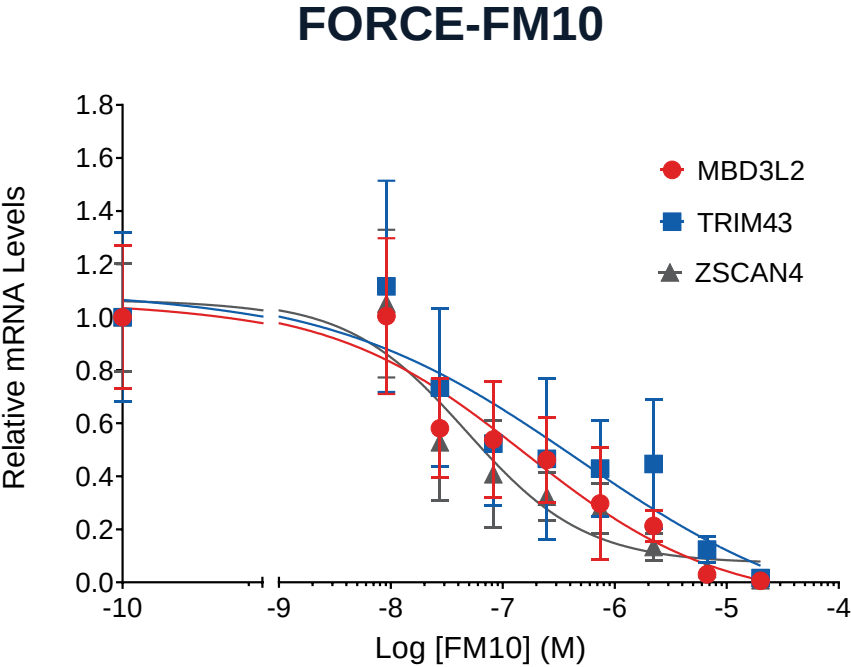
NO
approved
therapies

OUR APPROACH

Disease-Modifying DUX4 Knockdown

Targeting toxic *DUX4* mRNA expression to potentially **stop or reverse disease progression**

FORCE-FM10 Suppressed Expression of Key DUX4 Biomarkers in FSHD Patient Myotubes



Transcript	IC ₅₀ (nM) FORCE-FM10	IC ₅₀ (nM) Naked FM10	Fold Advantage of FORCE-FM10
ZSCAN4	67	643	9.6 x
MBD3L2	144	1208	8.4 x
TRIM43	352	1117	3.2 x



Three INDs
planned between
Q4 2021 - Q4 2022

Targeting the genetic basis of serious muscle diseases to

STOP OR REVERSE DISEASE PROGRESSION

FORCE
PLATFORM

Robust
PIPELINE

Delivering
FOR PATIENTS

Exceptional
TEAM