# Building the World's Leading Muscle Disease Company

40th ANNUAL J.P. MORGAN HEALTHCARE CONFERENCE
JANUARY 12, 2022

Ravi, *living with DMD*

# 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 Therapeutics, Inc.'s (the "Company") strategy, future operations, prospects, plans and objectives of management, the expected timeline for submitting investigational new drug applications and dosing patients, the potential advantages of the Company's FORCE platform and programs, expectations regarding the translation of preclinical findings to human disease and plans to conduct additional preclinical studies and clinical trials, the anticipated design of clinical trials 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. The Company 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 conduct of research activities, the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical studies; the timing of and our ability to submit and obtain regulatory approval for investigational new drug applications; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical trials; the Company's ability to obtain sufficient cash resources to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; the impact of the COVID-19 pandemic on the Company's business and operations; 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 the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company 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 the Company's views as of any date subsequent to the date of this presentation.

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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
- Significant exon skipping & dystrophin expression in DMD
- Significant market opportunities

## Delivering for Patients

- Developing multiple first-in-class or best-in-class therapies
- Precision medicine strategy
- Driving three programs to the clinic in 2022

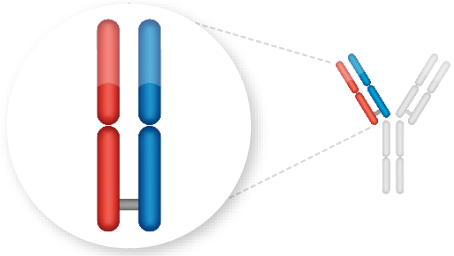
## Exceptional Team

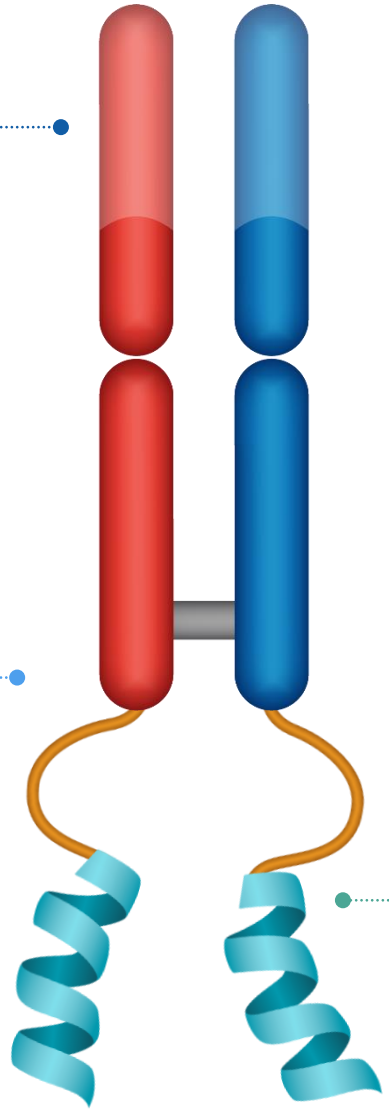
- Deep knowledge of muscle diseases and novel therapeutic modalities
- World-class scientific advisory board
- Supported by leading healthcare investors

# Dyne FORCE™ Platform: Modern Oligo Therapeutics for Muscle Diseases

## ANTIBODY

Proprietary Fab targets TfR1 to enable muscle delivery



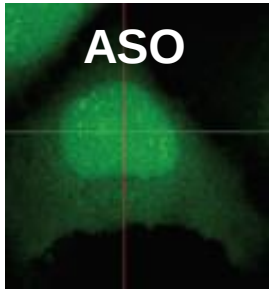


## LINKER

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

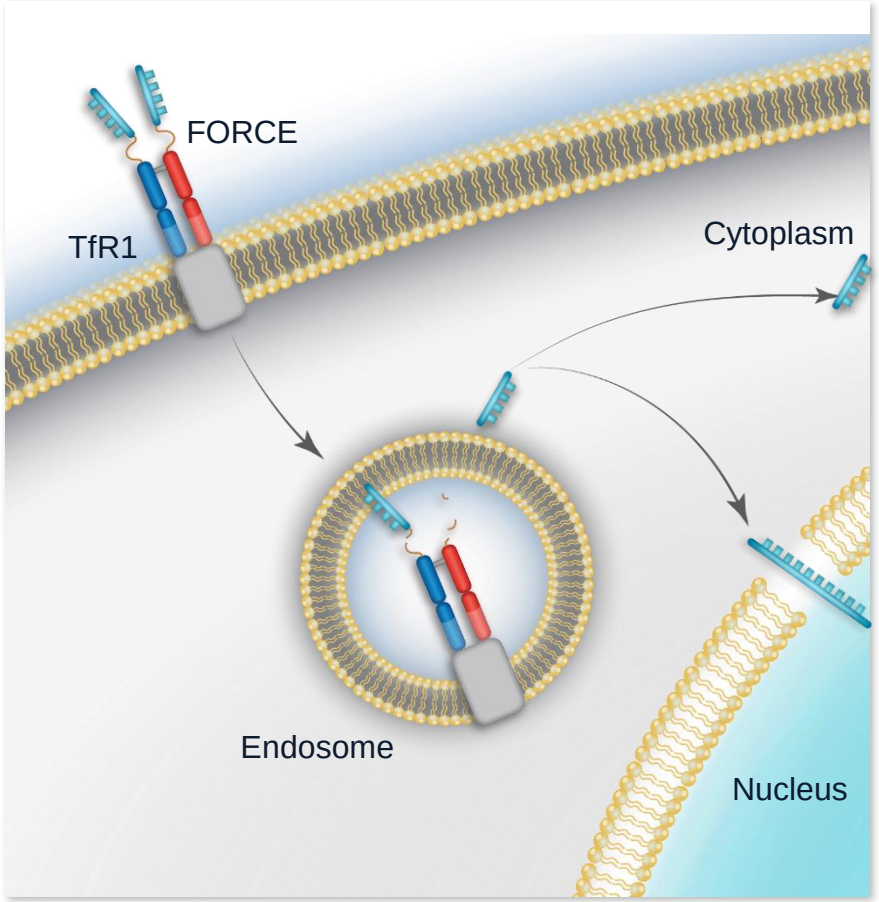



Nuclear localization


Cytoplasmic localization

Adapted from Ohrt T., et al. *Nucleic Acids Res* 2006;34:1369.

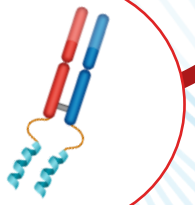
# FORCE Platform Harnesses Cell Biology to Modify Disease




- 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

# FORCE Platform Designed to Deliver Significant Advantages

**Stop or Reverse Disease Progression**



### Targeted Muscle Delivery

Leverages TfR1 expression on skeletal, cardiac and smooth muscle

### Targets Genetic Basis of Disease

Rationally select payloads to match target biology

### Redosable Administration

Potential for individualized patient titration and longer-term efficacy

### Enhanced Tolerability

Targeted delivery limits systemic drug exposure

### Extended Durability

Potential for prolonged disease-modifying effects, enabling less frequent dosing

### Reduced Development and Manufacturing Costs

A single Fab and linker utilized across all programs

# FORCE Platform Delivered Validating Data Across Three Programs Heading to the Clinic in 2022

## DMD

***In vitro:***

- Enhanced exon skipping

***In vivo:***

- Robust, durable exon skipping and dystrophin expression in *mdx* model
- Transformative exon skipping in NHP cardiac and skeletal muscles
- NHP GLP tox results support advancement to the clinic

## DM1

***In vitro:***

- *DMPK* KD, reduction in nuclear foci, splicing correction

***In vivo:***

- Correction of splicing & reversal of myotonia in $HSA^{LR}$ model
- Robust knockdown of toxic nuclear *DMPK* in hTfR1/DMSXL model, foci reduction & correction of splicing
- NHP GLP tox results support advancement to the clinic

## FSHD

***In vitro:***

- Reduced expression of key DUX4 biomarkers

***In vivo:***

- Enhanced tissue distribution in NHP

# Robust Portfolio Focused on Muscle Diseases

| DISEASE | TARGET | DISCOVERY / PRECLINICAL / PHASE 1/2 | ESTIMATED PATIENTS |
|---|---|---|---|
| **Myotonic Dystrophy Type 1 (DM1)** | DMPK | **DYNE-101** — *IND Submission Expected Q1 2022; FIH Expected by Mid-2022* | US: **>40,000**<br>Europe: **>74,000** |
| **Duchenne Muscular Dystrophy (DMD)** | Exon 51 | **DYNE-251** — *FIH Expected by Mid-2022* | US: **~12,000-15,000**<br>Europe: **~25,000** |
| | Exon 53 | | |
| | Exon 45 | | |
| | Exon 44 | | |
| | Other Exons | | |
| **Facioscapulohumeral Muscular Dystrophy (FSHD)** | DUX4 | **DYNE-301** — *IND Submission Expected H2 2022* | US: **~16,000-38,000**<br>Europe: **~35,000** |

**Pipeline Expansion Opportunities**

**Rare Skeletal**

**Cardiac**

**Metabolic**

# 2021: Focused on Driving Multiple Programs Towards the Clinic

**Key Milestones Achieved in 2021**

- **Submitted IND for DYNE-251 (DMD)**, Dyne's first IND
- Presented **validating preclinical data** across DM1, DMD, and FSHD
- **Successful financing** in January 2021, raising $168MM in gross proceeds
- **Building an exceptional team** to deliver upon our strategic vision

**A Year of Significant Progress Across Platform, Pipeline and Company**

# 2022: Focused on Execution in the Clinic Across Multiple Programs

**Key Expected Milestones for Patients & Shareholders in 2022**

- **Submit IND for DYNE-101 (DM1)** in Q1 2022
- **Dose patients in two clinical trials (DMD, DM1)** by mid-2022
- **Submit IND for DYNE-301 (FSHD)** in H2 2022
- **Expand muscle disease portfolio**, starting with a global DMD franchise, by leveraging the FORCE platform

**A Year of Advancing Multiple Transformational Therapies for Patients with Serious Muscle Diseases**

# Building a Global DMD Franchise of Transformative Therapies

## 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 <1%**

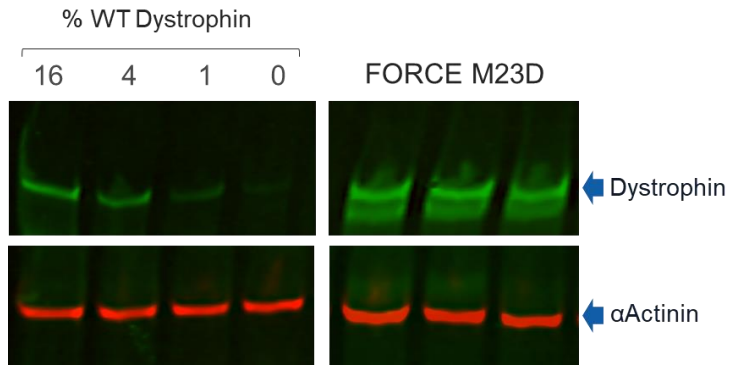
## OUR APPROACH

## Best-in-class Targeted Exon Skipping

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

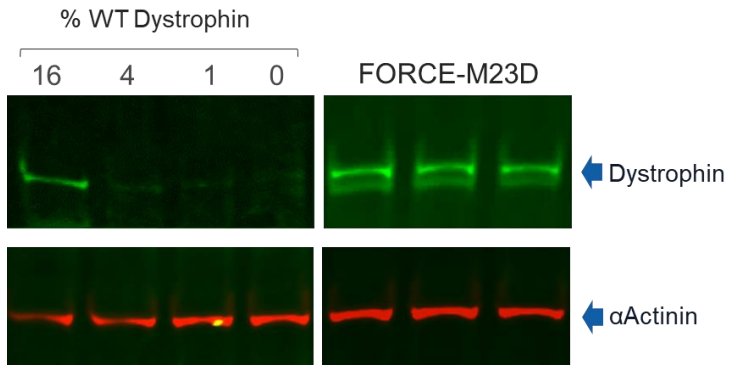
# FORCE Achieved Robust and Durable Dystrophin Expression and Sarcolemma Localization in Muscle in *mdx* Model

## Quadriceps



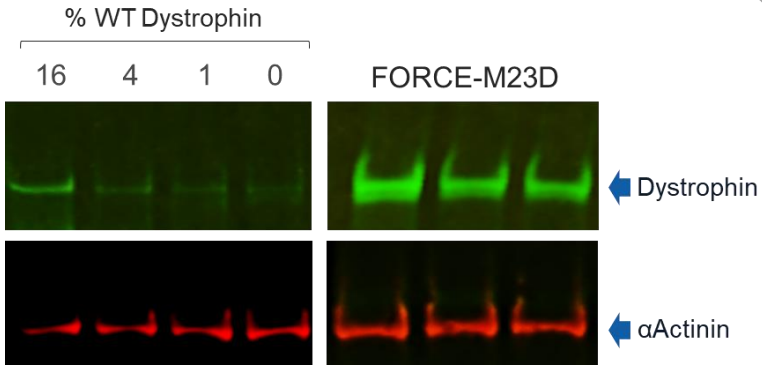

46% of wild-type dystrophin

## Diaphragm

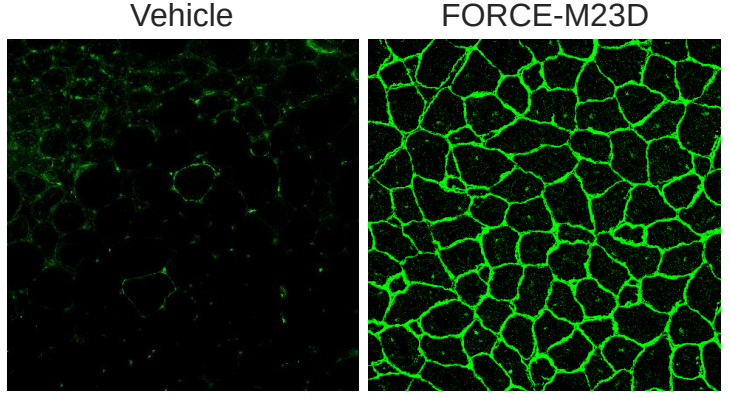



90% of wild-type dystrophin

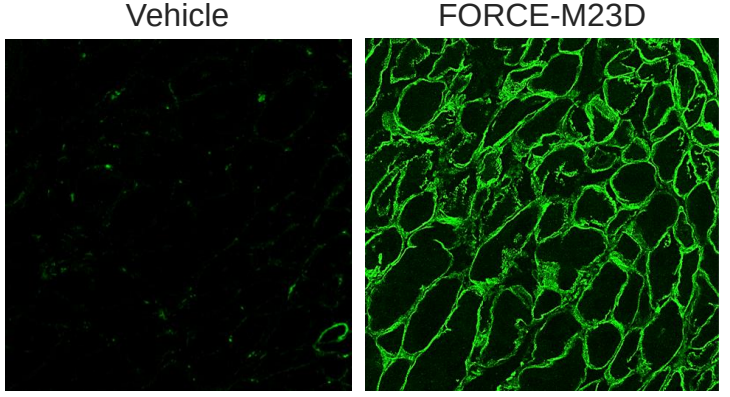
## Heart



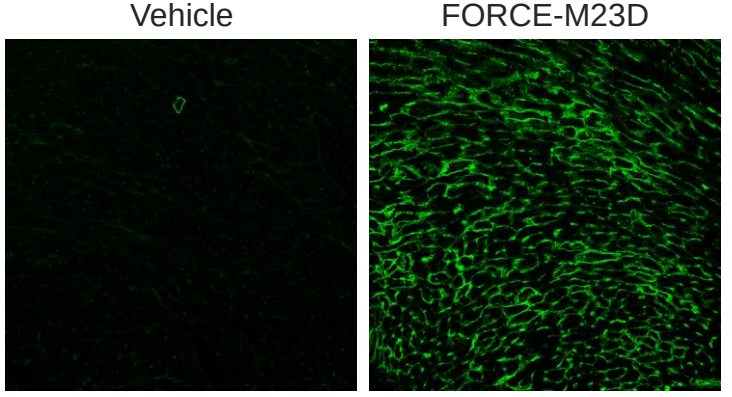

78% of wild-type dystrophin




68% dystrophin-positive fibers



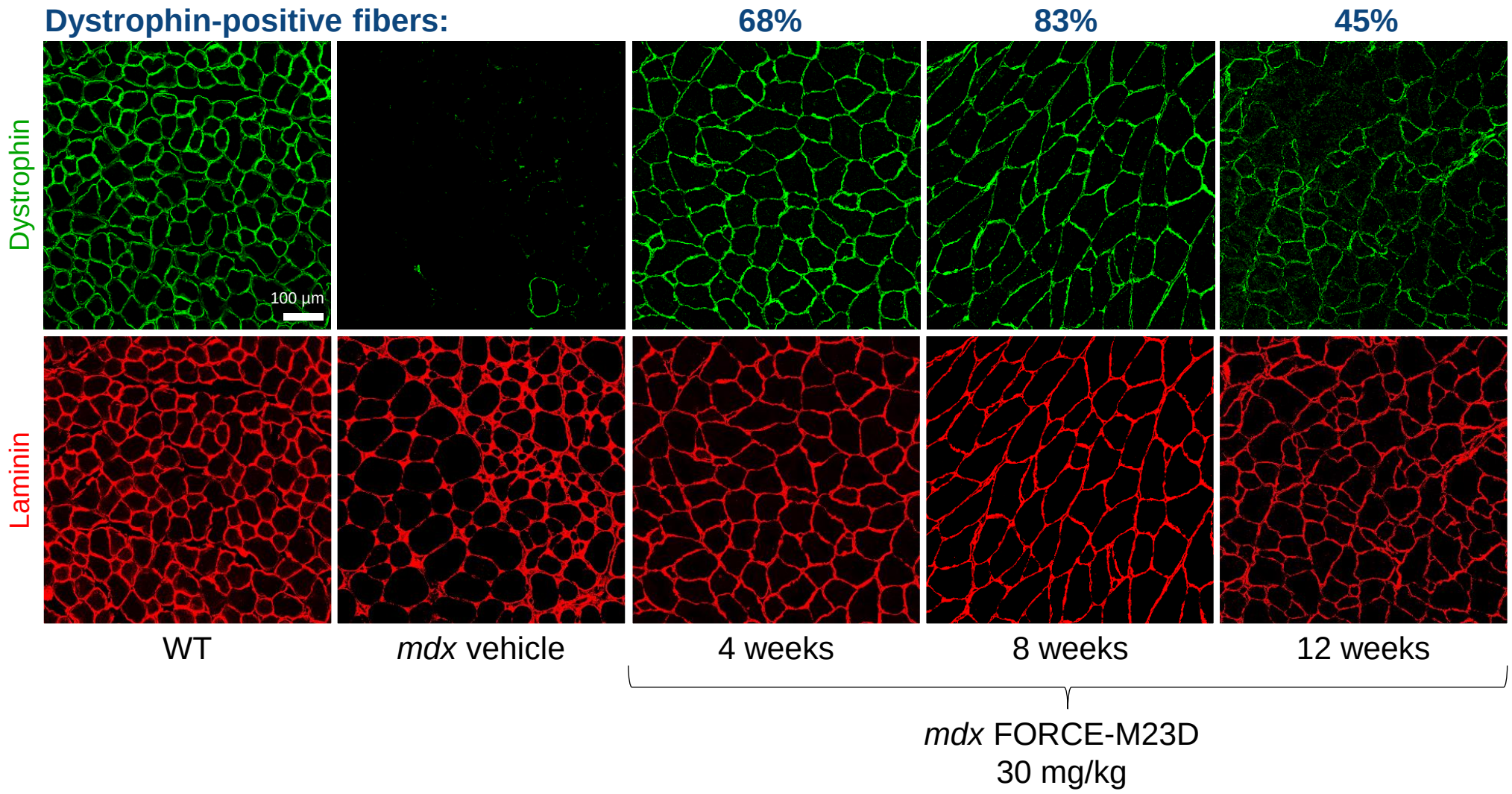

~80% dystrophin-positive fibers




~80% dystrophin-positive fibers

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

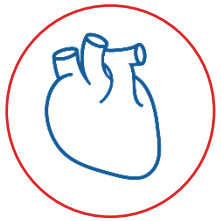
# FORCE Achieved Durable Dystrophin Localization to Sarcolemma in Quadriceps in *mdx* Model



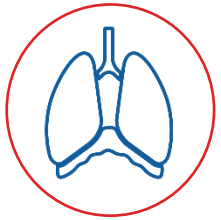

Note: Single IV 30 mg/kg dose of FORCE-M23D in *mdx* mouse model on day 0, analysis at specified time intervals.

# DYNE-251 Demonstrated Robust Exon Skipping & Favorable Safety Profile in NHPs

## High Level of Exon 51 Skipping Achieved in Key Muscles at 2 Months



**43% in heart**



**52% in diaphragm**

**18% in quadriceps**

## GLP Toxicology Study

- No dose limiting toxicity observed after five weekly doses 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

NOAEL: No-observed-adverse-effect level

# Proposed Clinical Trial to Evaluate DYNE-251 in Patients with DMD

**MULTIPLE ASCENDING DOSE (MAD)** | **LONG-TERM EXTENSION (LTE)**

## Design

- Multiple Ascending Dose
- Placebo Controlled
- Global
- LTE

## Population

- Patients with symptomatic DMD and mutation amenable to exon 51 skipping therapy
- Ages 4 to 16 years
- ~30-40 male participants
- Ambulant and non-ambulant

## Endpoints*

- Safety and tolerability
- PK/PD
- Dystrophin by Western Blot
- Measures of muscle function
  - Upper and lower limbs
  - Respiratory

**Anticipate Dosing Patients by Mid-2022**

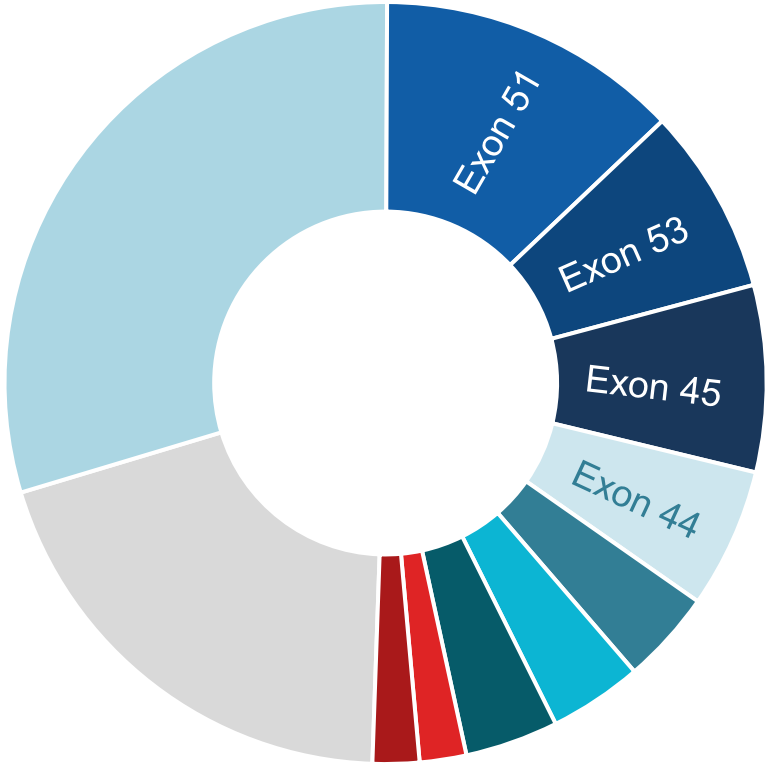
* Proposed endpoints include primary, secondary and exploratory

# Dyne is Committed to Developing Global DMD Franchise

Approximately

**80% of patients**

have genotypes amenable to exon skipping




- Exon 51 – **13%**
- Exon 53 – **8%**
- Exon 45 – **8%**
- Exon 44 – **6%**
- Exon 50 – **4%**
- Exon 52 – **4%**
- Exon 43 – **4%**
- Exon 55 – **2%**
- Exon 8 – **2%**
- Other exon skips – **~30%**
- May not be amenable to exon skipping – **~20%**

# Developing Transformative Therapies for People Living with DM1

## 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)

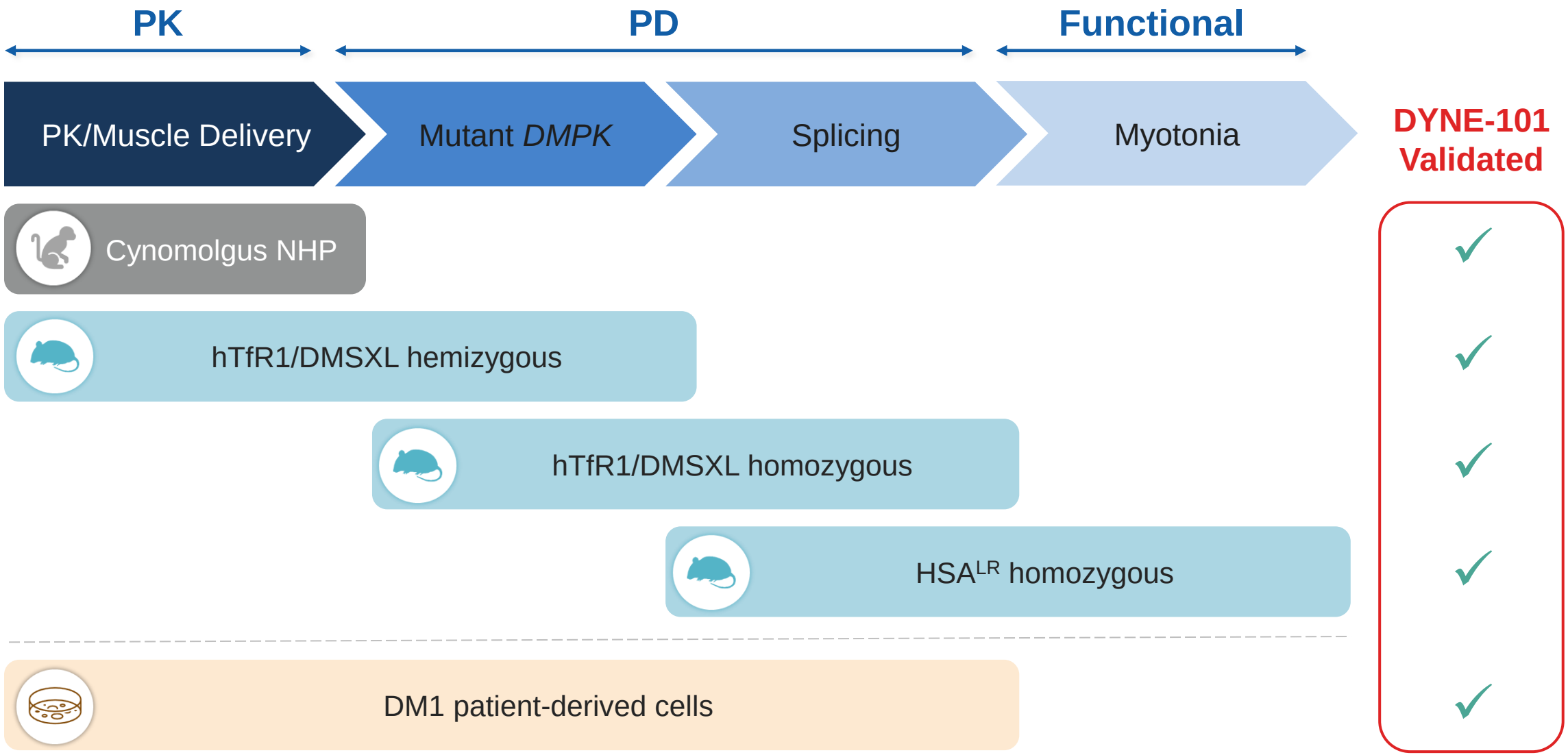
**NO approved therapies**

## OUR APPROACH

## Disease-Modifying Nuclear *DMPK* Knockdown

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

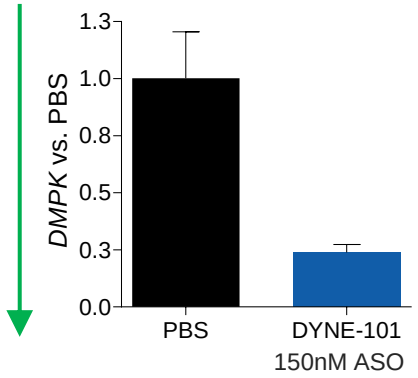
# Data from Multiple DM1 Models Demonstrate that FORCE Delivers to Muscle and Drives Disease Modification



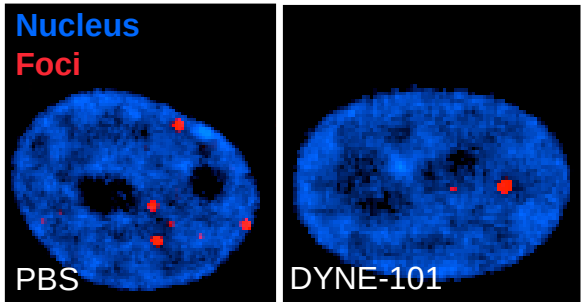
# DYNE-101 Demonstrated Robust Dose-dependent *DMPK* KD, Foci Reduction, and Splicing Correction

## 380 CTG Repeats DM1 Myotubes

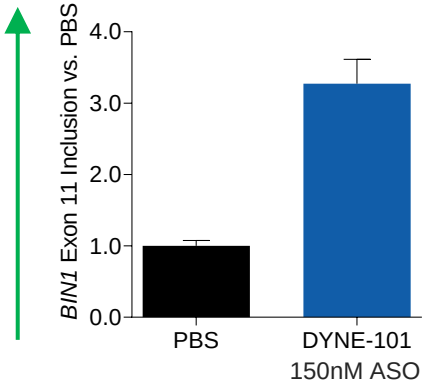
### *DMPK* mRNA KD by qPCR




### *DMPK* foci reduction by FISH

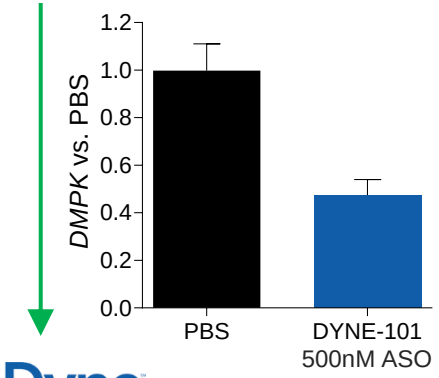



### *BIN1* mis-splicing correction by qPCR

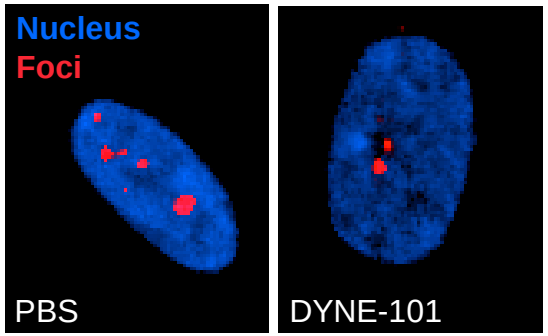



## 2,600 CTG Repeats DM1 Myotubes

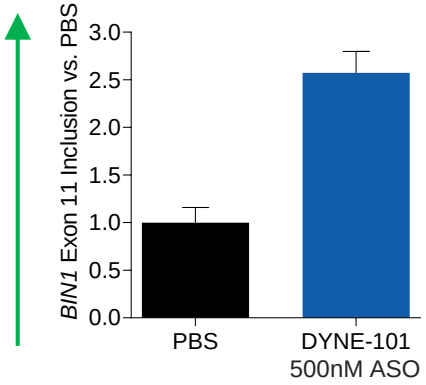
### *DMPK* mRNA KD by qPCR




### *DMPK* foci reduction by FISH



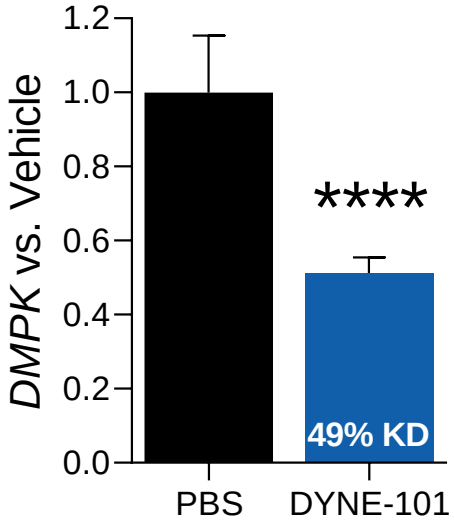

### *BIN1* mis-splicing correction by qPCR



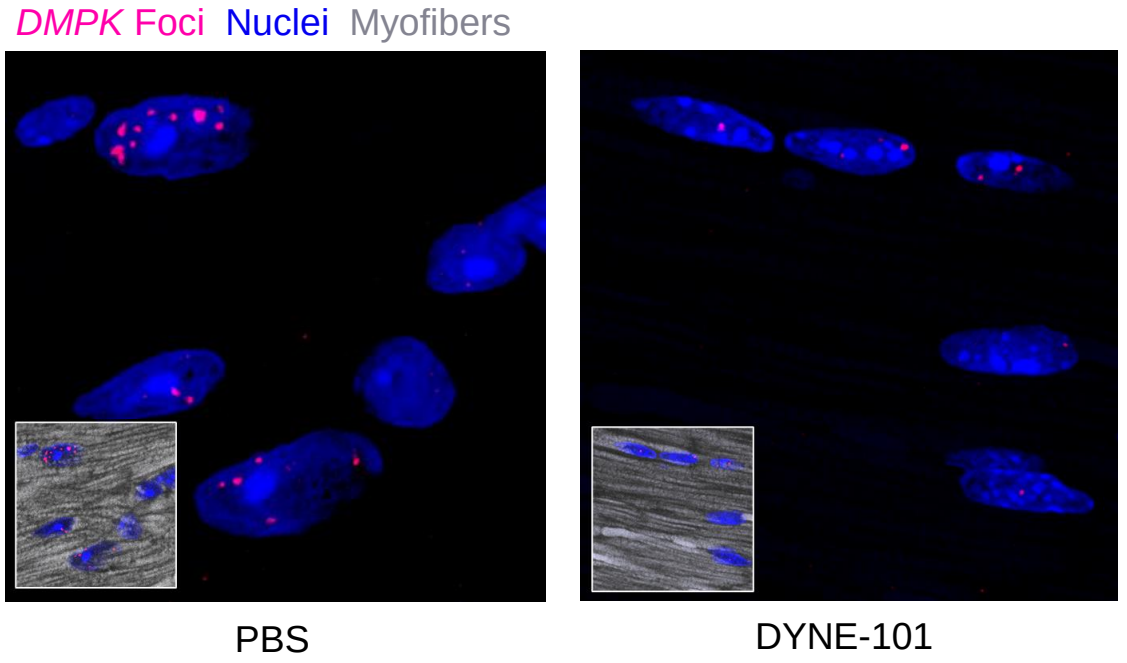

Note: Data are mean ±SD, n=4. Foci reduction based on foci area corrected for nuclear area

# DYNE-101 Demonstrated Toxic *DMPK* KD, Foci Reduction and Splicing Correction in Heart of hTfR1/DMSXL Homozygous Model

## Toxic Human *DMPK* RNA KD

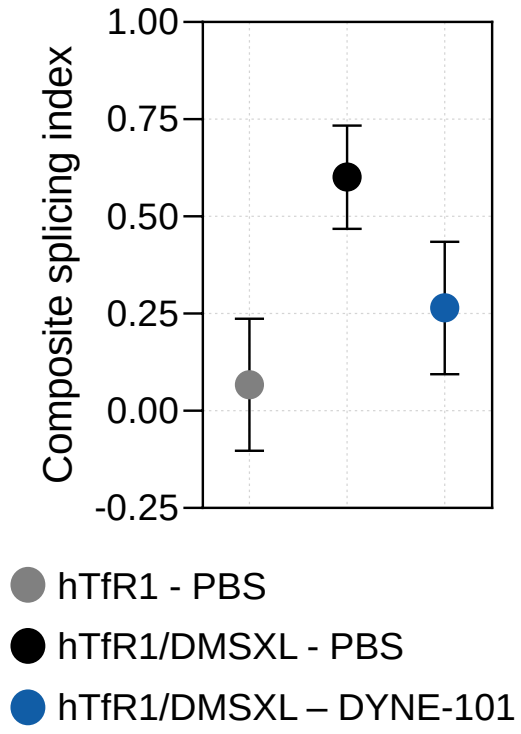



## Toxic Human *DMPK* Foci Reduction




**DYNE-101 reduces foci area by 49%***

## Splicing Correction




Note: hTfR1/DMSXL homozygous model. 2 x 10 mg/kg on d0 and d7, analyzed d28.
Composite splicing index includes changes in *Ldb3* exon (E) 11, *Mbnl2* E6, and *Nfix* E7. Data are mean ± SD, n = 6 - 7.; * $p$ <0.05; **** $p$ < 0.0001

# DYNE-101 Achieved *DMPK* Knockdown & Well Tolerated in NHPs

## Robust WT *DMPK* KD Achieved in Skeletal, Cardiac and Smooth Muscles

- Up to 60% *DMPK* KD at 1 month after a single dose

## 13-Week GLP Toxicology Study

- No dose limiting toxicity observed up to a maximally feasible dose[1]
- 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

1: Dosed once every three weeks
NOAEL: No-observed-adverse-effect level

# Proposed Clinical Trial to Evaluate DYNE-101 in Patients with DM1

**MULTIPLE ASCENDING DOSE (MAD)** | **LONG-TERM EXTENSION (LTE)**

## Design

- Multiple Ascending Dose
- Placebo Controlled
- Global
- LTE

## Population

- Patients with symptomatic DM1
- Ages 18+
- ~40-50 participants

## Endpoints*

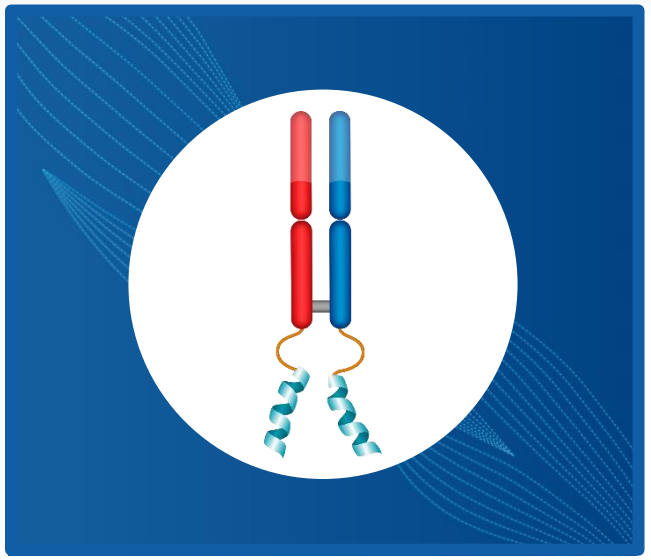
- Safety and tolerability
- PK/PD
- Splicing Index
- Measures of muscle strength and function
  - Myotonia
  - Ambulation
  - Respiratory

**Planned IND Submission in Q1 2022**
**Anticipate Dosing Patients by Mid-2022**

* Proposed endpoints include primary, secondary and exploratory

# Building the World's Leading Muscle Disease Company

**Win in DM1, DMD, FSHD**



**Own Muscle Delivery**

**Unparalleled Team & Culture**