



FORCE™ Platform for Targeted Delivery of Oligonucleotide Therapeutics in Muscle Diseases

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Ravi, living with DMD

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Dyne's Mission: Life-Transforming Therapies for Patients with Serious Muscle Diseases

Rare Muscle Disease Focus and Delivering for Patients

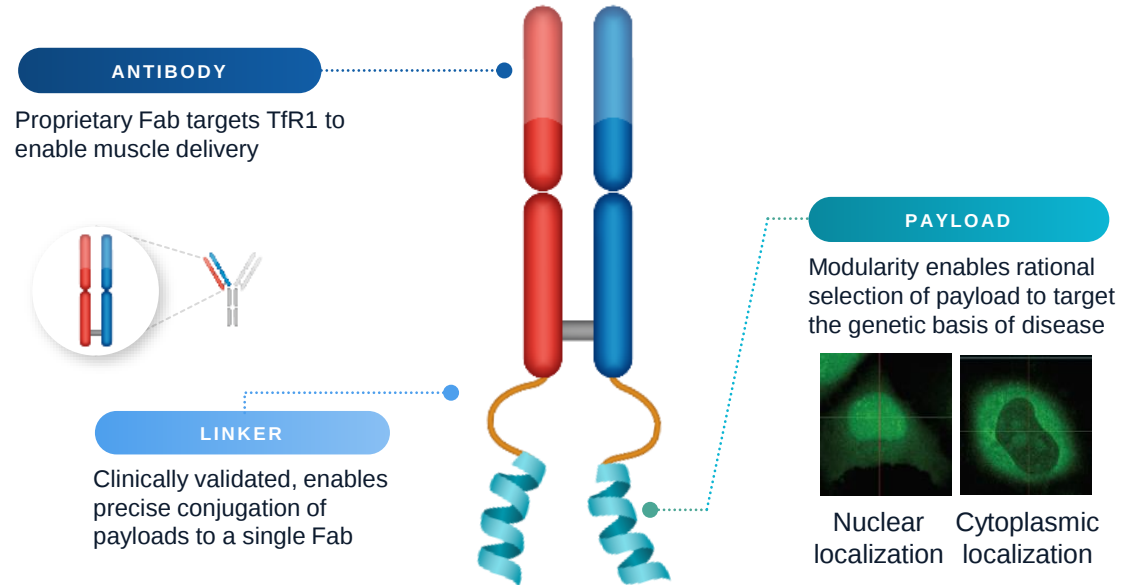


- Robust pipeline: DM1, DMD, and FSHD
- Developing multiple first-in-class or best-in-class therapies
- Precision medicine strategy
- Driving three programs to the clinic in 2022

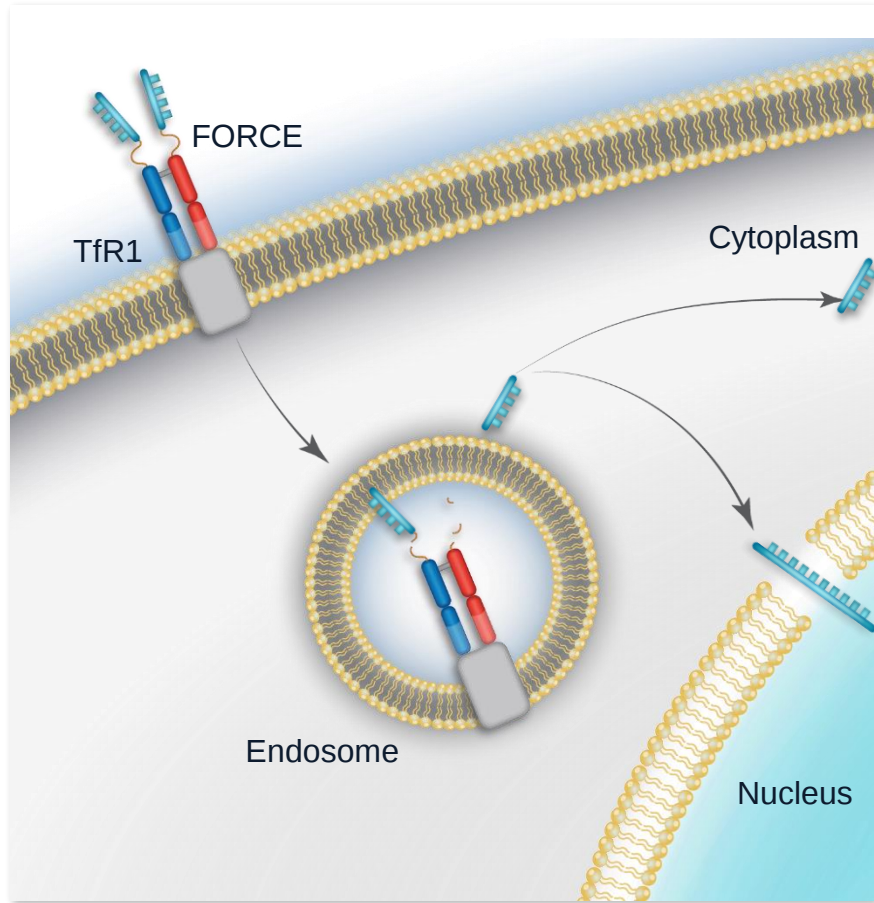
Proprietary FORCE Platform



- 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



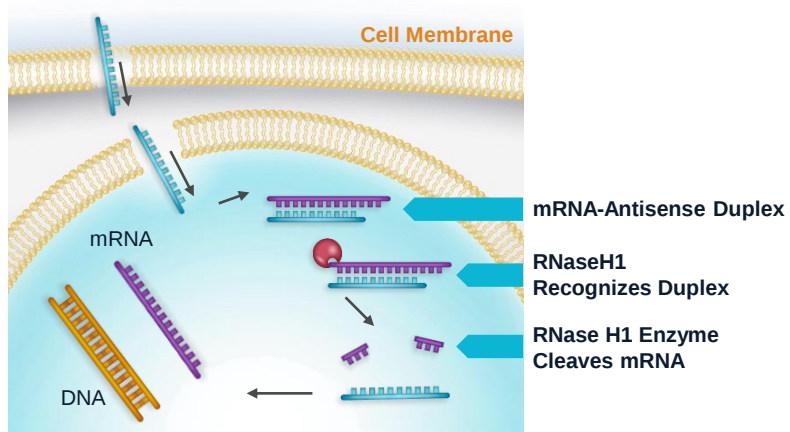
FORCE Platform Harnesses Cell Biology to Modify Disease



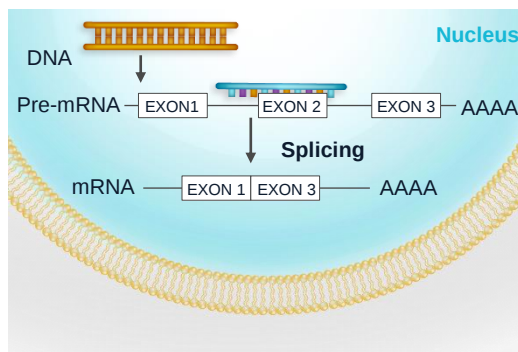
- Harnesses natural mechanism of TfR1 receptor-mediated delivery to transport therapeutics across the cell membrane
- Achieves endosomal escape without any membrane-destabilizing agents
- Distinctive pharmacokinetic profile creates opportunity for durable target engagement and wide therapeutic index

Rationally Select Payload to Target Genetic Basis of Disease

ASO acts in the nucleus and cytoplasm

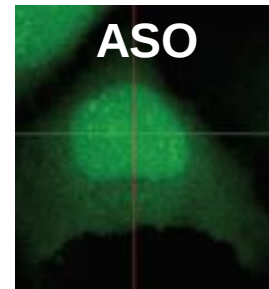


Splice-modulating ASO



Single-Stranded Antisense

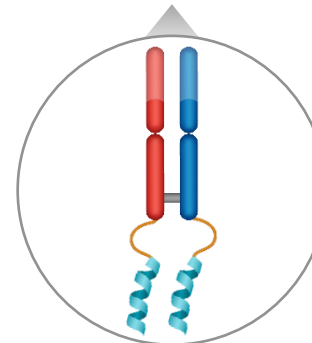
Subcellular distribution of ASO and siRNA



Nuclear localization

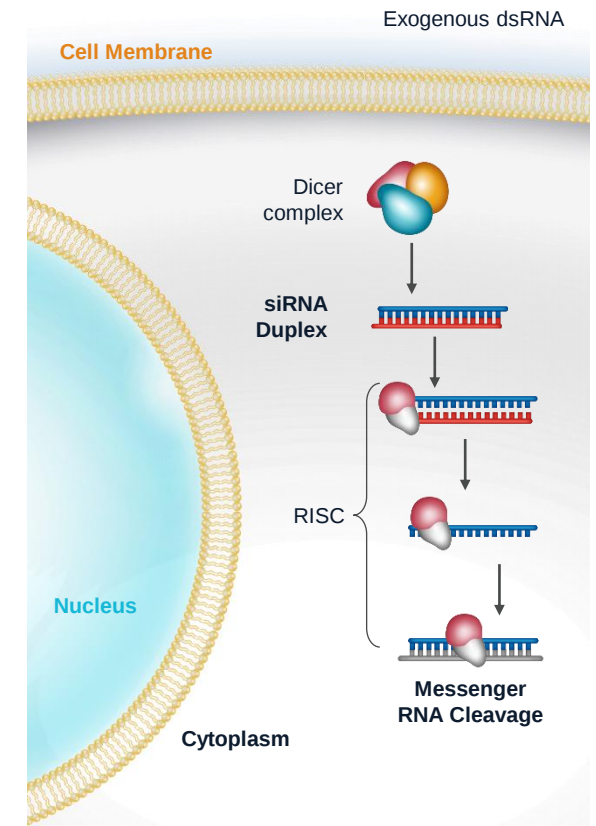


Cytoplasmic localization



FORCE delivers **ASO** payload for nuclear targets, **siRNA** payload for cytoplasmic targets

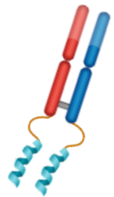
siRNA acts in the cytoplasm



Double-Stranded Antisense (siRNA)

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

Robust Portfolio Focused on Muscle Diseases

DISEASE	TARGET	DISCOVERY	PRECLINICAL	PHASE 1/2	ESTIMATED PATIENTS
Myotonic Dystrophy Type 1 (DM1)	DMPK	DYNE-101			US: >40,000 Europe: >74,000
Duchenne Muscular Dystrophy (DMD)	Exon 51	DYNE-251			US: ~12,000-15,000 Europe: ~25,000
	Exon 53				
	Exon 45				
	Exon 44				
	Other Exons				
Facioscapulohumeral Muscular Dystrophy (FSHD)	DUX4	DYNE-301			US: ~16,000-38,000 Europe: ~35,000

Pipeline Expansion Opportunities

Rare Skeletal
Cardiac
Metabolic

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)



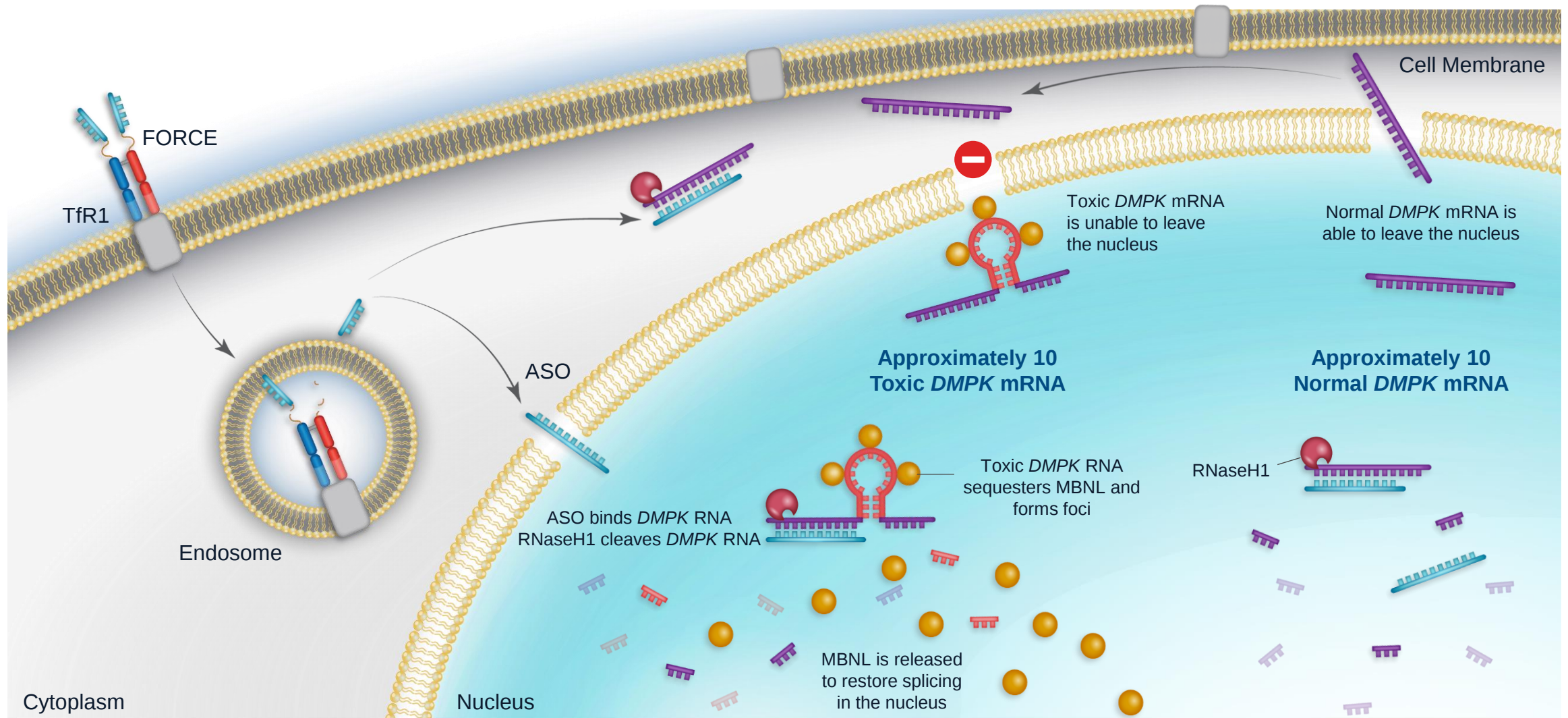
NO
approved
therapies

OUR APPROACH

Disease-Modifying Nuclear *DMPK* Knockdown

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

FORCE Targets Toxic Nuclear *DMPK* RNA



DM1 Program Summary

Validating Data

- ✓ **Targeted** toxic *DMPK* in the nucleus in patient cells
- ✓ **Robust and durable toxic human *DMPK* KD** in novel hTfR1/DMSXL model
- ✓ **Reduced nuclear foci** *in vitro* & *in vivo*
- ✓ **Corrected splicing** changes *in vitro* & *in vivo*
- ✓ **Reversed myotonia** in HSA^{LR} model
- ✓ **Delivered *DMPK* targeting ASO** to mouse and NHP muscle tissues
- ✓ **Favorable safety profile in NHP GLP tox study**

Potential Advantages

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

**Multiple Regulatory Filings
Planned in Q2 2022¹
Anticipate Dosing Patients in Mid-2022**

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)



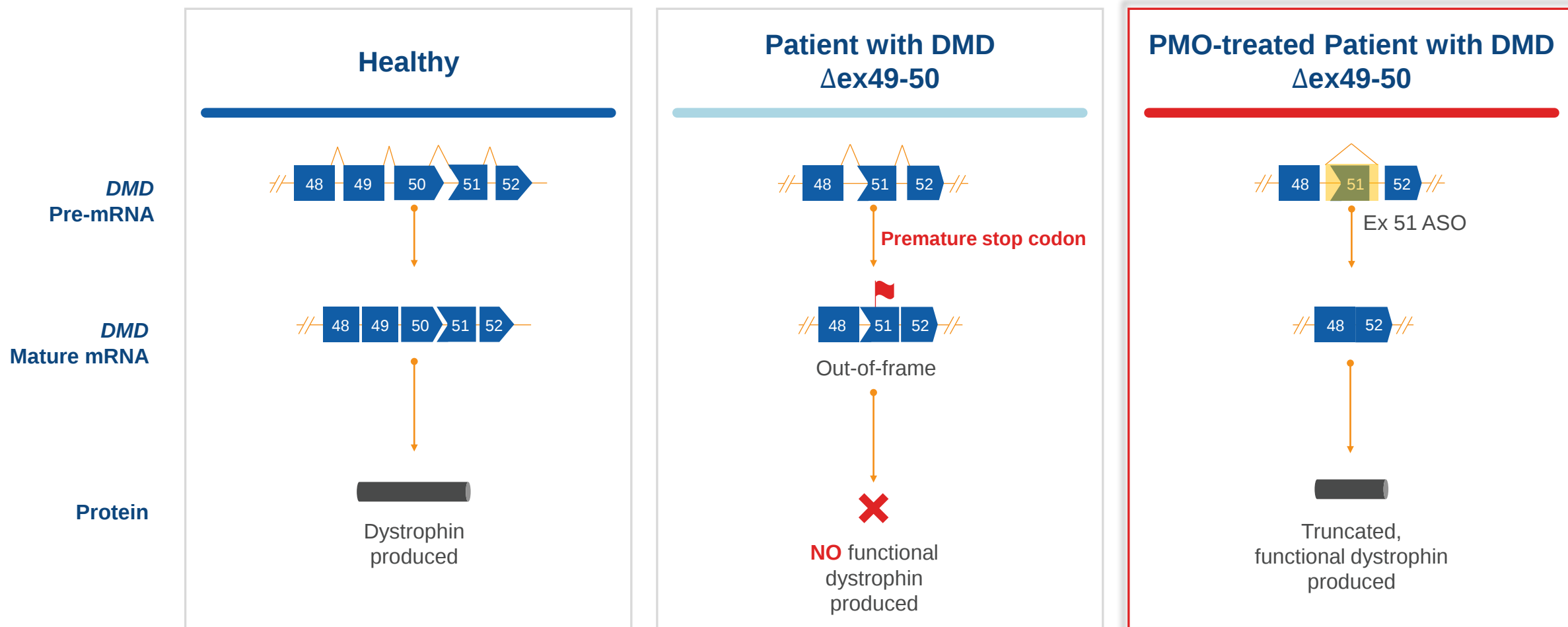
OUR APPROACH

Best-in-class Targeted Exon Skipping

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%

Targeting the Genetic Basis of DMD with a Proven Mechanism



Optimized with FORCE Platform

DMD Program Summary

Validating Data

mdx Model

- ✓ **Achieved robust and durable** exon skipping in skeletal and cardiac muscle
- ✓ **Dose-dependently increased dystrophin** expression up to 90% of WT based on western blot and ~80% dystrophin-positive fibers
- ✓ **Reduced serum CK levels**
- ✓ **Demonstrated functional benefit** in multiple standardized assessments

DYNE-251

- ✓ **Robust and dose-dependent exon skipping** in patient DMD patient myotubes (exon 51)
- ✓ **Transformative exon skipping in NHP** cardiac and skeletal muscles
- ✓ **Favorable safety profile in NHP GLP tox study**

Potential Advantages

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

Anticipate Dosing Patients in Mid-2022¹

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)



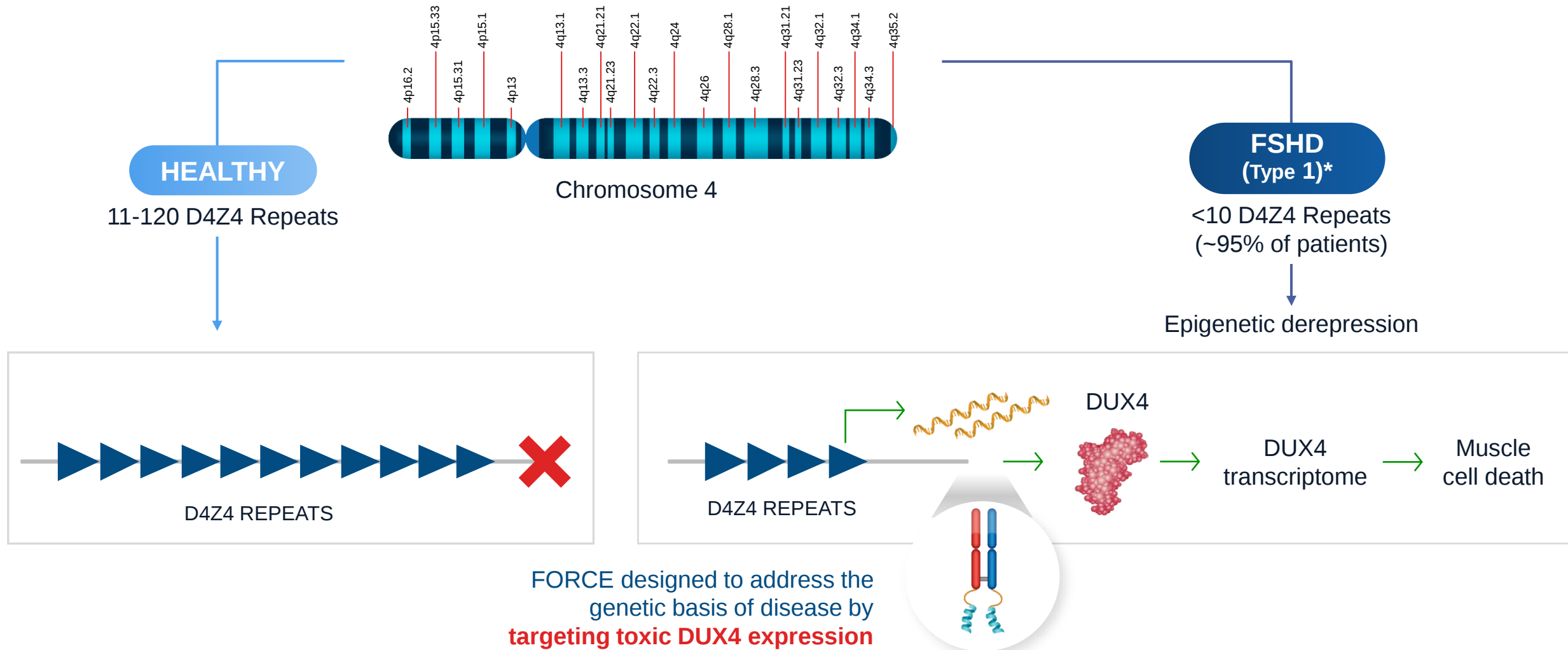
NO
approved
therapies

OUR APPROACH

Disease-Modifying DUX4 Knockdown

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

FORCE Targets the Genetic Basis of FSHD



FSHD Program Summary

Validating Data

- ✓ **Reduced** toxic gain-of-function *DUX4* mRNA
- ✓ **Superior** suppression of *DUX4* biomarkers observed over naked ASO
- ✓ **Enhanced** muscle distribution
- ✓ **Translatability** to primates expected; based on platform data in multiple NHP studies

Potential Advantages

- **Exclusive license** to potent *DUX4* targeting payloads
- **Tractable development** with rapid path to human PoC

Planned IND Submission in H2 2022



Targeting the genetic basis of serious muscle diseases to
STOP OR REVERSE DISEASE PROGRESSION



FORCE
PLATFORM

Robust
PIPELINE

Delivering
FOR PATIENTS

Exceptional
TEAM