

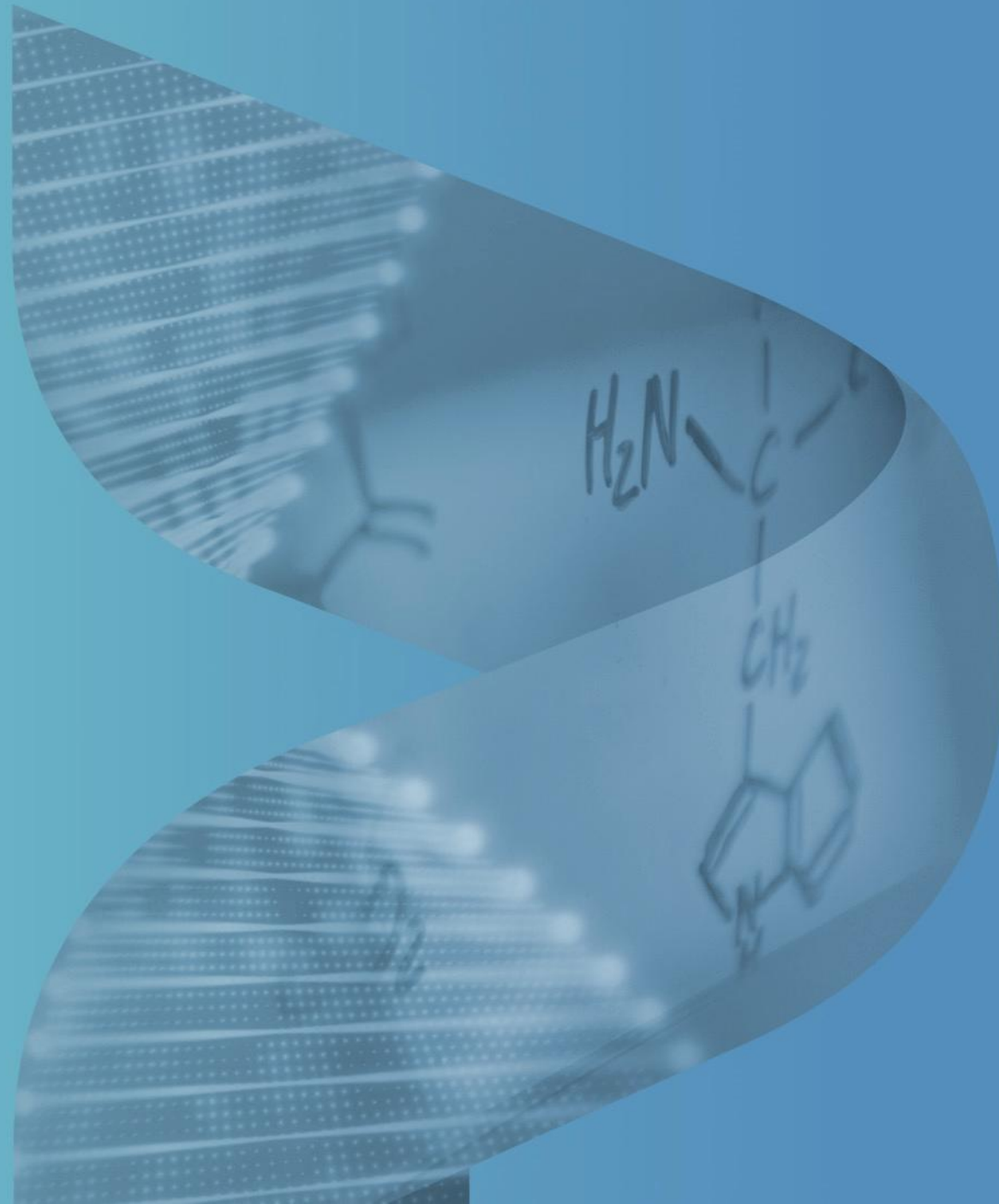


## PGN-EDODM1, in Development for Myotonic Dystrophy Type 1

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## Disclosures

- Jane Larkindale is a full-time employee of PepGen Inc
- Jane Larkindale receives compensation, equity and benefits from PepGen Inc
- The study and current analysis were sponsored by PepGen Inc



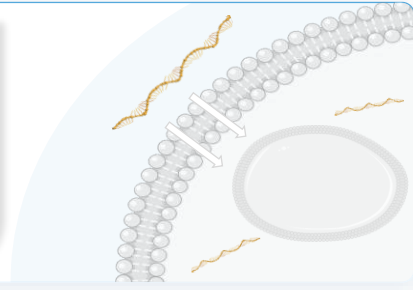
PepGen is committed to transforming the lives of people with severe neuromuscular and neurological disorders with our Enhanced Delivery Oligonucleotides (EDOOs)



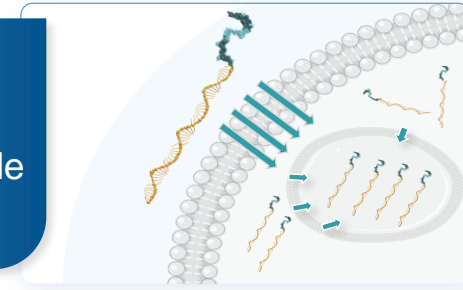
Jubal and family

# Enhanced Delivery Oligonucleotide Platform Enhances Nuclear Delivery and Uptake of Oligonucleotides

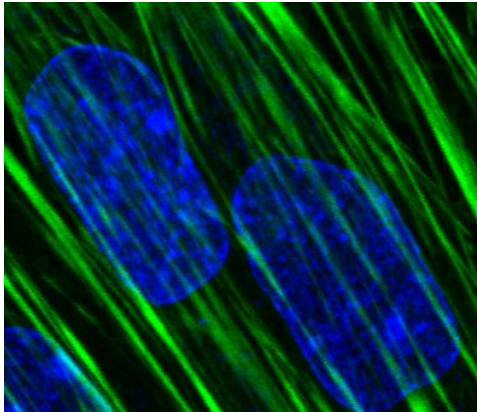
Naked oligonucleotides not efficiently taken up into muscle cells & nucleus



EDOs enhance nuclear delivery of oligonucleotide therapeutics

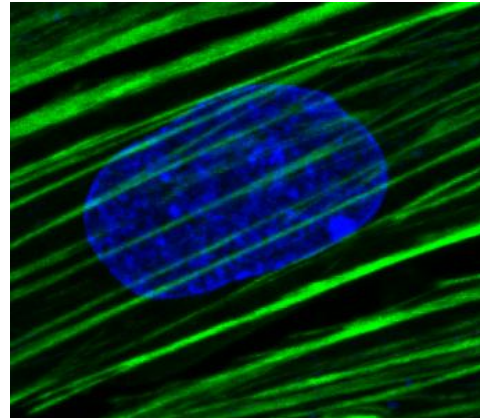


Not treated



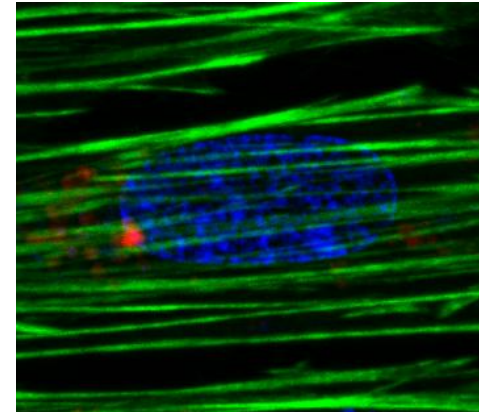
0  $\mu$ M

PGN-PMODM1

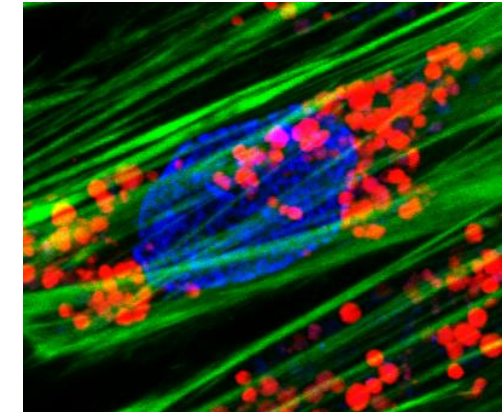


20  $\mu$ M

PGN-EDODM1



2  $\mu$ M

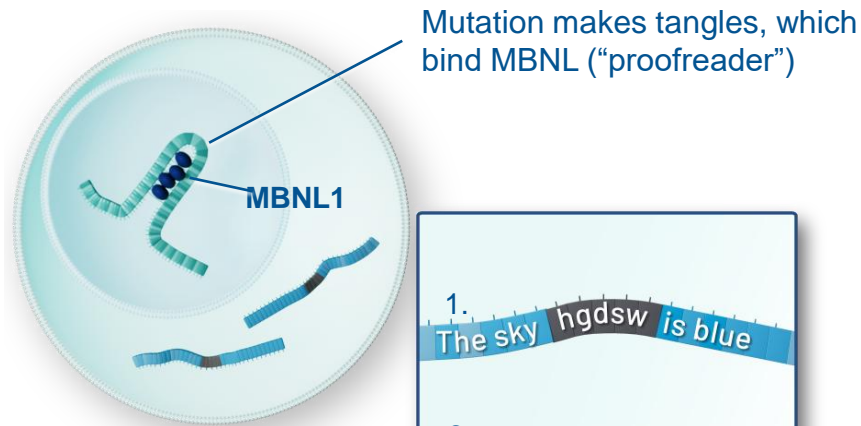


10  $\mu$ M

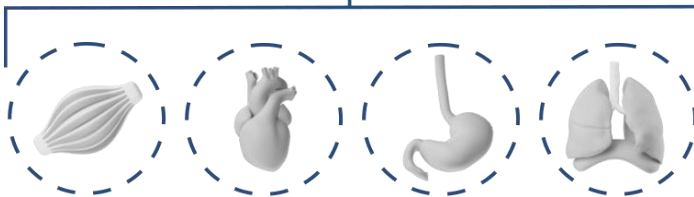
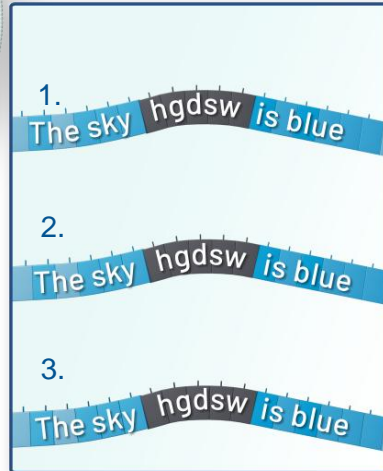
PGN-EDODM1 / Actin / Nucleus

# PGN-EDODM1 Mechanism of Action - Approach in DM1

## DM1

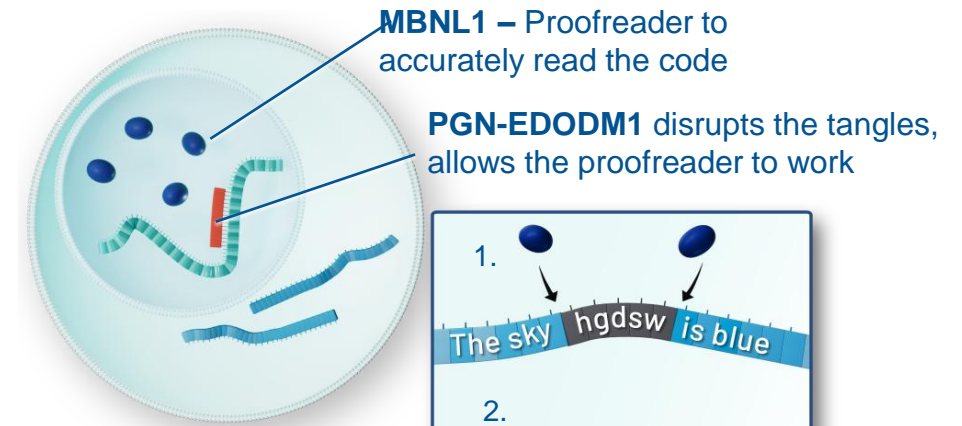


Proofreader not available.  
Splicing is incorrect and  
proteins are not made correctly

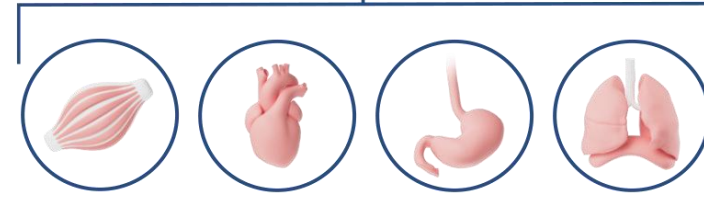
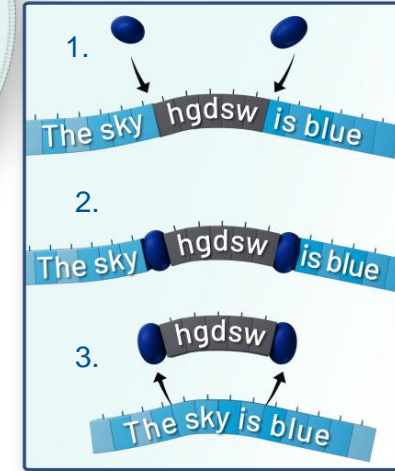


Skeletal muscle   Heart   Digestive system   Respiratory system

## DM1+ PGN-EDODM1



Proofreader available.  
Splicing is correct and  
proteins are made correctly

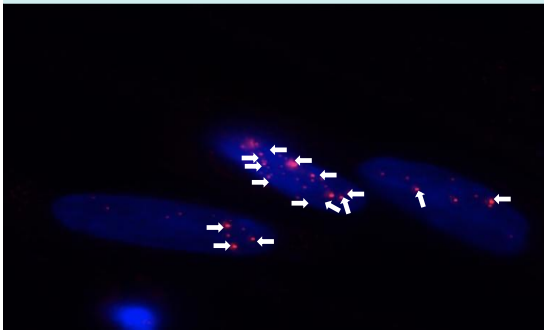


Skeletal muscle   Heart   Digestive system   Respiratory system

# PGN-EDODM1 Reduced Foci, Liberated MBNL1 and Corrected Mis-Splicing in Patient Cells with Long CTG Repeats

## FOCI REDUCTION

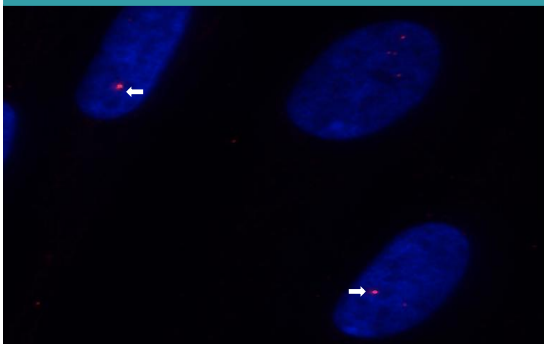
Not treated (NT)



**54%**  
reduction in  
toxic foci

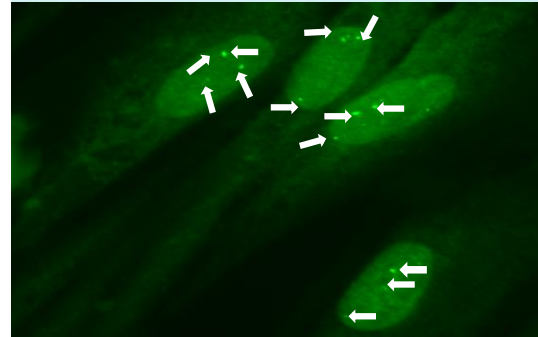


PGN-EDODM1 treated

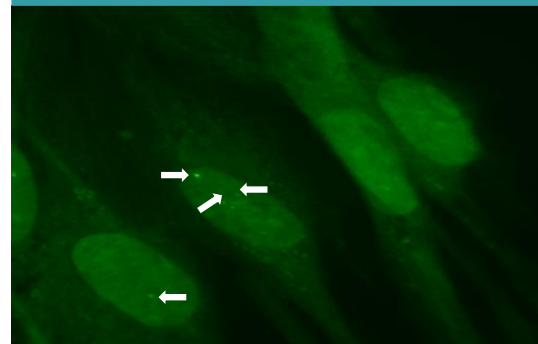


## MBNL1 LIBERATION

Not treated (NT)



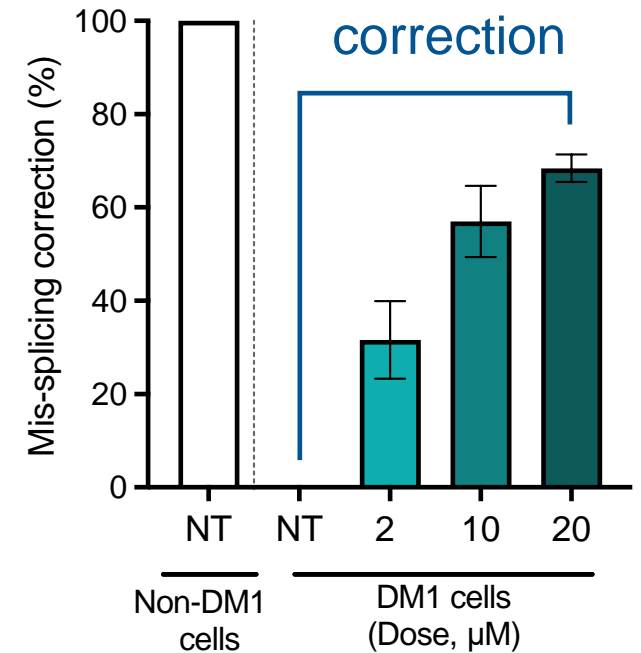
PGN-EDODM1 treated



## MIS-SPLICING CORRECTION

*Across multiple transcripts*

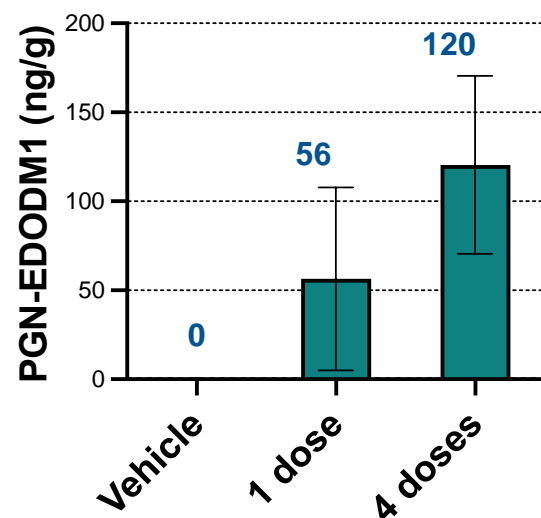
**69%**  
correction



# Multiple Doses of PGN-EDODM1 Led to Greater Improvement in Splicing Correction and Myotonia vs Single Dose in Preclinical Studies

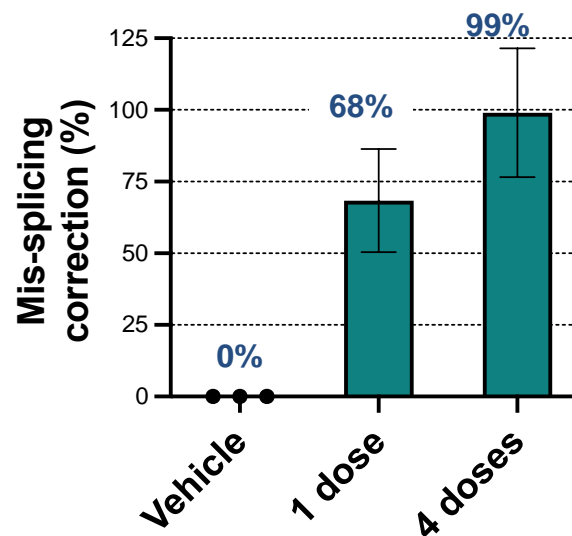
## Tissue Concentration

### Skeletal muscle



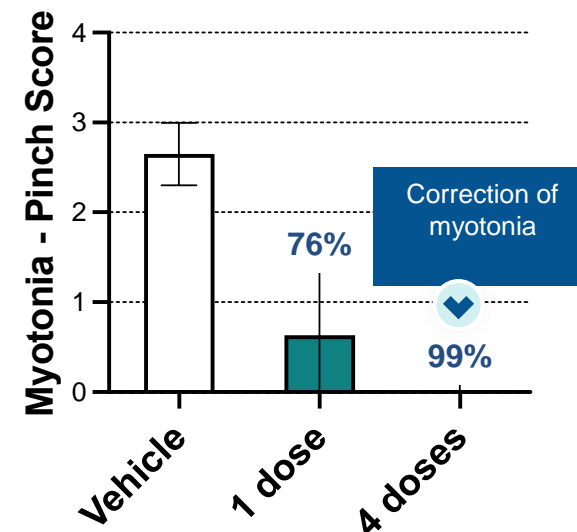
## Mis-Splicing Correction

### Across multiple transcripts



## Correction of Myotonia

### Pinch test



# FREEDOM: Phase 1 PGN-EDODM1 Single-Ascending Dose Study Design



## FREEDOM Study Overview

Multinational, randomized, double-blind, placebo-controlled SAD study in people with DM1

Single IV administration of PGN-EDODM1

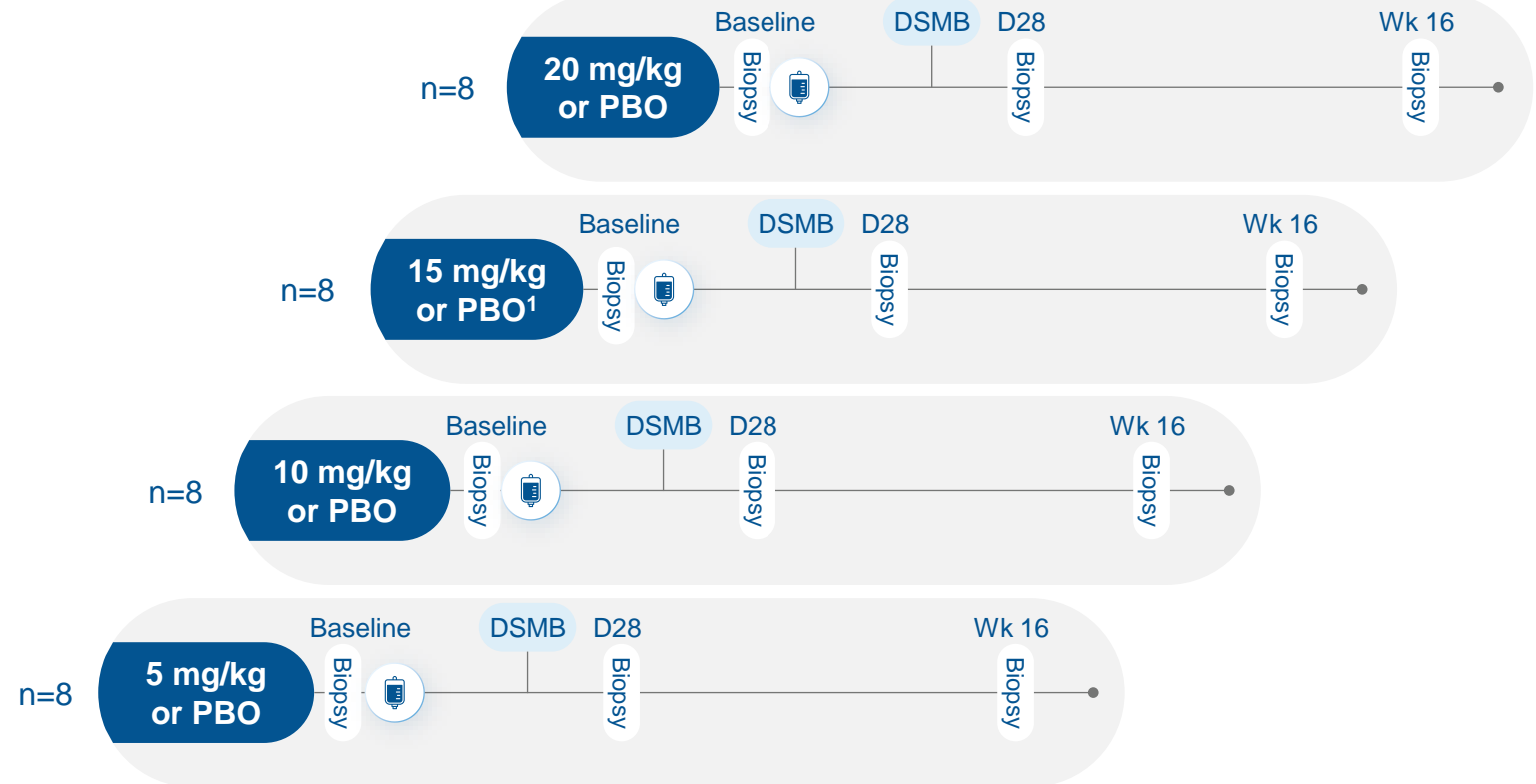
Muscle biopsies in tibialis anterior at Baseline, Day 28, Week 16

Safety, PK, correction of mis-splicing, initial functional assessments

## Single Dose PGN-EDODM1 or Placebo (randomized 3:1)

Dosing

Dosed



# FREEDOM: Demographics and Baseline Characteristics in First Two Cohorts

	Mean (SD) or n (%)		
	Placebo (n=4)	5 mg/kg (n=6)	10 mg/kg (n=6)
Age (years)	39.0 (10.9)	36.3 (9.0)	34.7 (8.2)
Female, n (%)	3 (75%)	3 (50%)	3 (50%)
BMI (kg/m <sup>2</sup> )	20.0 (3.3)	22.8 (5.0)	22.8 (5.7)
Splicing Index	72.3 (16.3)	73.7 (15.2)	53.6* (26.0)
vHOT – middle finger (sec)	14.1 (5.6)	12.6 (7.3)	9.3 (2.8)
10MWRT (sec)	4.3 (1.6)	3.9 (1.5)	4.4 (1.5)

# Favorable Emerging Safety Profile of PGN-EDODM1<sup>1</sup>

## Summary of Treatment Emergent Adverse Events (TEAEs)

	5 mg/kg (n=8) <sup>2</sup> n(%)	10 mg/kg (n=8) <sup>2</sup> n(%)	Total (n=16) <sup>2</sup> n(%)
Any TEAE	4 (50.0)	6 (75.0)	10 (62.5)
Any related TEAE	1 (12.5)	3 (37.5)	4 (25.0)
Any SAE	1 (12.5)	2 (25.0)	3 (18.8)
Any related SAE	0	1 (12.5)	1 (6.3)
Any AESI or dose-limiting toxicities	0	0	0
Any TEAE leading to study withdrawal	0	0	0
Any TEAE leading to death	0	0	0

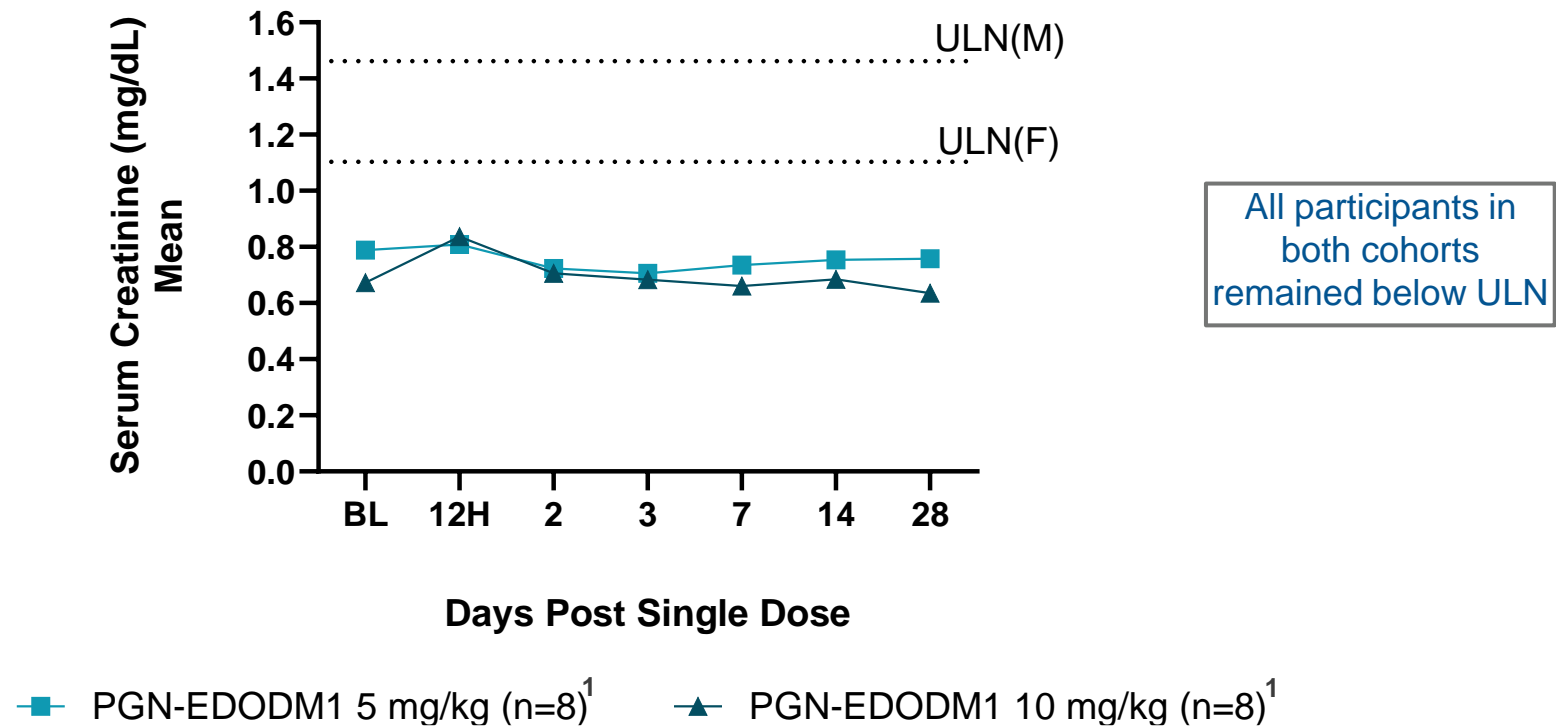
## PGN-EDODM1 was Generally Well-Tolerated, with Most TEAEs Mild or Moderate in Severity

### All treatment related TEAEs:

- Nausea (n=2), vomiting (n=1), dizziness (n=1), headache (n=1), feeling hot (n=1), abdominal pain (n=1)
- SAE related to study drug:
  - Abdominal pain (10 mg/kg) potentially confounded by use of prohibited, off-label drug taken on the morning of PGN-EDODM1 dosing<sup>3</sup>
- SAEs unrelated to study drug:
  - Appendicitis (5 mg/kg)
  - Right anterior tibial artery pseudoaneurysm (10 mg/kg) related to muscle biopsy procedure
- No adverse events related to electrolytes or renal biomarkers

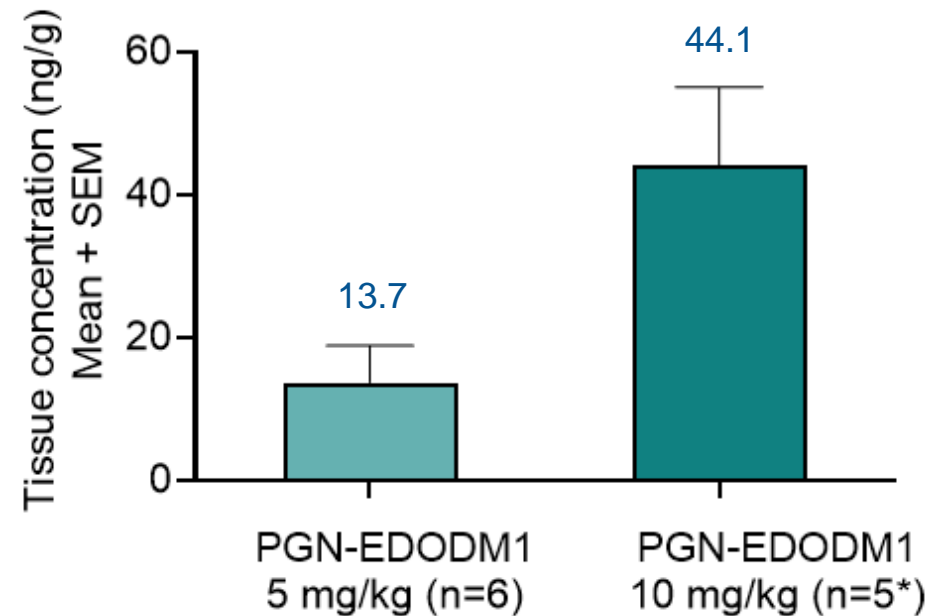
# PGN-EDODM1 Demonstrated Normal Mean Serum Creatinine Levels

## Serum Creatinine



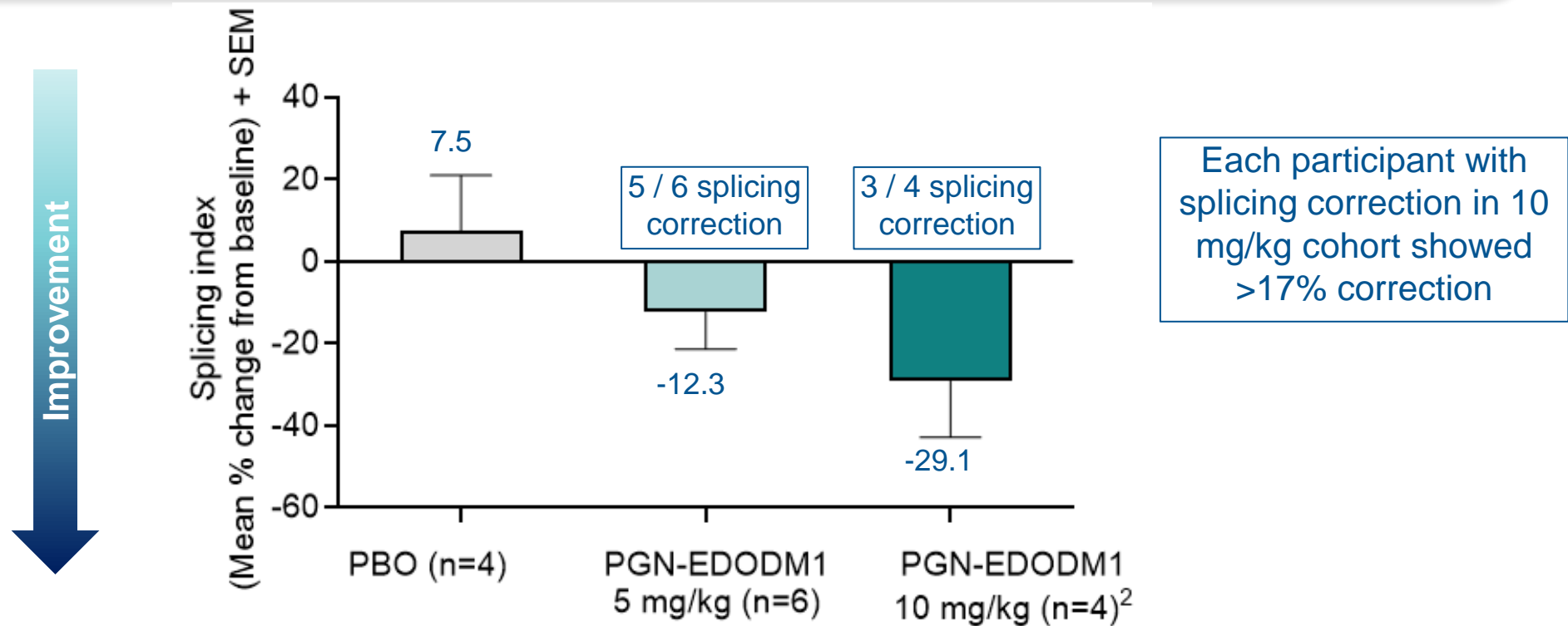
# PGN-EDODM1 Observed to Have Robust and Dose-Dependent Increases in Muscle Tissue Concentration Following a Single Dose

## Muscle Tissue Concentration at D28



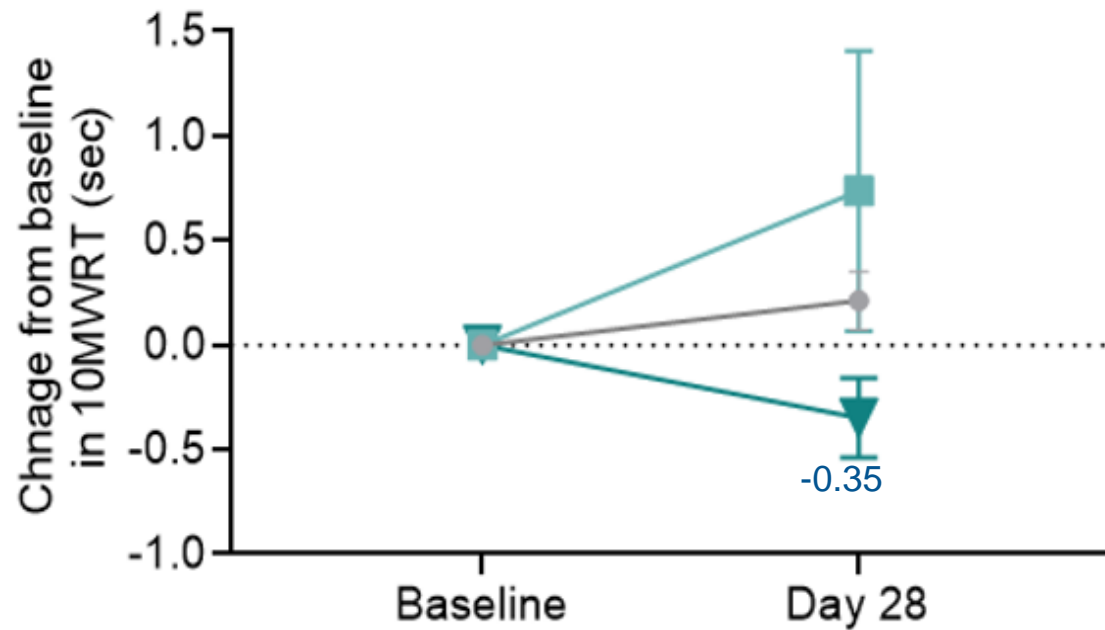
# PGN-EDODM1 Produced Mean 29% Splicing Correction Following Single 10 mg/kg Dose

## Splicing Index Changes: 22-Gene Panel<sup>1</sup> at D28

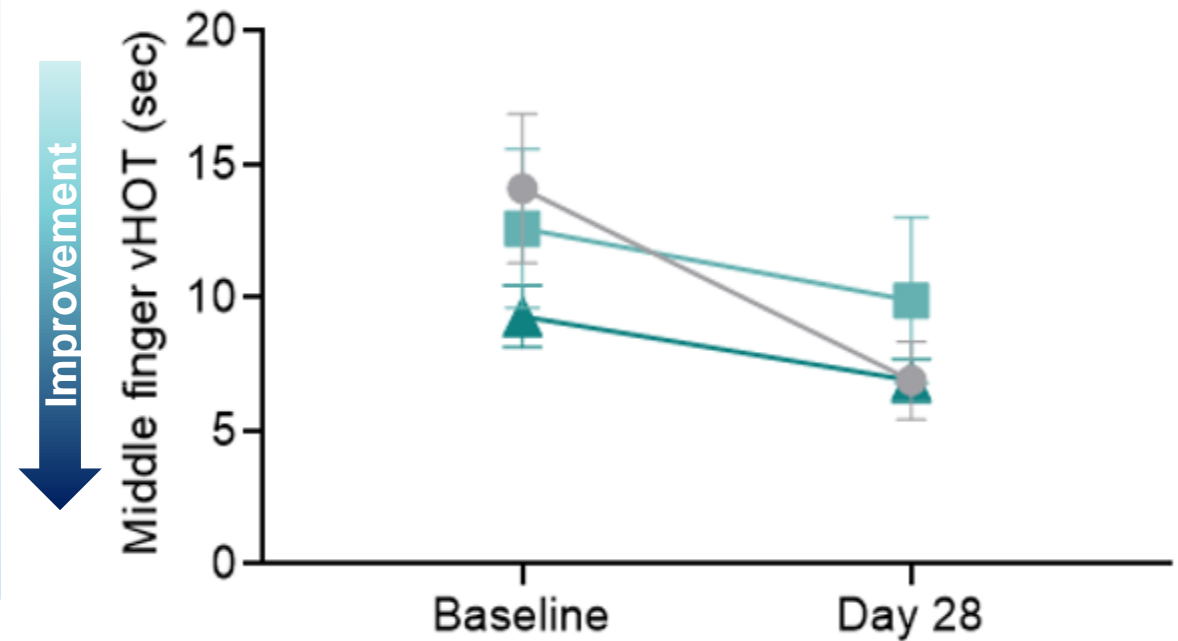


# Functional Outcomes Data After a Single Dose

## 10-Meter Walk Run Test (10MWRT) at D28



## Myotonia (vHOT) at D28



● PBO (n=4) ■ PGN-EDODM1 5 mg/kg (n=6) ▲ PGN-EDODM1 10 mg/kg (n=6)

# PGN-EDODM1 Selectively Targets Only Pathogenic *DMPK* to Correct RNA Mis-Splicing



**Favorable emerging safety profile<sup>1</sup>** in people with myotonic dystrophy type 1



Dose-dependent increase in drug **tissue concentration** observed in first two cohorts



Dose-dependent increases in evaluable people<sup>2</sup> in mean **splicing correction** following single dose

**~29%** at 10 mg/kg

**~12%** at 5 mg/kg

# FREEDOM2 Phase 2 MAD Study Underway



## FREEDOM2 Study Overview

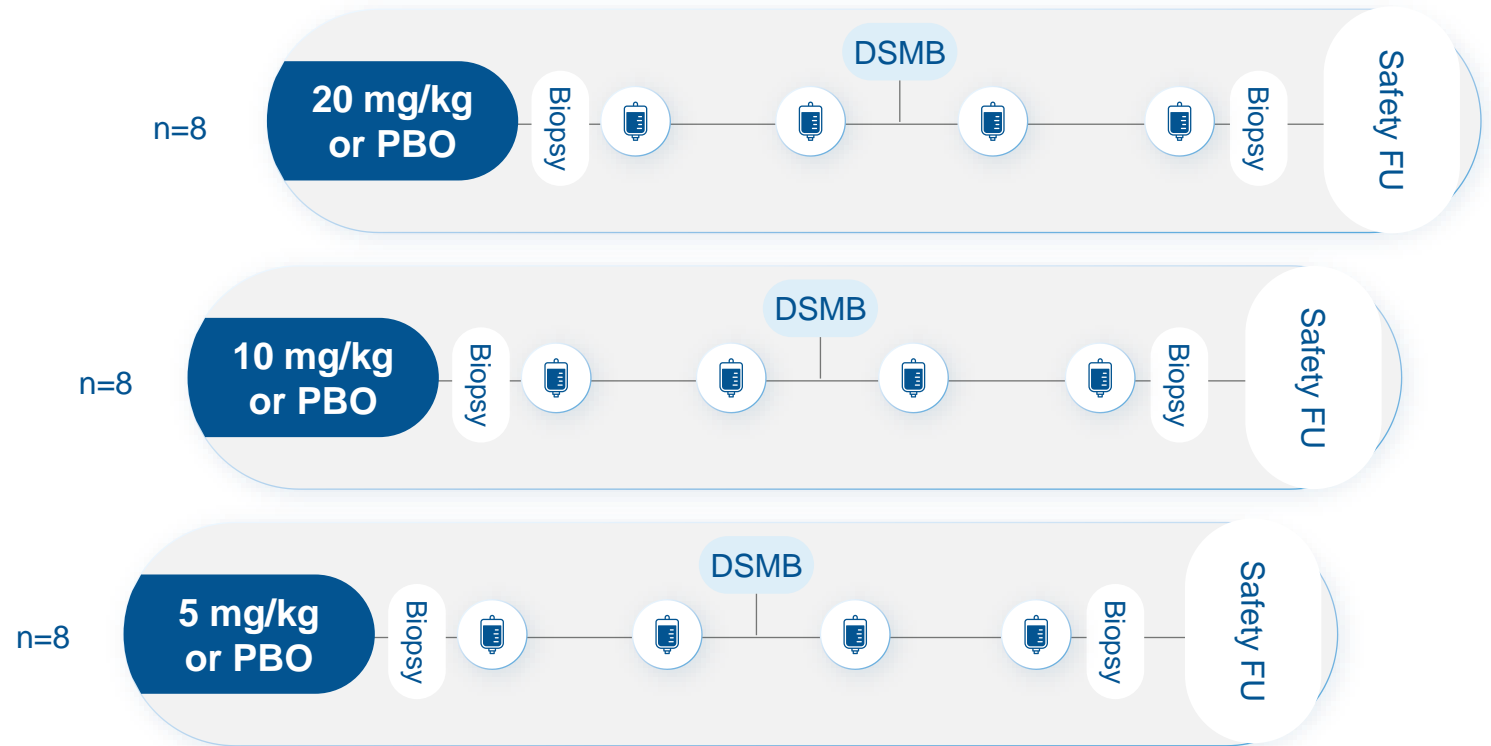
Multinational, randomized, double-blind, placebo-controlled, MAD study open in UK and Canada

IV administration of PGN-EDODM1 or placebo every 4 weeks for a period of 12 weeks

Key endpoints: Safety, PK, correction of splicing, functional assessments: vHOT, hand grip, 10-meter walk run test

### 4 Doses of PGN-EDODM1 or Placebo (randomized 3:1)

Dosing



# Thank you!



**Clinical study  
participants and  
their families**



**Clinical site staff  
and investigators**



**Community  
and clinical  
advisors**



**Preclinical  
collaborators**



# Q&A

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