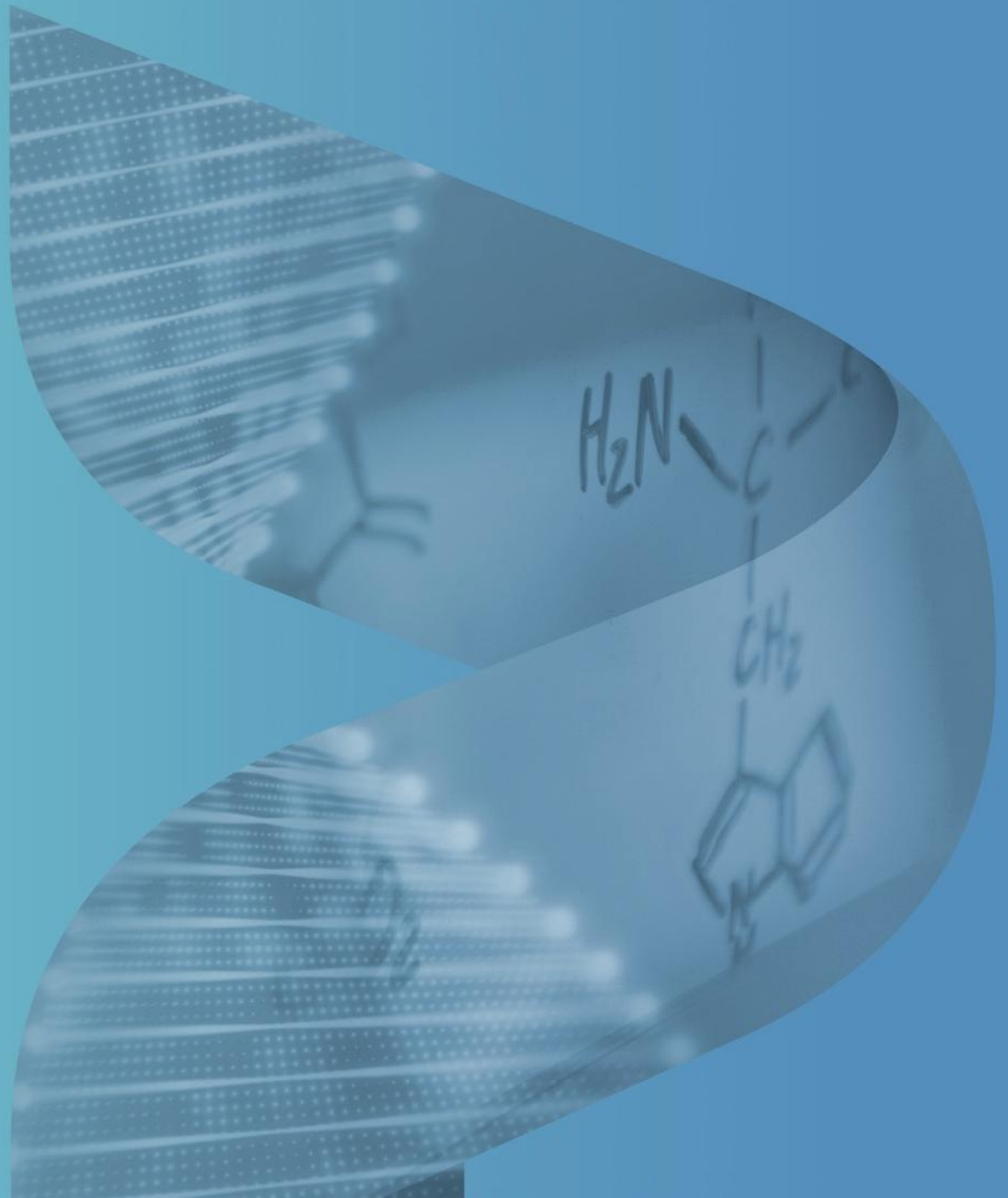
PepGen™

FREEDOM-DM1 5 and 10 mg/kg Clinical Data Update

February 24, 2025



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This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These statements may be identified by words such as “aims,” “anticipates,” “believes,” “could,” “estimates,” “expects,” “forecasts,” “goal,” “intends,” “may,” “plans,” “possible,” “potential,” “seeks,” “will,” and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this presentation that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include, without limitation, statements regarding the potential of our EDO platform to deliver higher levels of oligonucleotide to the nuclei, the therapeutic potential and safety profile of PGN-EDODM1 based on data from the 5 and 10 mg/kg cohorts of the FREEDOM-DM1 study, our expectations regarding the potential for significant correction of mis-splicing with more doses of PGN-EDODM1 over a longer treatment period to potentially provide improved functional benefit for patients with DM1, the design, initiation and conduct of clinical trials, including expected timelines for our FREEDOM1-DM1 Phase 1 and FREEDOM2-DM1 Phase 2 trials and our CONNECT1-EDO51 and CONNECT2-EDO51 Phase 2 trials, the expected timing for additional data reports from our FREEDOM Phase 1 trial and CONNECT1 Phase 2 trial, and ongoing and planned regulatory interactions.

Any forward-looking statements in this presentation are based on current expectations, estimates and projections only as of the date of this presentation and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: delays or failure to successfully initiate or complete our ongoing and planned development activities for our product candidates, including PGN-EDODM1 and PGN-EDO51; our ability to enroll patients in our clinical trials, including FREEDOM, FREEDOM2, CONNECT1 and CONNECT2; that our interpretation of clinical and preclinical study results may be incorrect, or that we may not observe the levels of therapeutic activity in clinical testing that we anticipate based on prior clinical or preclinical results, including for PGN-EDODM1 and PGN-EDO51; our product candidates, including PGN-EDODM1 and PGN-EDO51, may not be safe and effective or otherwise demonstrate safety and efficacy in our clinical trials; adverse outcomes from our regulatory interactions, including delays in regulatory review, clearance to proceed or approval by regulatory authorities with respect to our programs, including clearance to commence planned clinical studies of our product candidates, or other regulatory feedback requiring modifications to our development programs, including in each case with respect to our including FREEDOM, FREEDOM2, CONNECT1 and CONNECT2 clinical trials; changes in regulatory framework that are out of our control; our ability to obtain, maintain and protect our intellectual property; our ability to enforce our patents against infringers and defend our patent portfolio against challenges from third parties; competition from others developing therapies for the indications we are pursuing; unexpected increases in the expenses associated with our development activities or other events that adversely impact our financial resources and cash runway; and our dependence on third parties for some or all aspects of our product manufacturing, research and preclinical and clinical testing. Additional risks concerning PepGen's programs and operations are described in our most recent annual report on Form 10-K that is filed with the SEC. PepGen explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

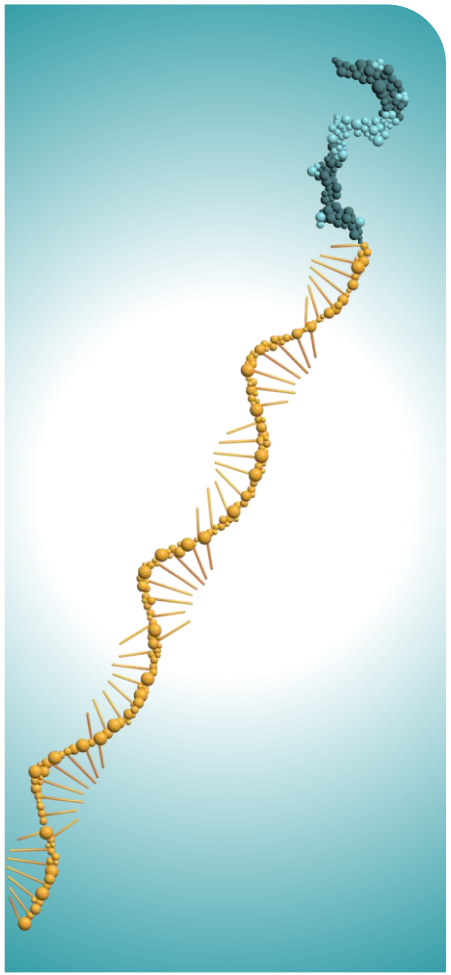
This presentation discusses PGN-EDODM1 and PGN-EDO51, investigational therapies that have not been approved for use in any country, and is not intended to convey conclusions about their efficacy or safety. There is no guarantee that PGN-EDODM1, PGN-EDO51 or any other investigational therapy will successfully complete clinical development or gain regulatory authority approval.

Agenda

James McArthur, PhD
President and Chief Executive Officer
Key Takeaways, DM1 Overview, EDO Platform, Closing Remarks, and Q&A

Paul Streck, MD, MBA
Head of R&D
FREEDOM Clinical Trial Design, Clinical Data, and Q&A

Michelle Mellion, MD
Chief Medical Officer
Q&A



PGN-EDODM1 Initial Data FREEDOM-DM1 Study: Myotonic Dystrophy Type I Overview and EDO Platform

James McArthur, PhD
President and Chief Executive Officer

PGN-EDODM1 Has Demonstrated Robust Dose-Dependent Splicing Correction Following Single Dose in First Two Cohorts

Favorable emerging safety profile in patients with myotonic dystrophy type 1 (DM1)[1]

Dose-dependent increases in drug tissue concentration and mean splicing correction were observed in first two cohorts

Robust splicing correction at Day 28

Mis-splicing is the known cause of DM1, and we believe that with repeat and higher dosing, PGN-EDODM1 has the potential to produce greater splicing correction levels, which could lead to improved functional outcomes for patients

1. As of data cut-off date Dec 3, 2024

Myotonic Dystrophy Type 1 Overview and Unmet Medical Need

Overview

- CUG expansion in the *DMPK* gene
- Onset of symptoms variable-childhood to adulthood
  - Myotonia
  - Muscle weakness
  - Cardiac arrythmias
  - Loss of lung function
  - Fatigue
- Average life expectancy is 50-60 years for non-congenital forms of DM1

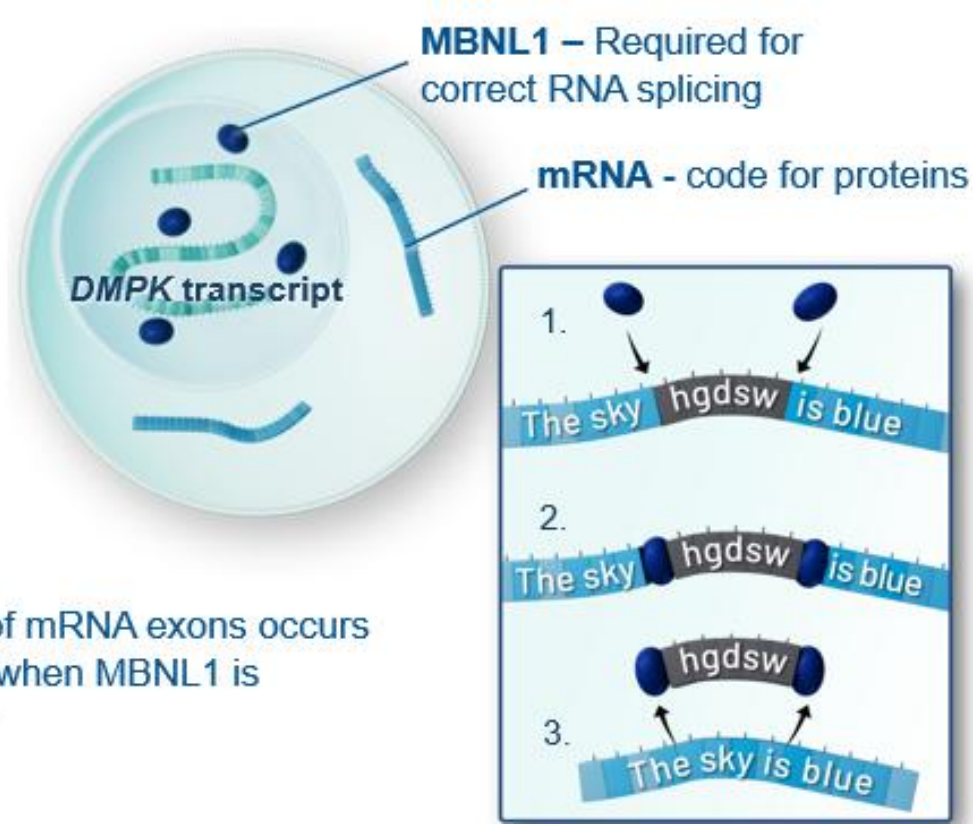
Market Opportunity

- U.S and EU over 110,000 patients
- No approved therapies that address underlying cause of the disease

Sources: Neuroepidemiology (2022) 56 (3): 163–173., Neurology 2021 Feb 16;96(7):e1045-e1053
CUG: cytosine-uracil-guanine; *DMPK*: dystrophia myotonica protein kinase

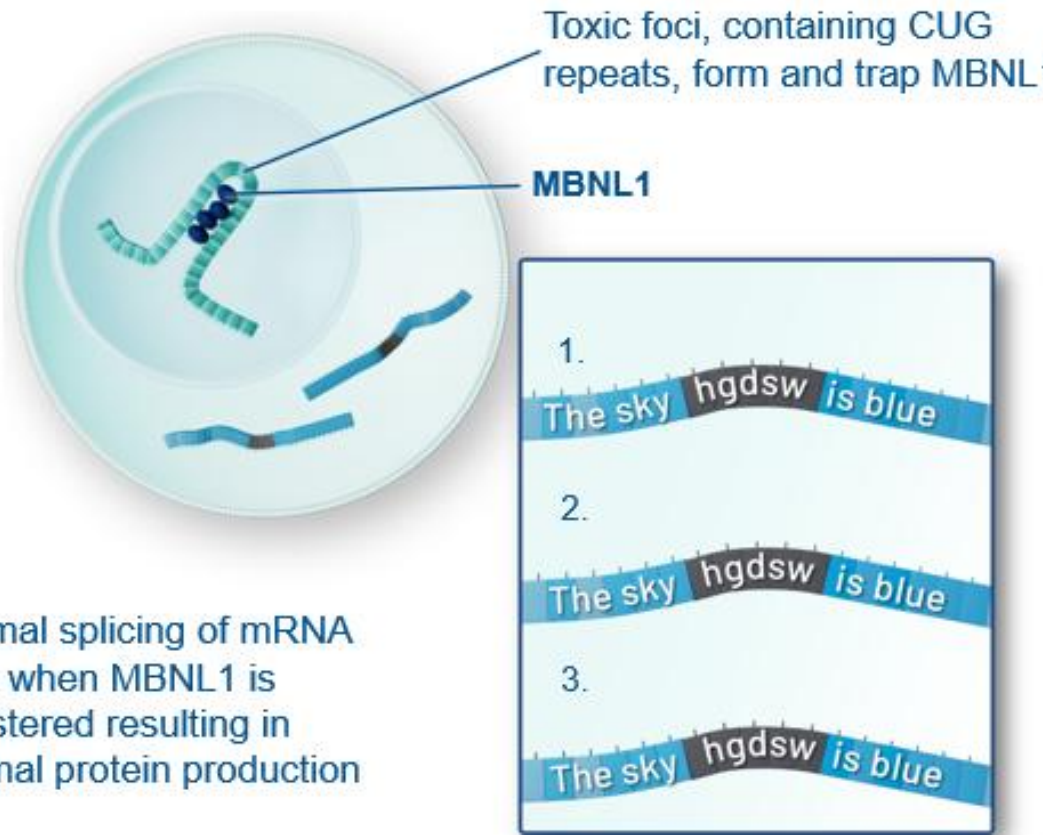
Mis-Splicing is the Underlying Cause of DM1

Unaffected Individual



Splicing of mRNA exons occurs normally when MBNL1 is available

DM1 Patient



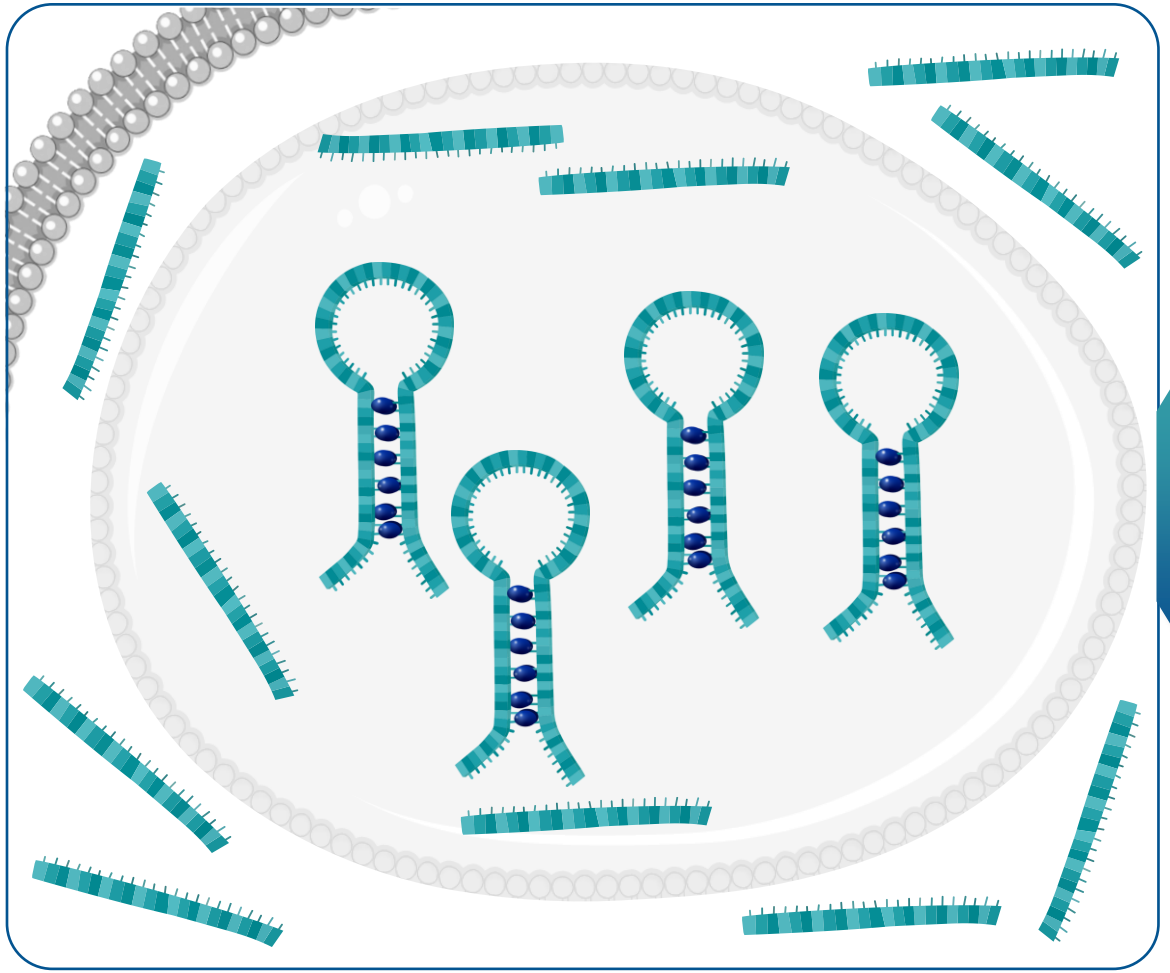
Abnormal splicing of mRNA occurs when MBNL1 is sequestered resulting in abnormal protein production

Lopez-Martinez, et al., An Overview of Alternative Splicing Defects Implicated in Myotonic Dystrophy Type 1, *Genes,* September 2020
Sznajder & Swanson, Short Tandem Repeat Expansions and RNA-Mediated Pathogenesis in Myotonic Dystrophy, *International Journal of Molecular Sciences,* July 2019

DM1 is Caused by Pathogenic CUG Repeats in *DMPK* RNA

DM1 is caused by pathogenic *DMPK* transcripts

- Approximately 50% of *DMPK* transcripts are pathogenic while the remaining *DMPK* transcripts are normal[1]
- Pathogenic *DMPK* transcripts containing cytosine-uracil-guanine (CUG) repeat sequences form hairpin loops
- These hairpin loops trap MBNL1 proteins
- MBNL1 is a splicing factor required for processing multiple RNAs into proteins accurately



DMPK transcript

Bound MBNL1 (inactive)

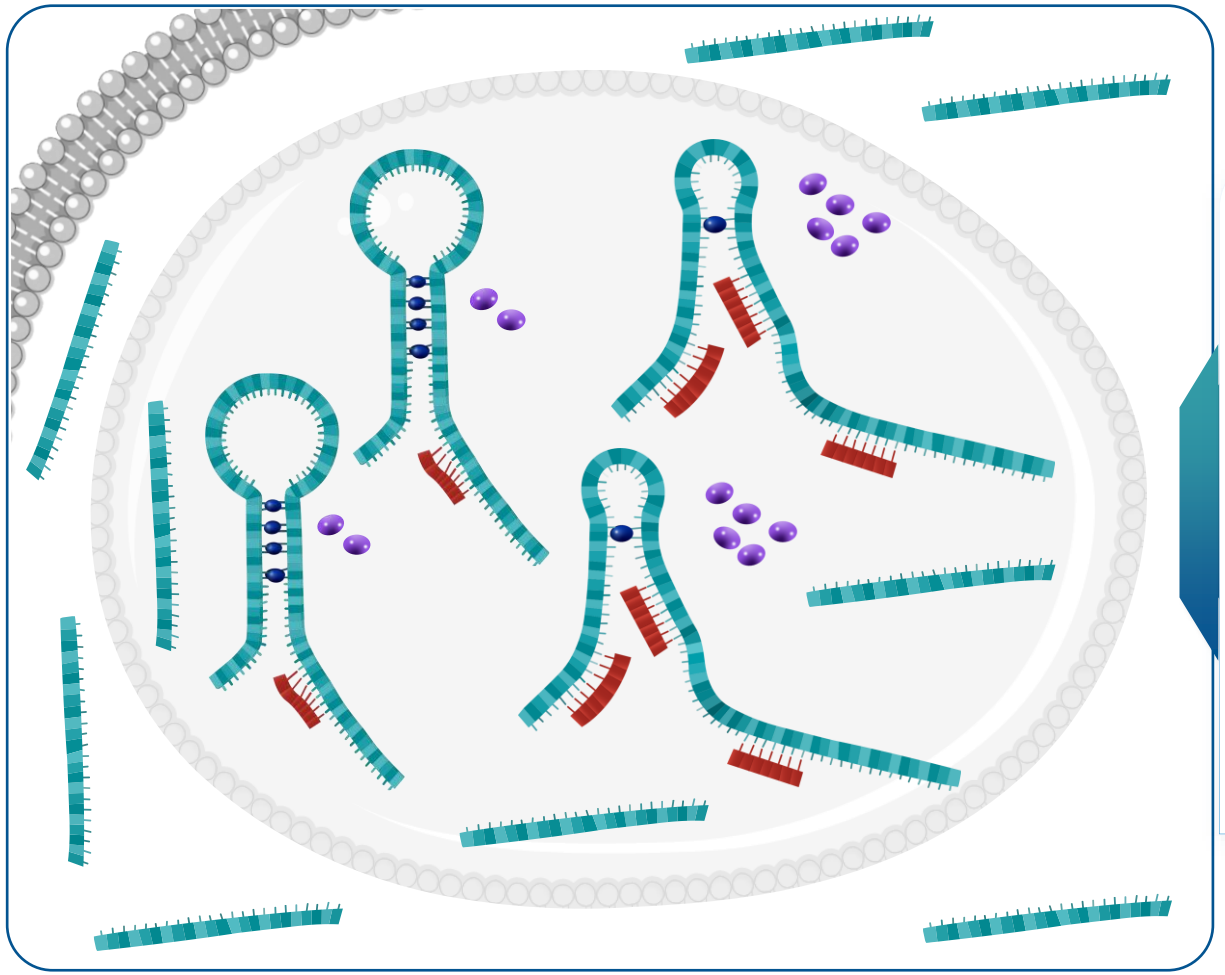
Trapped MBNL1 is inactive and results in mis-splicing

1. Wojciechowska, et al., Quantitative Methods to Monitor RNA Biomarkers in Myotonic Dystrophy, *Nature*, April 12, 2018

PGN-EDODM1 Blocking Approach Targets Only the Pathogenic *DMPK* RNA

PGN-EDODM1 binds selectively to the pathogenic *DMPK* transcript

- PGN-EDODM1 is engineered to bind selectively to the pathogenic CUG repeat expansion present in *DMPK* transcript
- This reduces the ability of these CUG repeats to form hairpin loops and sequester RNA splicing proteins, including MBNL1, in the nucleus

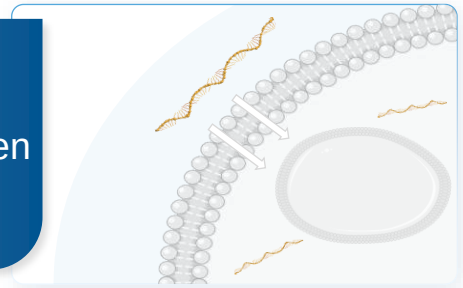


Liberated MBNL1 restores correct splicing

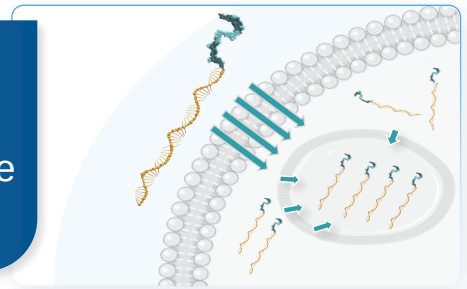
PGN-EDODM1 | Bound MBNL1 (inactive) | Free MBNL1 (active)

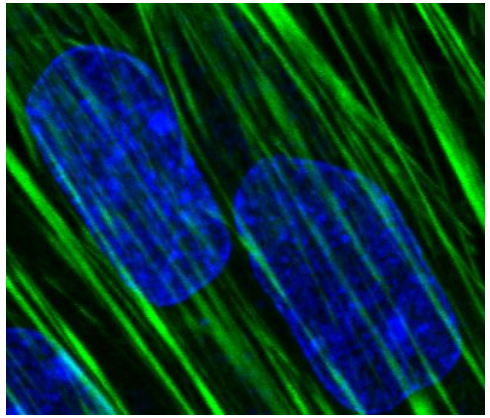
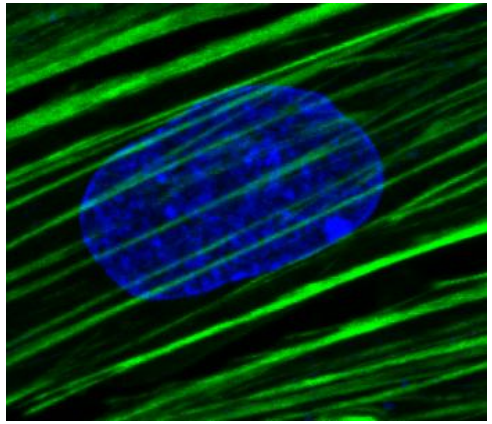
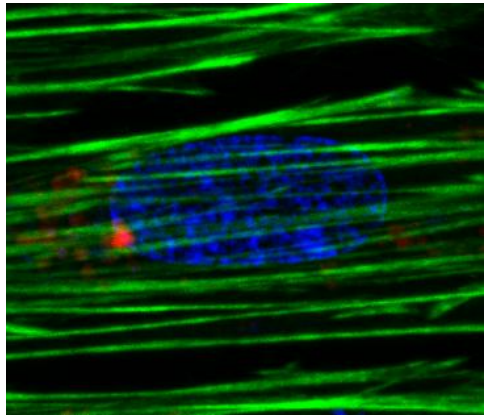
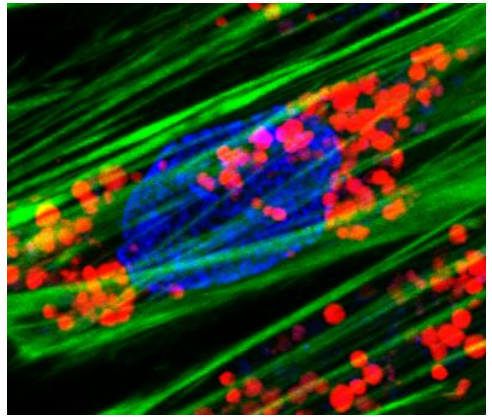
Enhanced Delivery Oligonucleotide (EDO) Platform Enhances Nuclear Delivery and Uptake of Oligonucleotides

Naked oligonucleotides not efficiently taken up into muscle cells & nucleus



EDOs enhance nuclear delivery of oligonucleotide therapeutics



Not treated	PGN-PMODM1	PGN-EDODM1	
			
0 µM	20 µM	2 µM	10 µM

PGN-EDODM1 / Actin / Nucleus

Immortalized myoblasts from a healthy individual or a DM1 patient with 2600 CTG repeats were cultured then differentiated for 4 days into myotubes and then treated with fluorescently tagged PGN-PMODM1 (PMO) or PGN-EDODM1 (PPMO) at concentrations detailed above. Cells were visualized by confocal microscopy 24h after treatment.

FREEDOM-DM1 Trial Design and Clinical Data

Paul Streck, MD, MBA
Head of R&D

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

Freedom
DM1

FREEDOM Study Overview

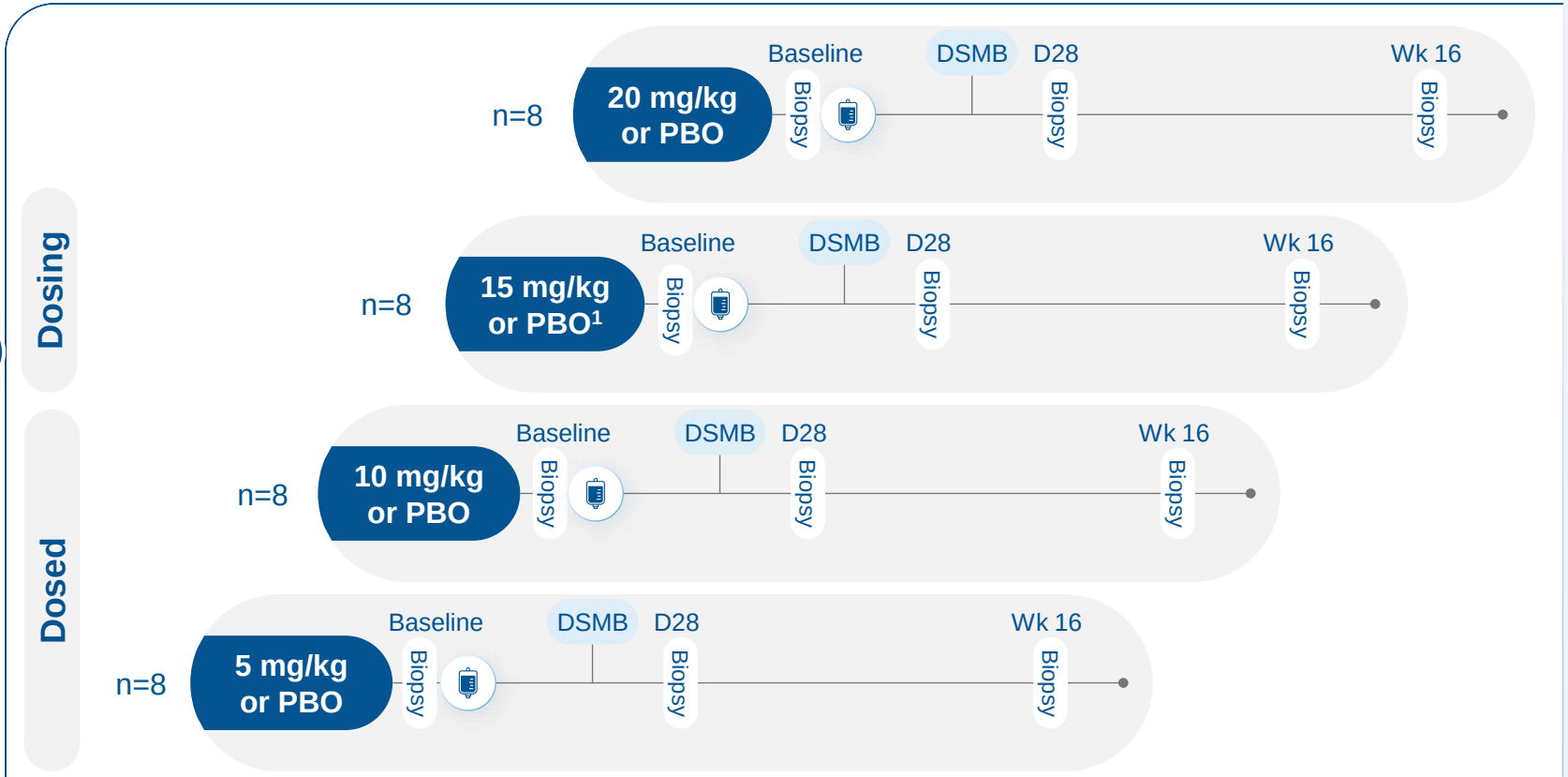
Multinational, randomized, double-blind, placebo-controlled SAD study in patients

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)



1.15 mg/kg cohort added to expand pharmacokinetic and pharmacodynamic understanding
DSMB: data safety monitoring board; IV: intravenous; PBO: placebo; SAD: single-ascending dose; PK: pharmacokinetics

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^2)	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)

*n=5 as one participant's sample showed splicing index outside the pre-specified assay range at Baseline (no detectable mis-splicing)
Splicing Index (SI) Mild = 0–0.4, SI Moderate = 0.41–0.75, and SI Severe = 0.76–1.0. Provenzano, et al.
SD: standard deviation; BMI: body mass index; PBO: placebo; vHOT: video hand opening time; 10MWRT: 10-meter walk run test

Favorable Emerging Safety Profile of PGN-EDODM1[1]

Summary of Treatment Emergent Adverse Events (TEAEs)

	5 mg/kg (n=8)[2] n(%)	10 mg/kg (n=8)[2] n(%)	Total (n=16)[2] 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)

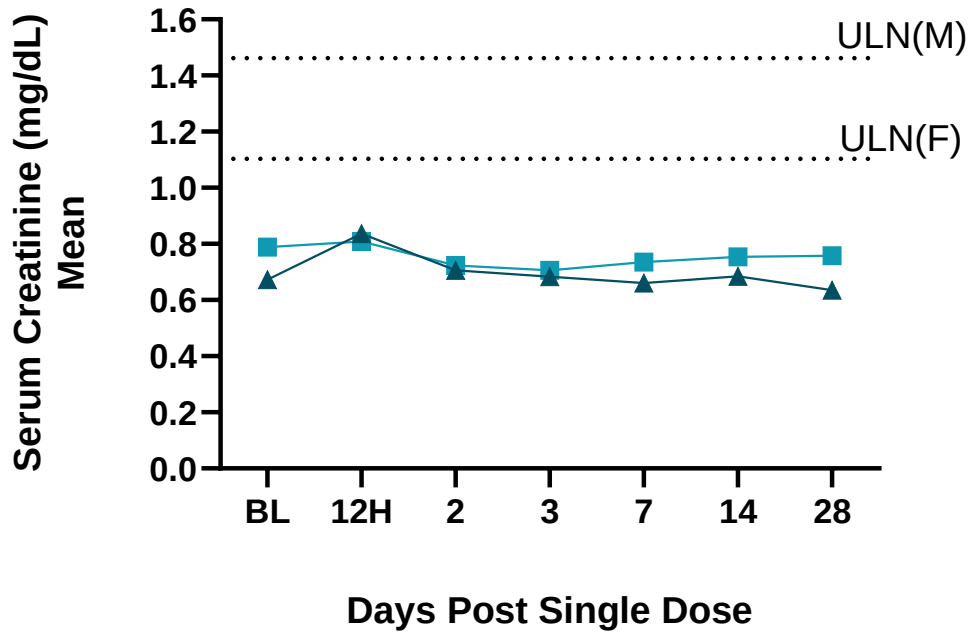
- SAE related to study drug:
  - Abdominal pain (10 mg/kg) potentially confounded by use of prohibited, off-label drug taken on the morning of PGN-EDODM1 dosing[3]
- SAEs unrelated to study drug:
  - Appendicitis (5 mg/kg)
  - Right anterior tibial artery pseudoaneurysm (10 mg/kg) in connection with biopsy procedure
- No adverse events related to electrolytes or renal biomarkers

1. As of December 3, 2024
2. Includes all participants (placebo and PGN-EDODM1 treated); cohorts remain blinded
3. Data Safety Monitoring Board reviewed event and recommended continuation of study/dosing

SAE: serious adverse event; AESI: adverse event of special interest

PGN-EDODM1 Demonstrated Normal Mean Serum Creatinine Levels

Serum Creatinine

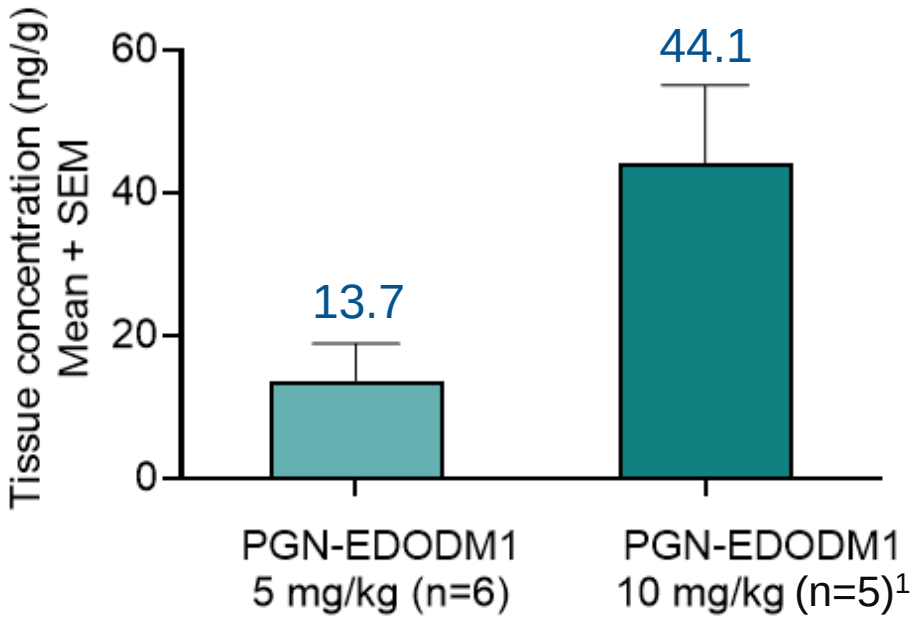


All participants in both cohorts remained below ULN

1. Includes all participants (placebo and PGN-EDODM1 treated); cohorts remain blinded
BL: baseline; ULN: upper limit of normal; M: male; F: female

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

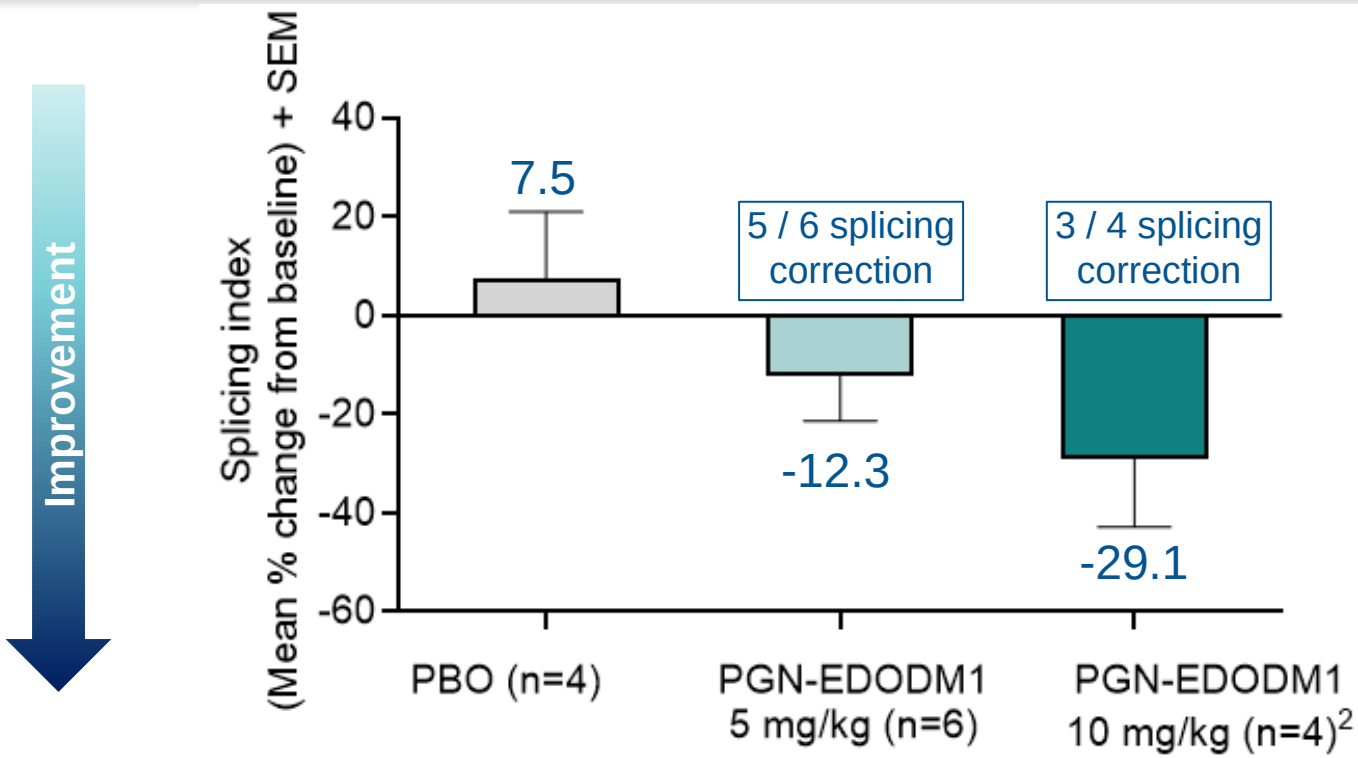
Muscle Tissue Concentration at D28



1. One participant's biopsy was not collected at Day 28 due to pseudoaneurysm in connection with biopsy procedure
SEM: standard error of the mean; Placebo tissue concentration was below level of quantification

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

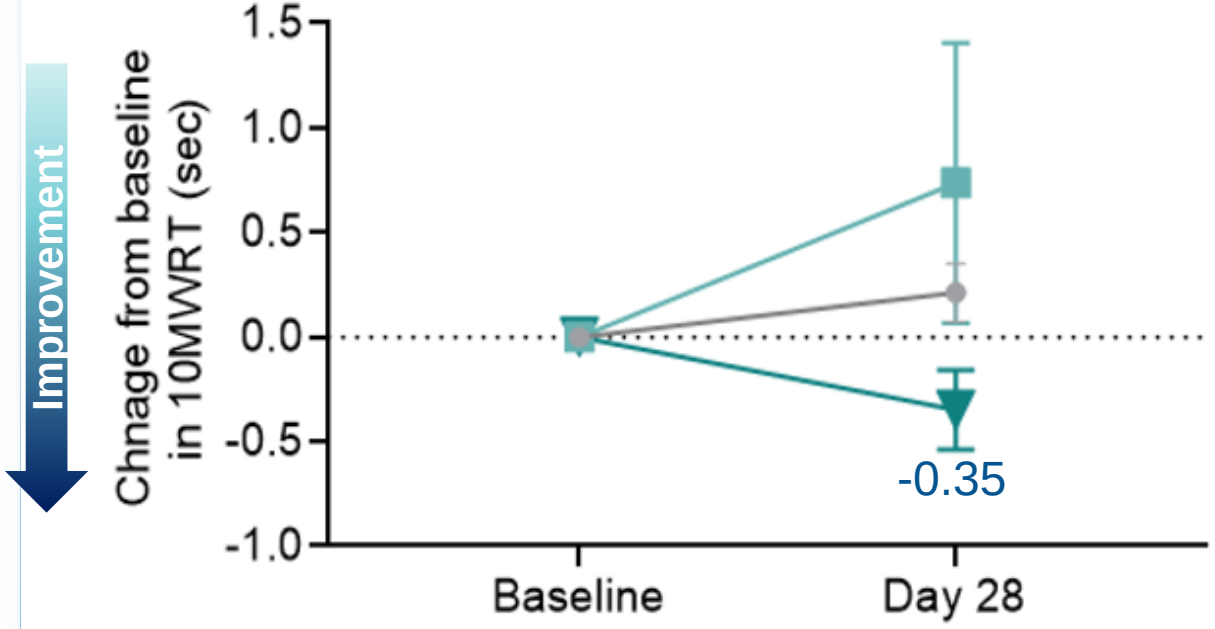
Splicing Index Changes: 22-Gene Panel[1] at D28



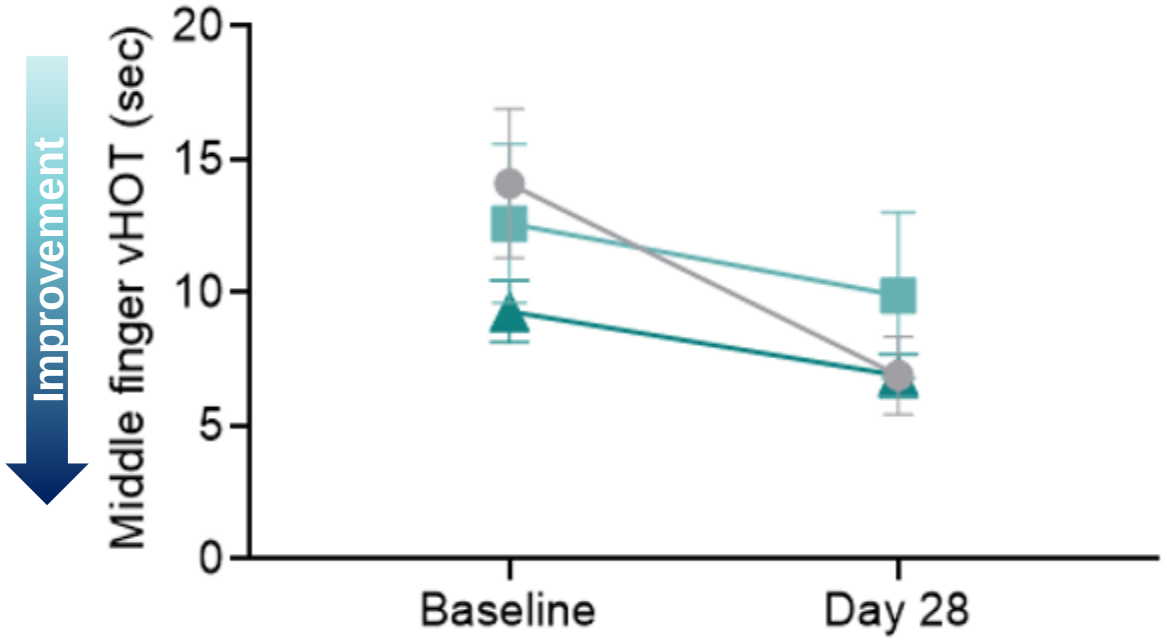
1. Provenzano et al., The Splice Index as a prognostic biomarker of strength and function in myotonic dystrophy type 1, *J Clin. Invest*. 2025
2. In 10 mg/kg cohort: One participant's biopsy was not collected at Day 28 due to pseudoaneurysm in connection with biopsy procedure and one participant's sample showed splicing index outside the pre-specified assay range at Baseline and Day 28 (no detectable mis-splicing) and was excluded from the analysis.

Functional Outcome Data After 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)

vHOT: video hand opening time

Closing Remarks

James McArthur, PhD
President and Chief Executive Officer

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

Favorable emerging safety profile[1] in patients with myotonic dystrophy type 1

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

Dose-dependent increases in evaluable patients[2] in mean **splicing correction** following single dose

~29% at 10 mg/kg

~12% at 5 mg/kg

1. As of data cut-off date Dec 3, 2024
2. Two participants in the 10 mg/kg cohort were excluded from the splicing correction assay. One participant's biopsy was not collected at Day 28 and the other participant's splicing index values were outside of the pre-specified assay range, both at Baseline and at Day 28.

FREEDOM2 Phase 2 MAD Study Underway

Freedom 2
DM1

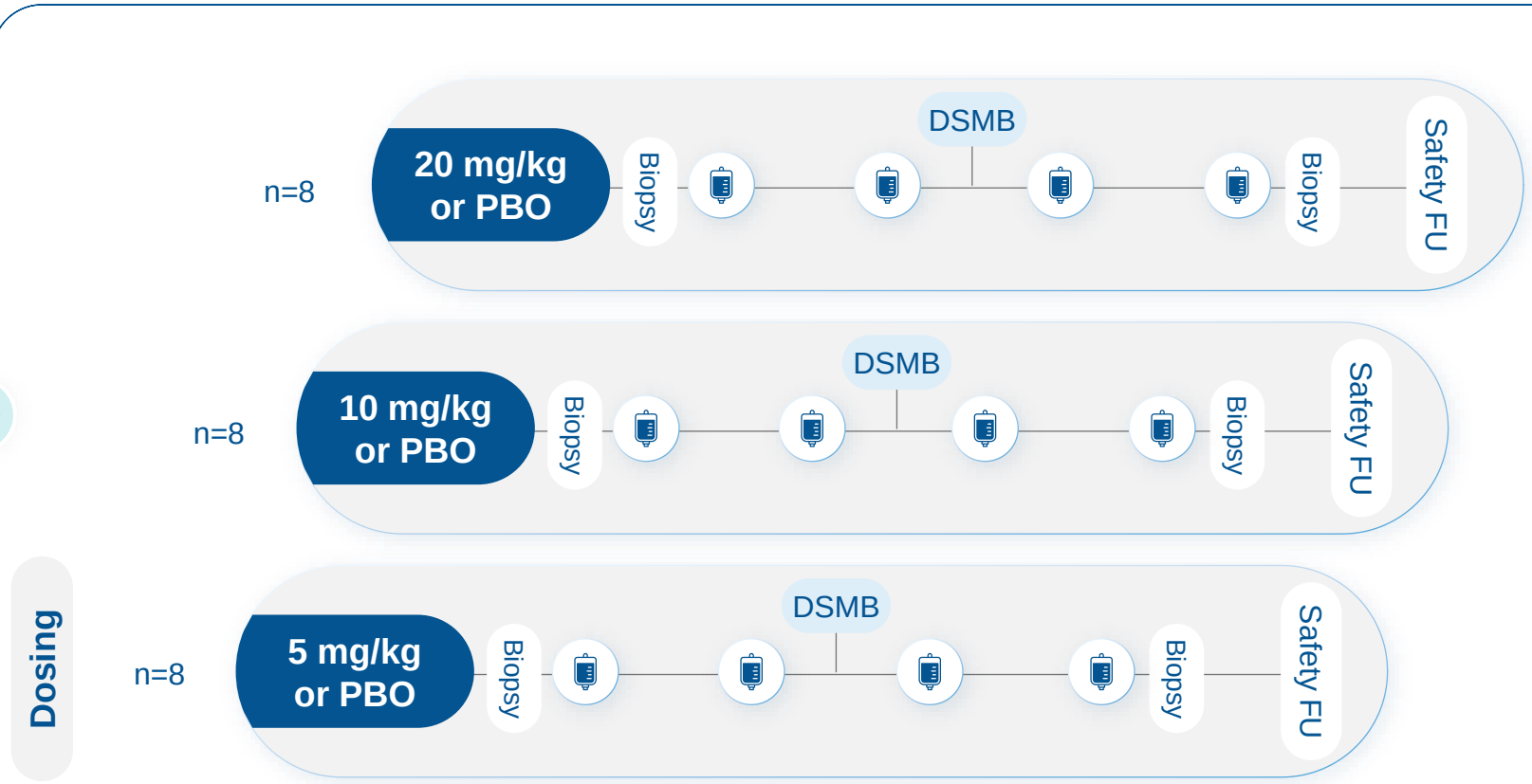
FREEDOM2 Study Overview

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)



DSMB: data safety monitoring board; FU: follow-up; IV: intravenous; MAD: multiple-ascending dose; PBO: placebo; PK: pharmacokinetics; vHOT: video hand opening test

PGN-EDODM1 dose every 4 weeks

Key Anticipated Milestones Ahead

Key Expected Data Readouts/ Milestones

Freedom

- **2H 2025:** FREEDOM 15 mg/kg clinical results
- **Q1 2026**: FREEDOM2 5 mg/kg clinical results

Connect

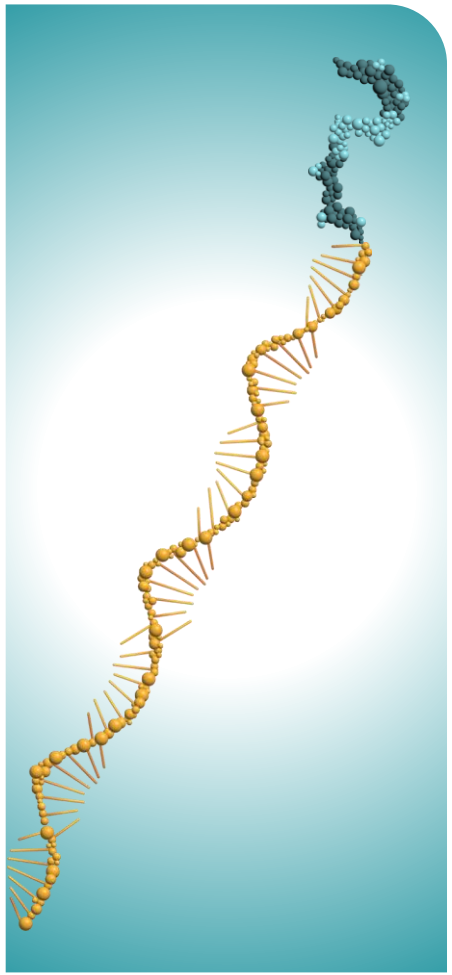
- **Q3 2025:** CONNECT1 10 mg/kg clinical results

Question and Answer Session

James McArthur, PhD
President and Chief Executive Officer

Paul Streck, MD, MBA
Head of R&D

Michelle Mellion, MD
Chief Medical Officer



Thank you!

Clinical study participants and their families

Clinical site staff and investigators

Community and clinical advisors

Preclinical collaborators