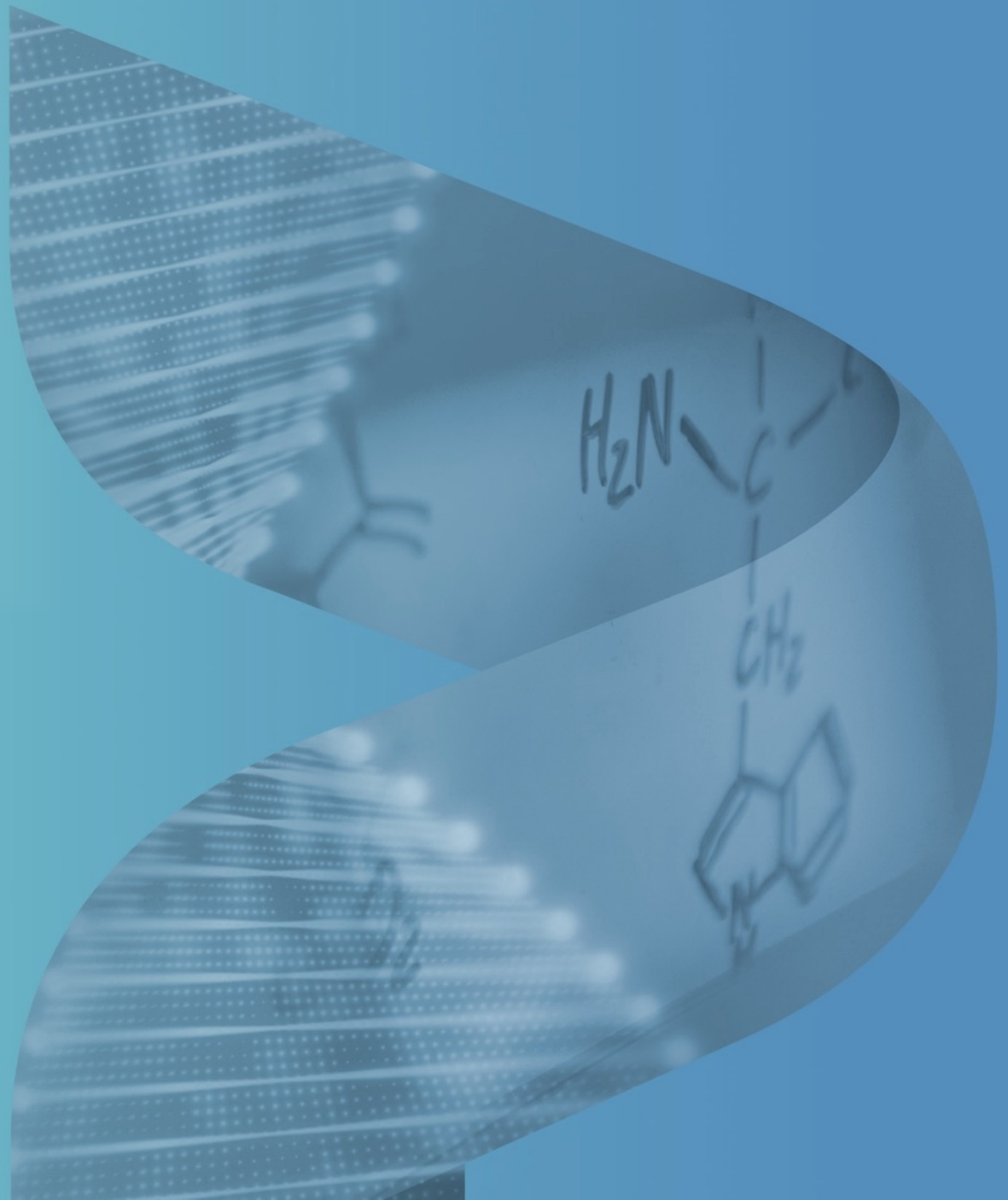
PepGen™

Company Presentation

March 2026



Forward-Looking Statements

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 high levels of oligonucleotide to the nuclei, the therapeutic potential and safety profile of PGN-EDODM1 based on data from the 5, 10 and 15 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 initial data report from our FREEDOM2-DM1 trial and the potential to extend dosing to the 12.5 mg/kg dose level, the potential for any functional improvements that may result from robust splicing correction with PGN-EDODM1, dose-dependent increases in splicing suggesting that PGN-EDODM1 is getting into the muscle and effectively binding to the target, the potential for PGN-EDODM1 to offer a best-in-class treatment option, ongoing and planned regulatory interactions and our financial resources and expected cash runway.

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; our ability to enroll patients in our clinical trials, including FREEDOM2, 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; our product candidates, including PGN-EDODM1, 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, including release of the partial clinical hold placed by FDA on the FREEDOM2 study, or other regulatory feedback requiring modifications to our development programs, including with respect to the FREEDOM2 program; 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 filings 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, an investigational therapy, that has 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 or any other investigational therapy will successfully complete clinical development or gain regulatory authority approval.

Leveraging EDO Platform to Drive Meaningful Impact for Patients

OUR VISION

Develop therapies that **address the root cause** of serious genetic neuromuscular and neurological diseases—driving meaningful, functional improvement

Backed by a team of **leading neuromuscular researchers** with deep expertise in genetic disease biology and oligonucleotide drug development

Cash runway into **2H 2027**

EDO PLATFORM

Achieving **superior nuclear delivery and uptake** of therapeutic oligonucleotides, overcoming key limitations of prior approaches

PGN-EDODM1: *Myotonic Dystrophy Type 1*

- Best-in-class potential; selectively targets only pathogenic *DMPK* RNA
- Favorable emerging safety profile and highest splicing correction ever reported in patients
- Regulatory clearance received in South Korea, Australia, and New Zealand; enrollment now open across Canada, UK, and South Korea
- Orphan Drug & Fast Track Designation (U.S.); Orphan Drug Designation (EU)

Anticipated Upcoming Milestones

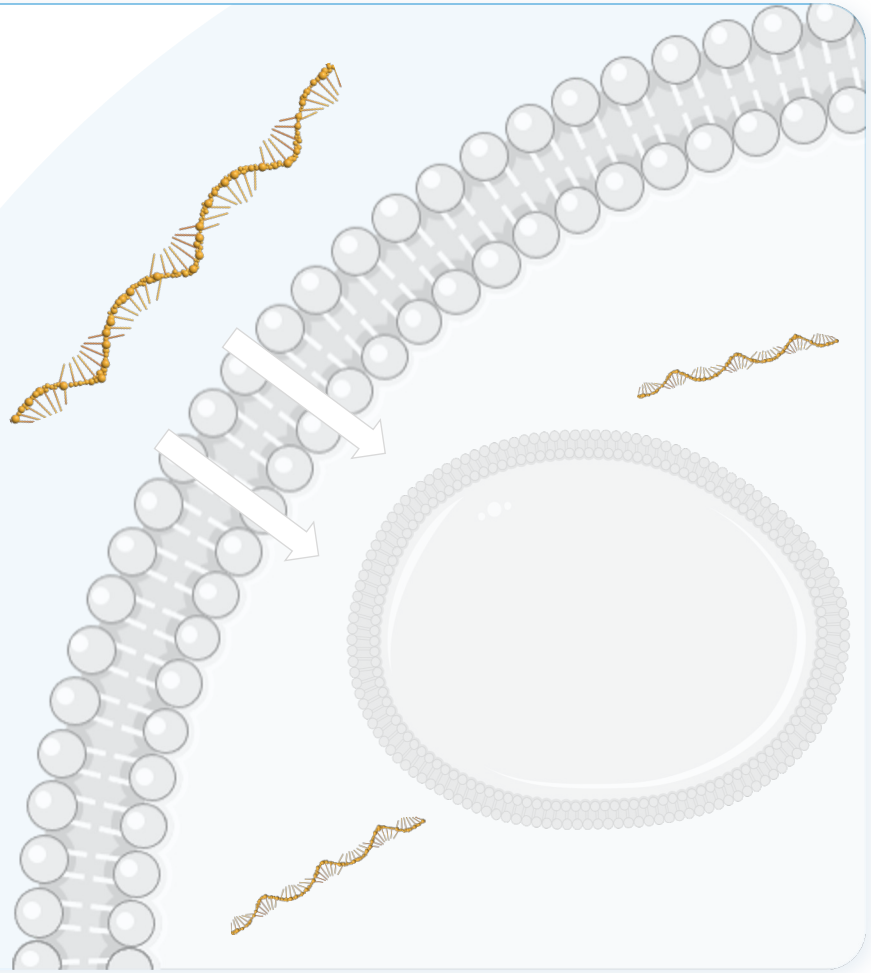
- **Q1 2026:** FREEDOM2 5 mg/kg clinical results
- **H2 2026:** FREEDOM2 10 mg/kg clinical results

Research Pipeline

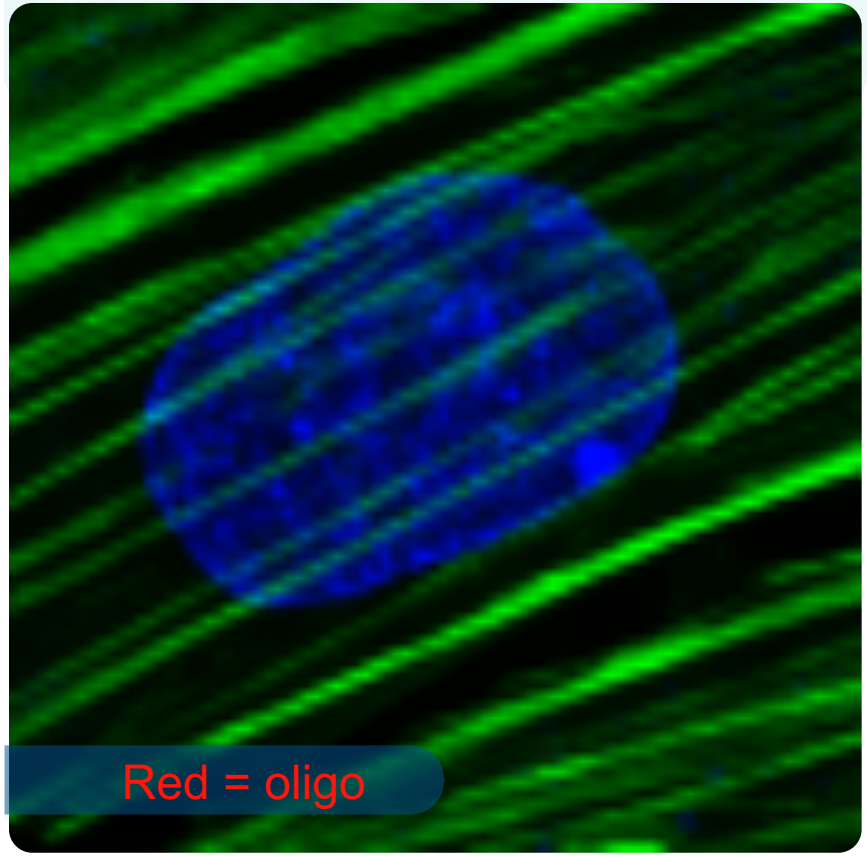
- Developing research pipeline that applies platform differentiators to address underlying neuromuscular disease drivers
- Exploring EDO's potential in genetic conditions, including Charcot-Marie-Tooth disease

The Challenge of Oligonucleotides

Naked oligonucleotides do not efficiently penetrate muscle cells and nucleus



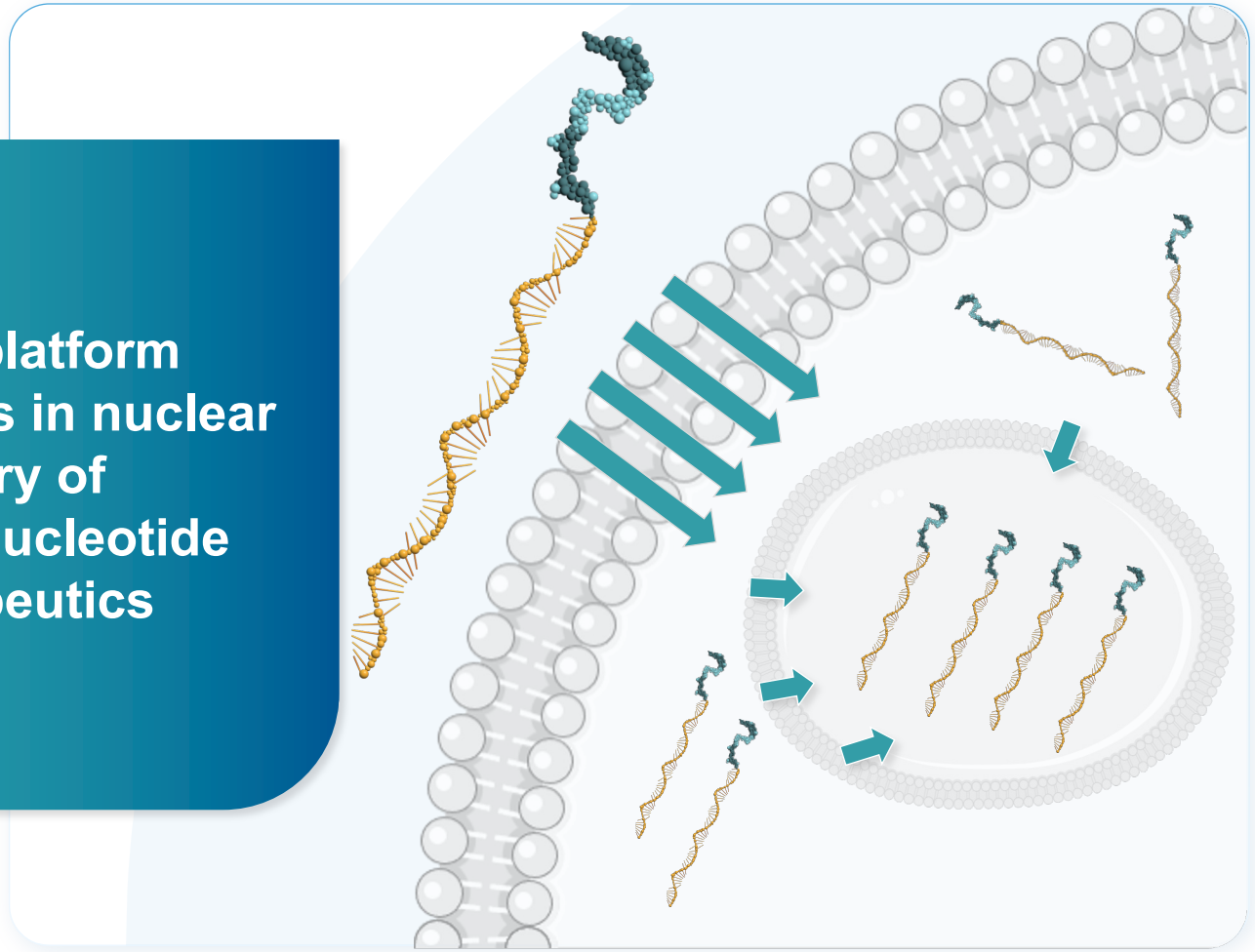
PGN-PMODM1 (Naked Oligo at 20 µM)



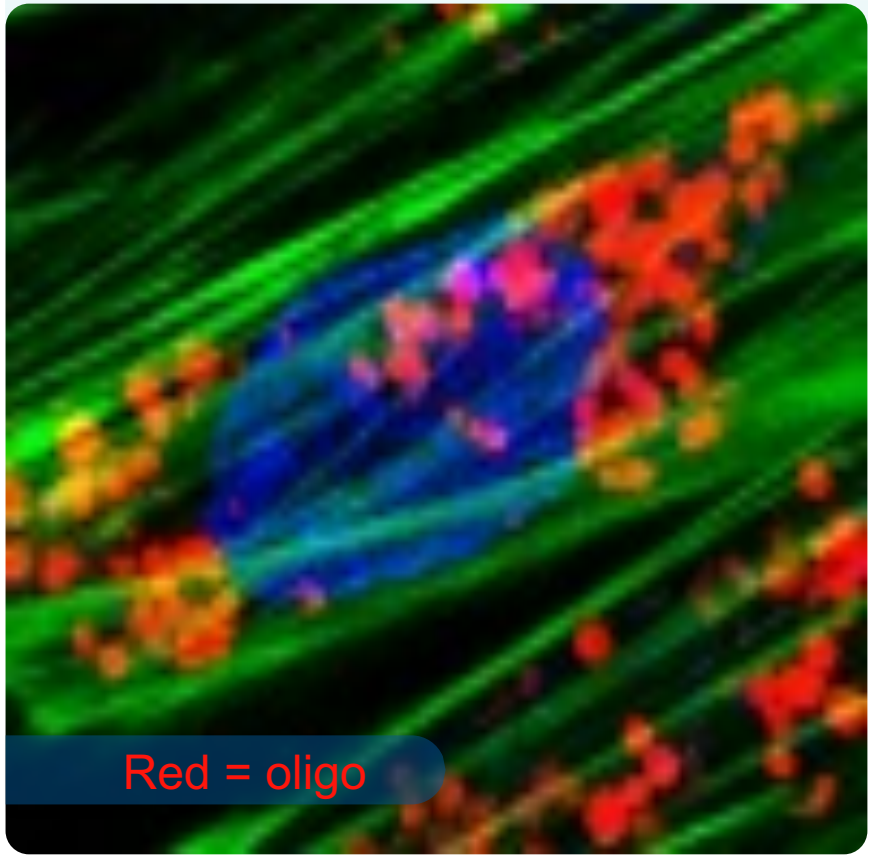
Immortalized myoblasts from a healthy individual or a DM1 patient with 2600 CTG repeats were cultured then differentiated for 4 days into myotubes and then treated with fluorescently tagged PGN-PMODM1 (PMO) or PGN-EDODM1 (PPMO) at concentrations detailed above. Cells were visualized by confocal microscopy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

PepGen's EDO Platform Has Been Designed and Developed to Solve this Decades Long Problem

EDO platform results in nuclear delivery of oligonucleotide therapeutics



PGN-EDODM1 (10 µM)



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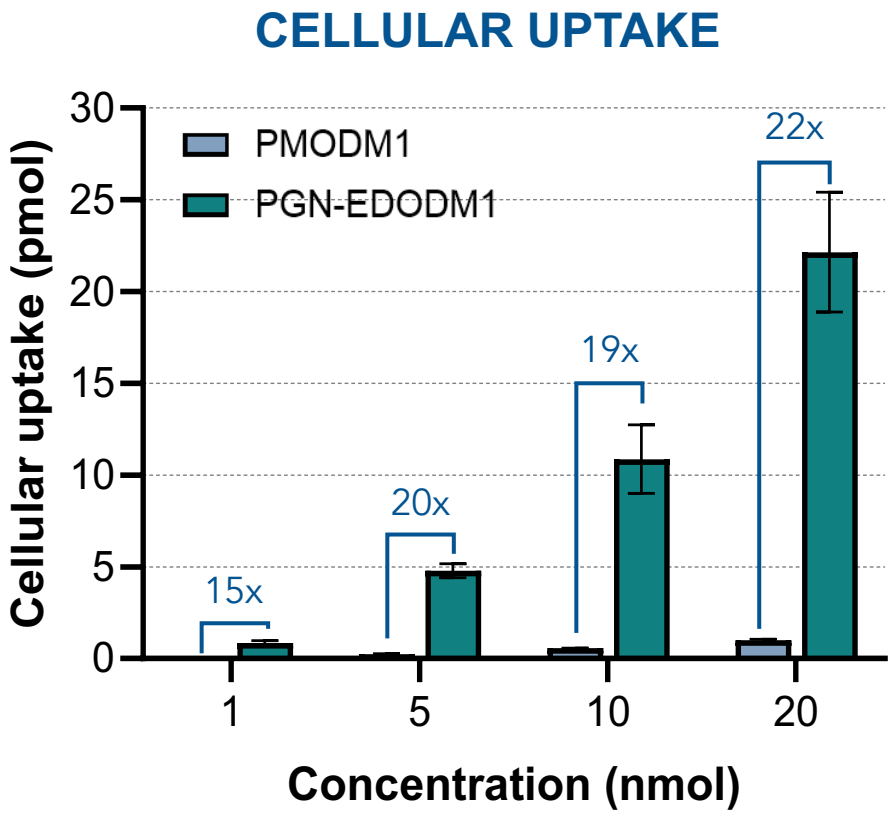
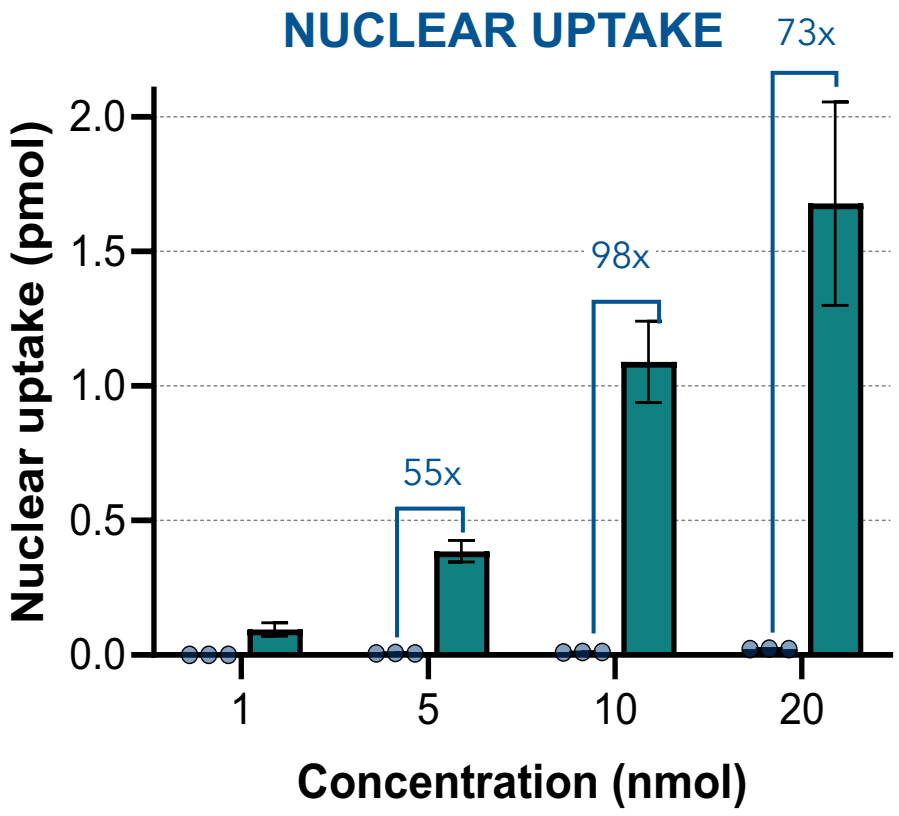
EDO Technology Can Improve Endosomal Escape and Has Been Shown to Increase Nuclear Uptake up to 98-Fold

PMO Delivery in DM1 Cells





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PGN-EDODM1: A Differentiated Drug with Best-in-Class Potential

1 Differentiated Delivery Technology

- **Receptor-independent EDO peptide delivery**
- Designed to escape the endosome – unlike TfnR targeting

2 Differentiated Target

- **Selectively targets pathogenic RNA** (CUG repeat in DMPK)
- Demonstrated highest rate of splicing correction ever reported in DM1 after only a single dose[1]

3 Cost Effective Manufacturing

- **EDO peptide is a short linear peptide** – not cell culture product

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1. FREEDOM 15 mg/kg data readout when compared with prior published data.

PGN-EDODM1 –
Myotonic Dystrophy Type 1 (DM1)

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

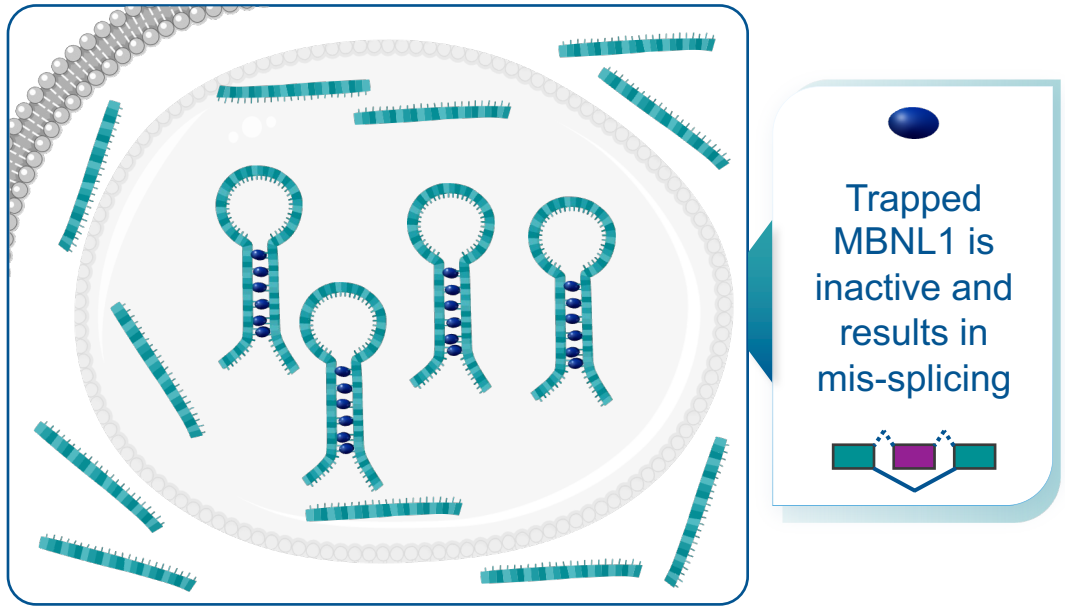
Market Opportunity

- U.S. and EU over 115,000 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

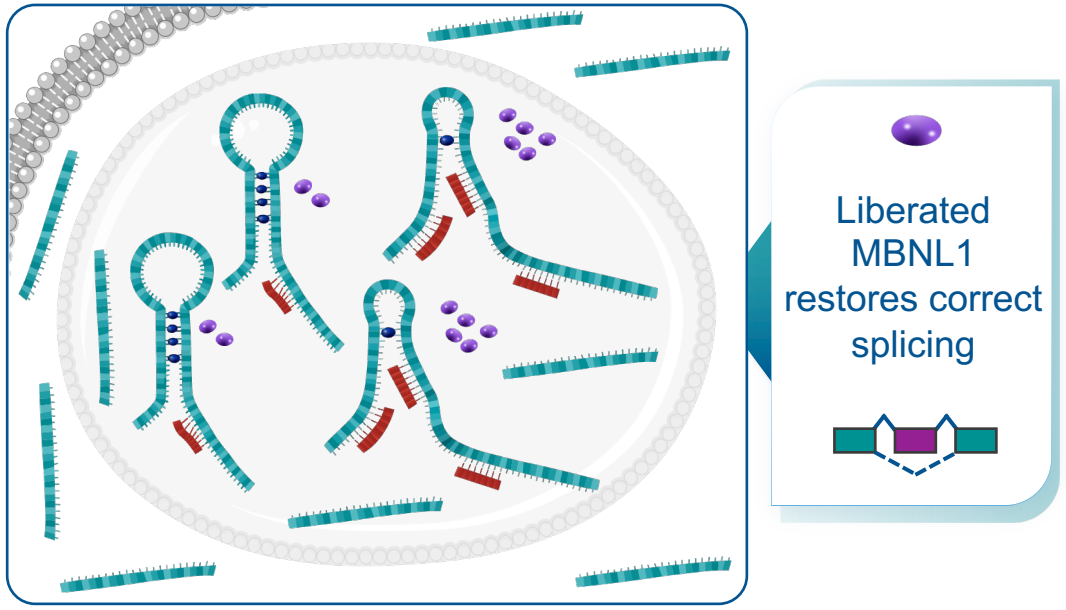
PGN-EDODM1 Blocking Approach Targets the Pathogenic CUG^{exp} Repeats *DMPK* RNA

DM1 is caused by pathogenic *DMPK* transcripts



- DM1 is caused by pathogenic *DMPK* transcripts containing CUG^{exp} repeat sequences that form hairpin loops
- These hairpin loops trap MBNL1 proteins that are needed for correct splicing of mRNAs

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



- PGN-EDODM1 binds selectively to the pathogenic *DMPK* transcript
- This reduces the ability of the CUG^{exp} repeats to form hairpin loops and sequester RNA splicing proteins

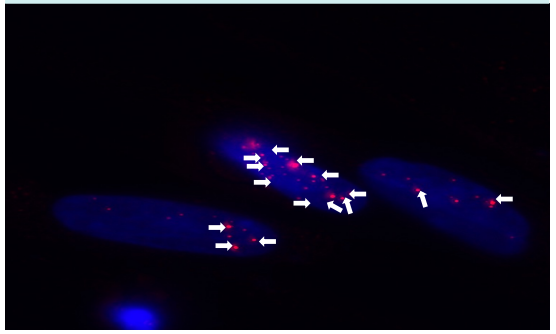
DMPK transcript | Bound MBNL1 (inactive) | PGN-EDODM1 | Free MBNL1 (active)

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

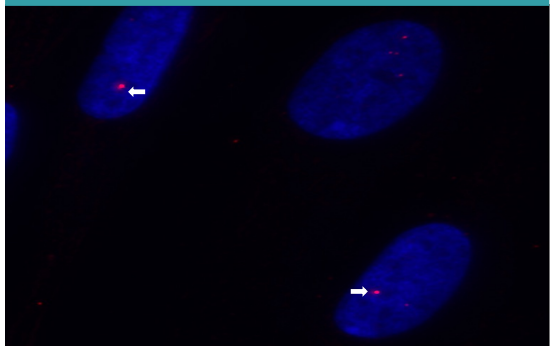
PGN-EDODM1 Reduced Pathogenic Nuclear Foci, Liberated MBNL1 and Corrected Mis-Splicing in Patient Cells with Long CUG Repeats

Foci Reduction

Not Treated



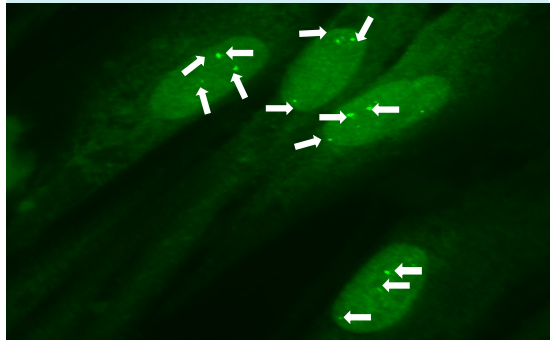
PGN-EDODM1 Treated



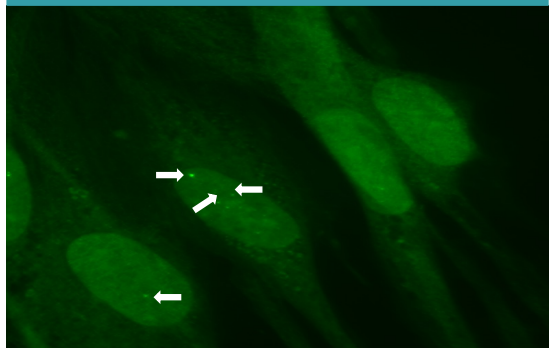
54%
reduction in toxic foci

MBNL1 Liberation

Not Treated



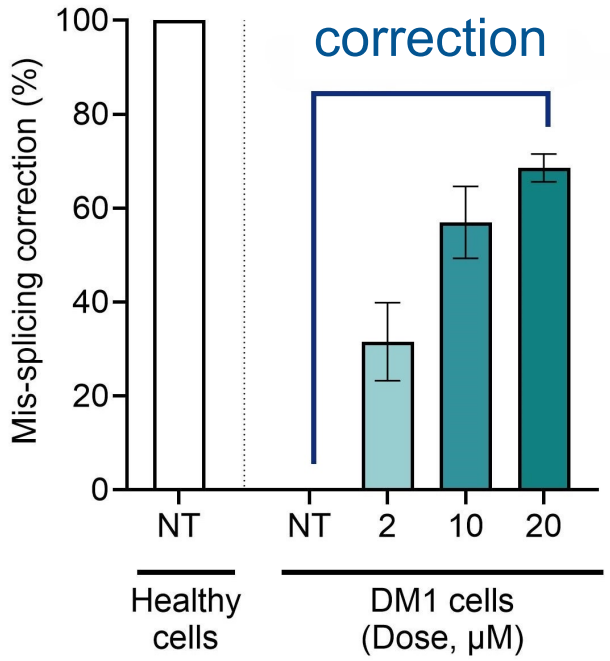
PGN-EDODM1 Treated



Mis-Splicing Correction

Across multiple transcripts

69%
correction



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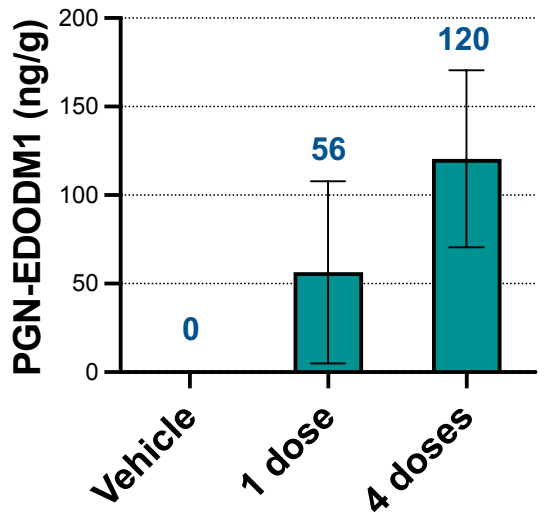
Immortalized myoblasts from healthy individual or DM1 patient with 2600 CTG repeats were cultured then differentiated for 4 days into myotubes. Treatment with peptide-PMO conjugates at concentrations given. Cells were harvested for analysis 24h after treatment. RNA isolation, RT-PCR and capillary electrophoresis (QIAxcel) analysis were performed. Visualization with FISH and immunofluorescence microscopy. Mean ± SD; n = 5 per group.

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

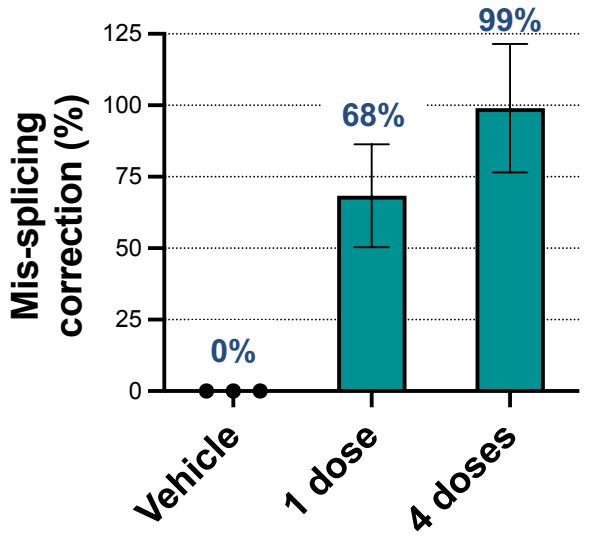
Tissue Concentration

Skeletal muscle



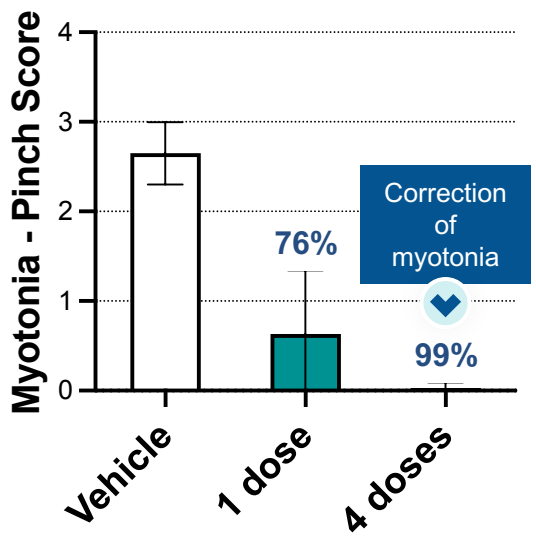
Mis-Splicing Correction

Across multiple transcripts



Correction of Myotonia

Pinch test



Protocol: HSA^{LR} mice received 1 or 4 doses of PGN-EDODM1, with 4-week intervals between doses. Skeletal muscle tissues were collected 4 weeks post-final dose. Skeletal muscle tissue concentration was measured by fluorescent based HPLC method. Graph is presented as mean ± SD; n = 8-12 per cohort. Mis-splicing analysis considers multiple transcripts. Graph is presented as mean ± SD; n = 8-12 per cohort per transcript. Action myotonia evaluation (pinch test) was performed 4 weeks post-final dose. Grade 3 = Clear sign of myotonia strong AND reproducible, Grade 2 = Clear sign of myotonia, strong OR reproducible, Grade 1 = Clear sign of myotonia but non reproducible, Grade 0 = No sign of myotonia. Graphs are presented as mean ± SD; n = 12-43 per cohort.

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

Freedom
DM1
FREEDOM Phase 1

Study Overview

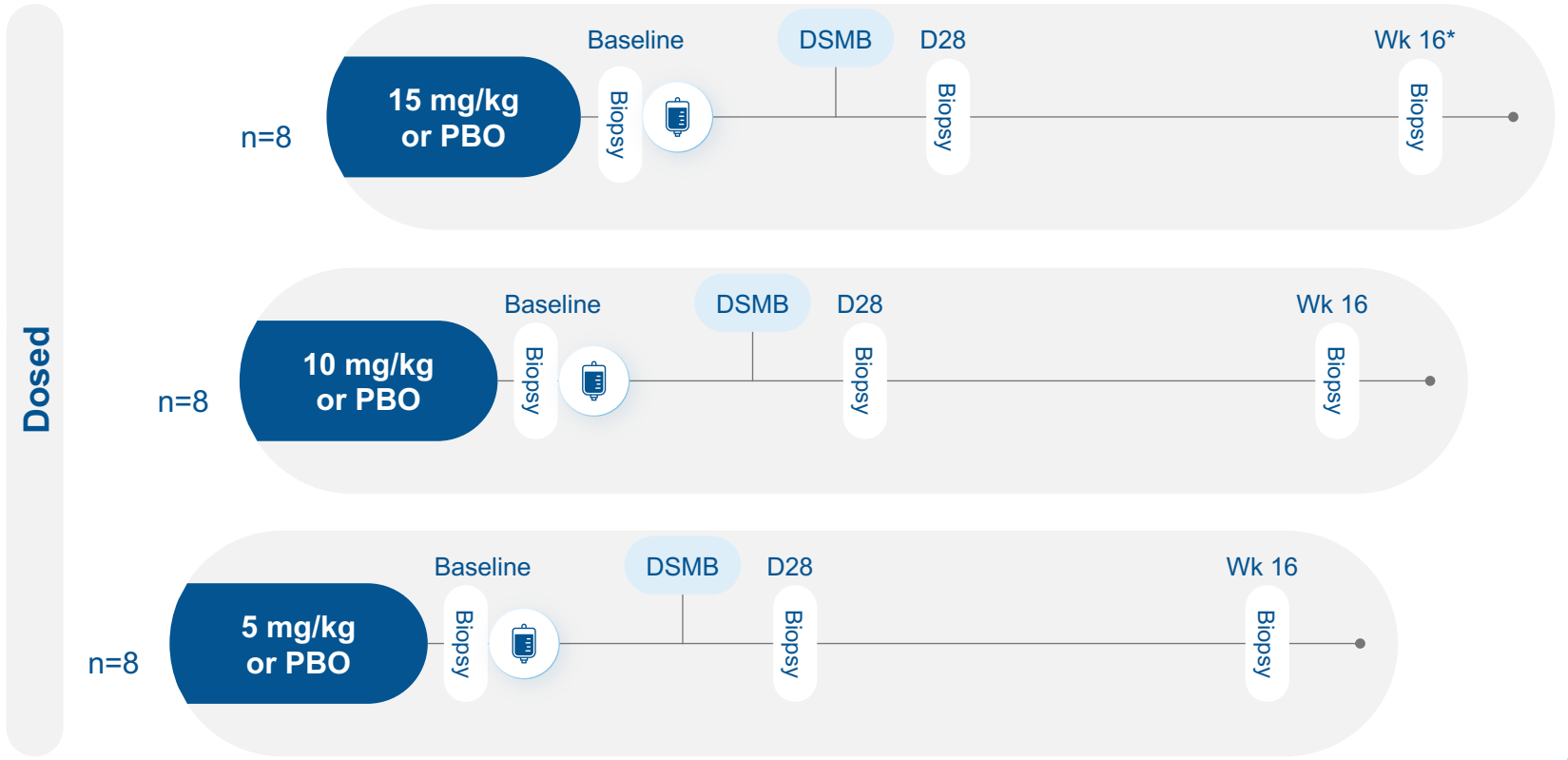
Multinational, randomized, double-blind, placebo-controlled SAD study in patients

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

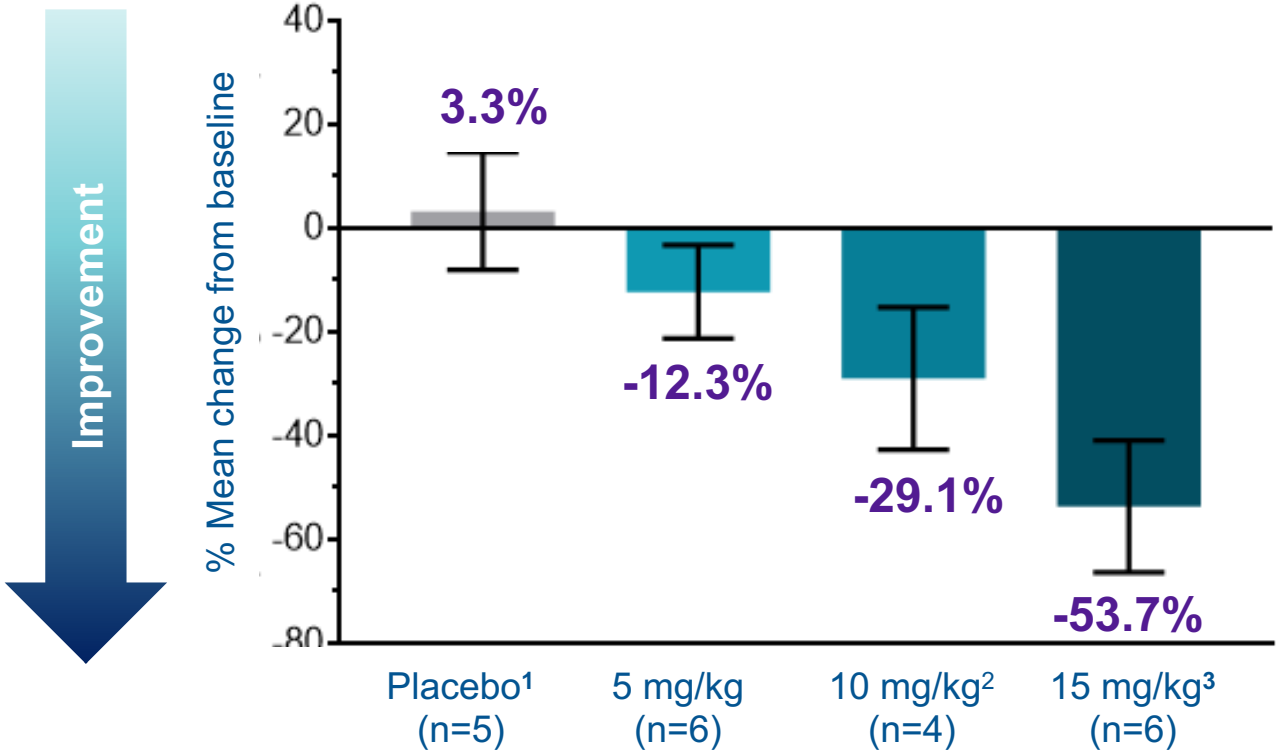
Single Dose PGN-EDODM1 or Placebo (randomized 3:1)



DSMB: data safety monitoring board; IV: intravenous; PBO: placebo; SAD: single-ascending dose; PK: pharmacokinetics

PGN-EDODM1 Produced Dose-Dependent Best-in-Class Splicing Correction Following Single Dose

Splicing Index Changes: 22-Gene Panel* at D28

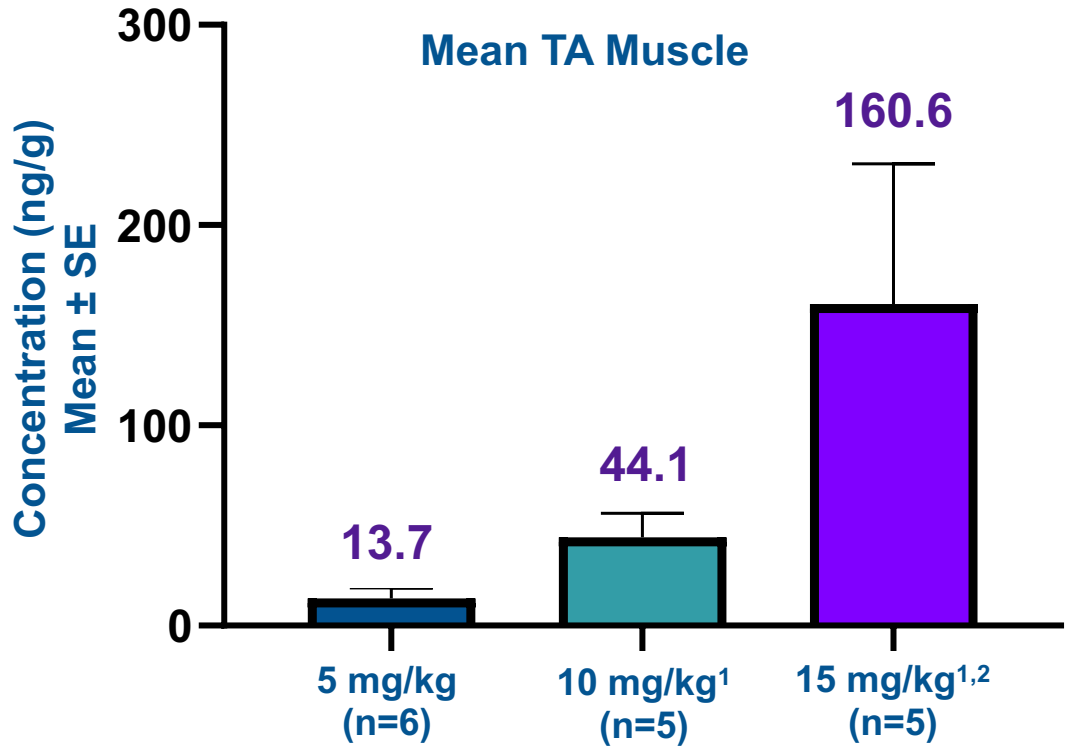


87.5%
of participants across all doses showed improved splicing

1.Missing samples due to unavailability of biopsy tissue or sample outside of assay window.
2. One subject at 10 mg/kg biopsy was not collected at day 28 due to pseudoaneurysm in connection with biopsy and one participant's splicing index fell below the pre-specified assay range at baseline and at day 28 (indicating no detectable mis-splicing)
3.One subject at 15mg/kg received 77% of the dose and was still included in the splicing index change analysis for the cohort
*Provenzano et al., The Splice Index as a prognostic biomarker of strength and function in myotonic dystrophy type 1,J Clin. Invest. 2025

Robust, Greater Than Dose-Proportional Increase in Muscle Tissue Concentration Following Single Dose

Muscle Tissue Concentration at D28



1.Missing samples due to unavailability of biopsy tissue
2.One subject at 15mg/kg received 77% of the dose and was still included in the muscle tissue concentration analysis for the cohort

PGN-EDODM1 Was Generally Well Tolerated, with TEAEs Primarily Mild to Moderate Across Dose Cohorts

	Placebo (n=6) N (events)	Cohort 1 5 mg/kg (n=6)	Cohort 2 10 mg/kg (n=6)	Cohort 3 15 mg/kg (n=6)	Total (n=24)
Any TEAE, n (events)	5 (16)	3 (20)	4 (16)	5 (18)	17 (70)
Any TEAE by Max Severity Mild/Moderate Severe	 5 0	 2 1	 2 2	 5 0	 14 3
Any related TEAE, n (events)	1 (3)	1 (1)	2 (4)	4 (14)	8 (22)
Any SAE (event)	1(2)	1 (1)	2 (2)	0 (0)	4 (5)
Any related SAE	0	0	1 (1)	0	1(1)
Any TEAE leading to study withdrawal	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0

- Most frequent TEAEs: nausea, nasopharyngitis, and headache
- No electrolyte-related TEAEs or hypomagnesemia observed across dose cohorts
- No renal-related TEAEs observed at 5 and 10 mg/kg; DLT at 15 mg/kg involving a transient decrease in eGFR(cys), resolving without intervention
- Transient moderate albuminuria observed at 15 mg/kg and mild albuminuria at 10 mg/kg; Normalized within 2-7 days without intervention
- One drug-related hypersensitivity reaction (rash) during infusion at 15 mg/kg, resolving within 2 hours with oral antihistamines
- One drug-related SAE of severe abdominal pain at 10 mg/kg, confounded by off-label medication use on the day of dosing

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*As of database lock on December 23, 2025. Unblinded FREEDOM safety data
TEAE: treatment-emergent adverse event, SAE: serious adverse event, DLT: Dose limiting toxicity, eGFR(cys): estimated glomerular filtration rate (cystatin equation)

FREEDOM2 Phase 2 MAD Study Underway

Freedom 2
DM1

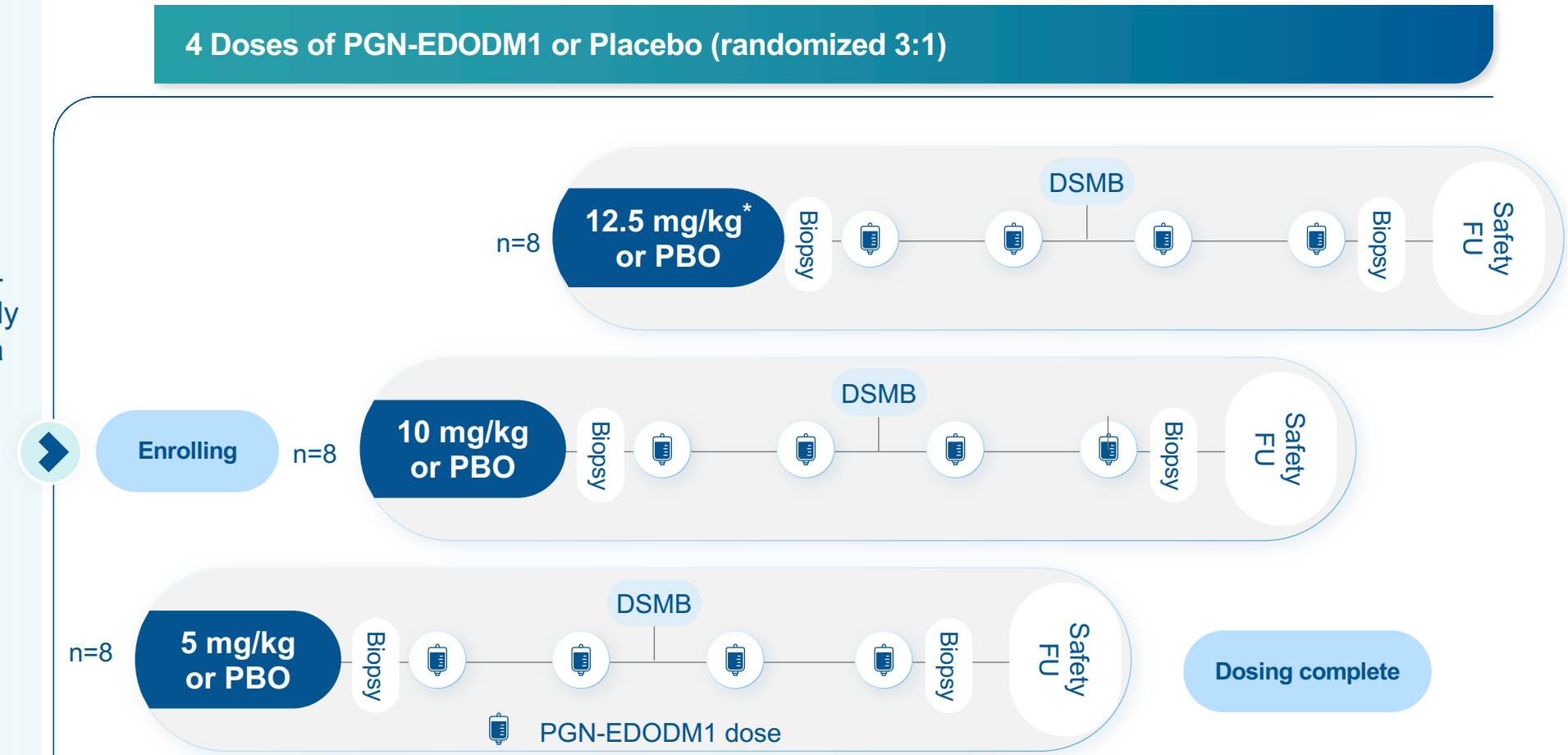
FREEDOM2 Study Overview

Multinational, randomized, double-blind, placebo-controlled, MAD study open in Canada, UK, NZ, Australia and South Korea**

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

OLE open in CA and UK



DSMB: data safety monitoring board; FU: follow-up; IV: intravenous; MAD: multiple-ascending dose; PBO: placebo; PK: pharmacokinetics; vHOT: video hand opening test; OLE: open label extension
* Dose dependent on recommendations of DSMB
**The U.S. FDA recently placed a partial clinical hold on FREEDOM2-DM1

Summary: PGN-EDODM1 Designed to Address the Underlying Cause of DM1

Safety & Tolerability:

PGN-EDODM1 was generally well-tolerated across all doses.

- One drug-related SAE (at 10 mg/kg), possibly confounded by concomitant medication
- Asymptomatic transient changes in renal biomarkers resolved without intervention
- No kidney-related TEAEs observed at 5 and 10 mg/kg

FREEDOM2 dosing at 10 mg/kg is ongoing, with the 5 mg/kg readout anticipated in Q1 2026 and 10 mg/kg readout in H2 2026

Highest Ever Reported Mean Splicing Correction in DM1

- 87.5% of participants across all doses showed improved splicing
- More than dose-proportionate increases in splicing correction observed across doses at Day 28
- Unprecedented splicing provides a window of pharmacodynamically active doses that can be assessed in the MAD study

12.3% at 5 mg/kg
29.1% at 10 mg/kg
53.7% at 15 mg/kg

Robust Single-Dose Splicing Correction Supports Evaluation of Optimized Dose Regimens in MAD Study

Splicing correction comparison is based on cross trial comparisons for exploratory purposes.

Summary of PGN-EDODM1 and FREEDOM Program

1. **Differentiated Delivery Technology**
2. **Differentiated Target**

FREEDOM STUDY :

PRIMARY: SAFETY

- ☑ Favorable emerging safety profile

EXPLORATORY: PD (SPLICING)

- ☑ Unprecedented splicing correction achieved with single dose

PHASE 2 FREEDOM2 (MAD)

- **Fully enrolled** 5 mg/kg cohort; All patients have completed dosing
- **Dosing patients** in 10 mg/kg cohort; 50% (4/8) of patients have received up to two doses

UPCOMING PLANNED READOUTS:

Q1 2026: FREEDOM2 5 mg/kg clinical results

H2 2026: FREEDOM2 10 mg/kg clinical results

Cash runway into **2H 2027**

Splicing correction comparison is based on cross trial comparisons for exploratory purposes

Thank you