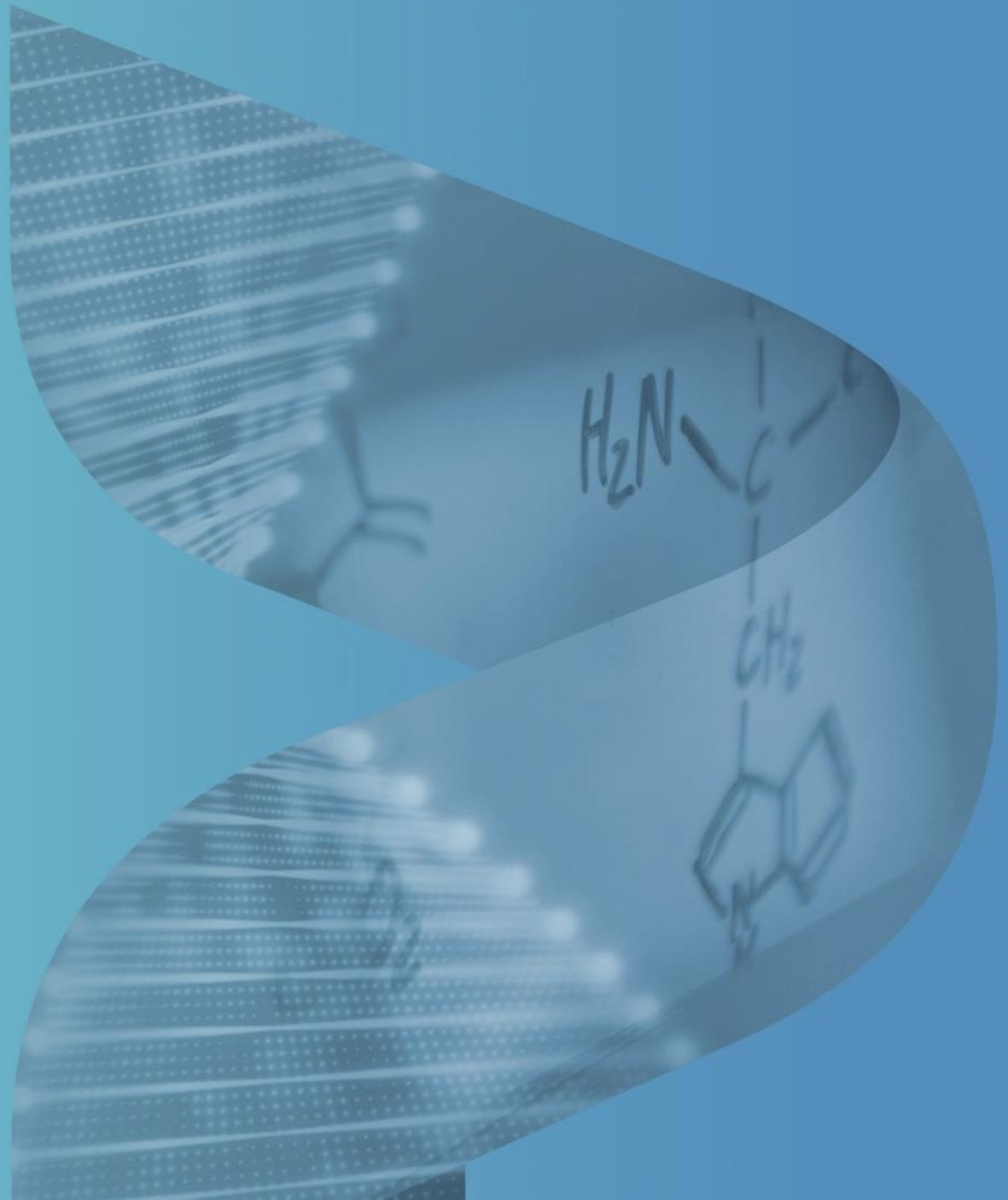
PepGen™

# Company Presentation

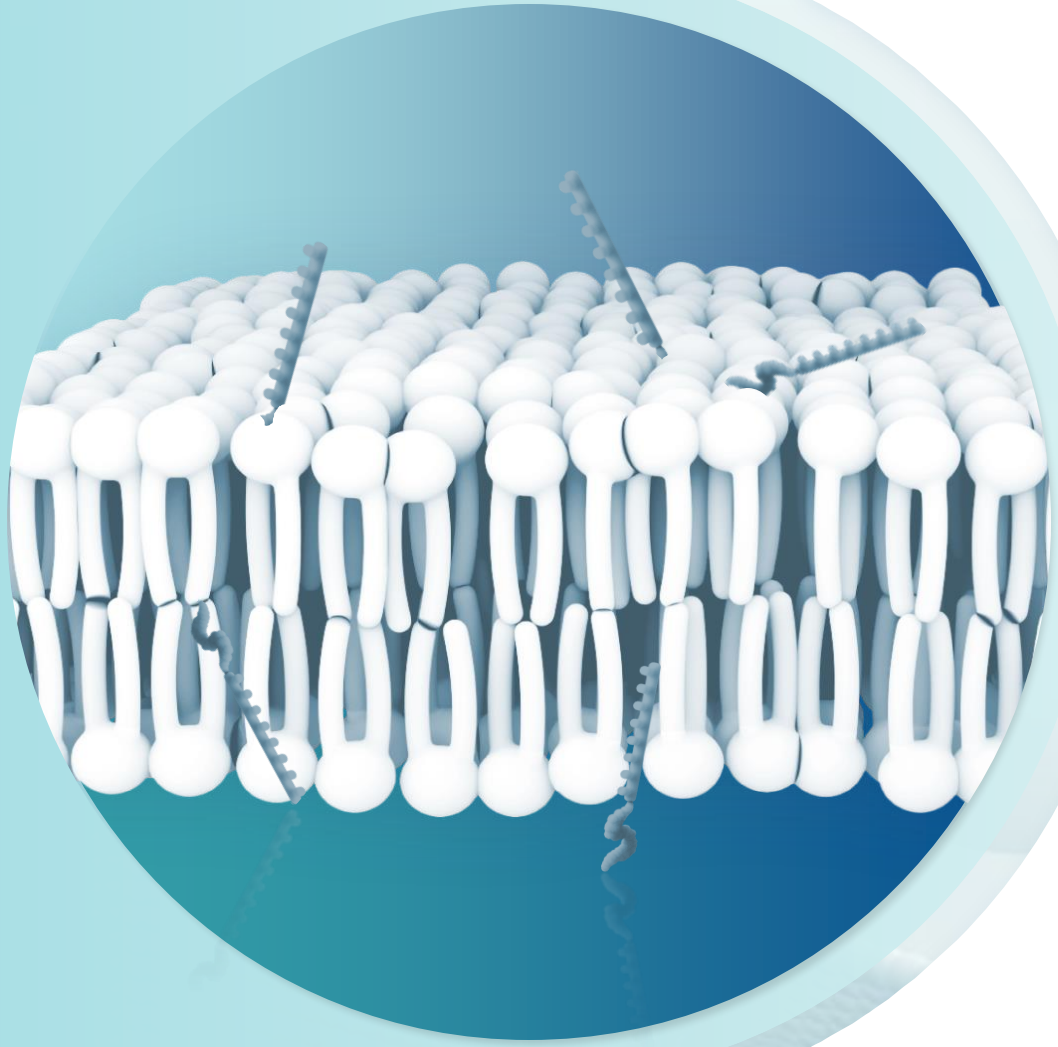
August 2024



# 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 higher levels of oligonucleotide to the nuclei and to dramatically improve the lives of people living with severe neuromuscular and neurological diseases, the therapeutic potential and safety profile of our product candidates, including PGN-EDODM1 and, based on early data, PGN-EDO51, the design, initiation and conduct of clinical trials, including expected timelines for our CONNECT2-EDO51 Phase 2 trial and FREEDOM2-DM1 Phase 2 trial, the expected timing for additional results from our CONNECT1-EDO51 Phase 2 trial and results from our FREEDOM-DM1 Phase 1 trial, ongoing and planned regulatory interactions, the advancement of PGN-EDO53 in IND/CTA enabling studies, and our financial resources and 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-EDO51, PGN-EDODM1 and PGN-EDO53; our ability to enroll patients in our clinical trials, including CONNECT1-EDO51, CONNECT2-EDO51, FREEDOM-DM1 and FREEDOM2-DM1; 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-EDO51 and PGN-EDODM1; our product candidates, including PGN-EDO51 and 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, or other regulatory feedback requiring modifications to our development programs, including in each case with respect to our including CONNECT1-EDO51, CONNECT2-EDO51, FREEDOM-DM1 and FREEDOM2-DM1 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 and quarterly report on Form 10-Q that are filed with the SEC. PepGen explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.



Driven by our proprietary Enhanced Delivery Oligonucleotide (EDO) platform, PepGen is creating a pipeline of disease-modifying therapeutics with the potential to safely and effectively target the underlying cause of serious genetic neuromuscular and neurological disorders.

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# PepGen's Pipeline Enabled by EDO Technology

| INVESTIGATIONAL CANDIDATES | CLINICAL PROGRAMS | INDICATIONS | PRECLINICAL | PHASE 1 | PHASE 2 | PIVOTAL |
|---|---|---|---|---|---|---|
| PGN-EDO51 | Connect | DMD – *Exon 51* | | | | |
| PGN-EDODM1 | Freedom | DM1 – *DMPK* | | | | |
| PGN-EDO53 | | DMD – *Exon 53* | | | | |

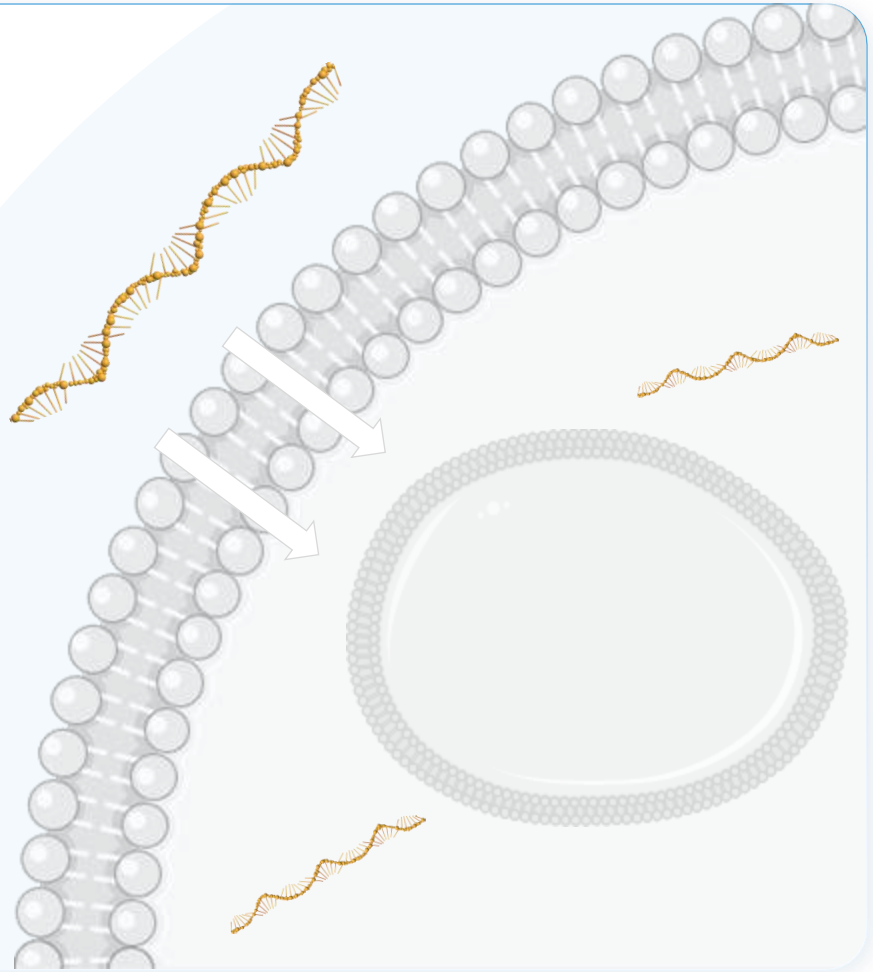
**Research**

- DMD *Exon 45, Exon 44*
- Additional neuromuscular diseases
- Neurological diseases

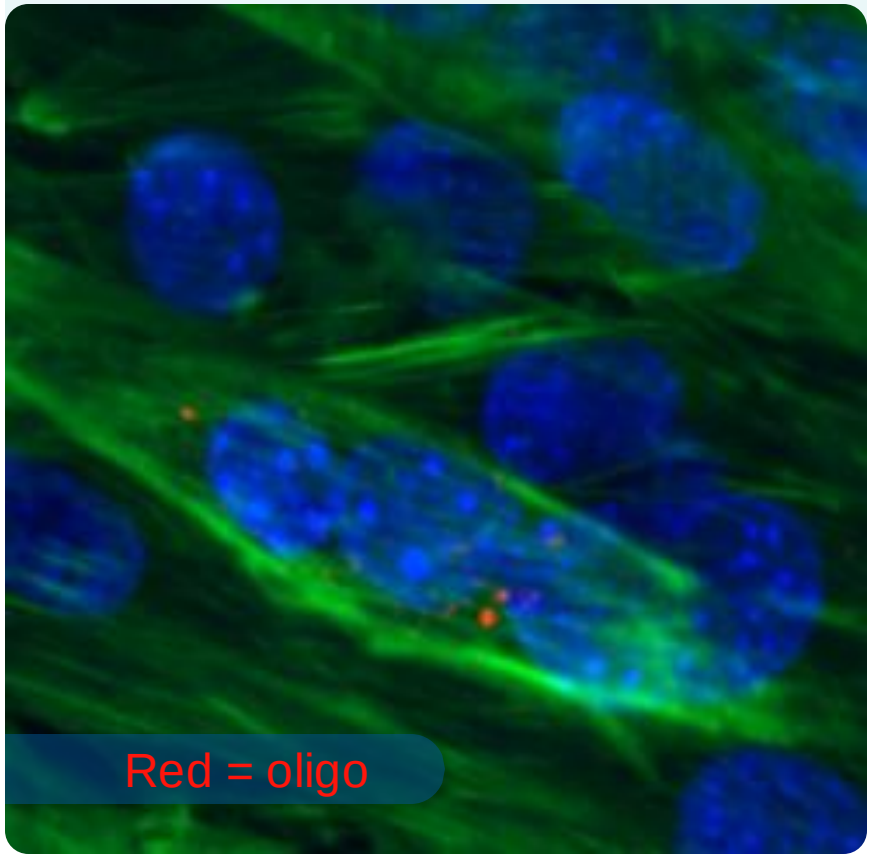
Note: Clinical plans are subject to alignment with regulatory authorities.

# The Challenge of Oligonucleotides

**Naked oligonucleotides do not efficiently penetrate muscle cells and nucleus**



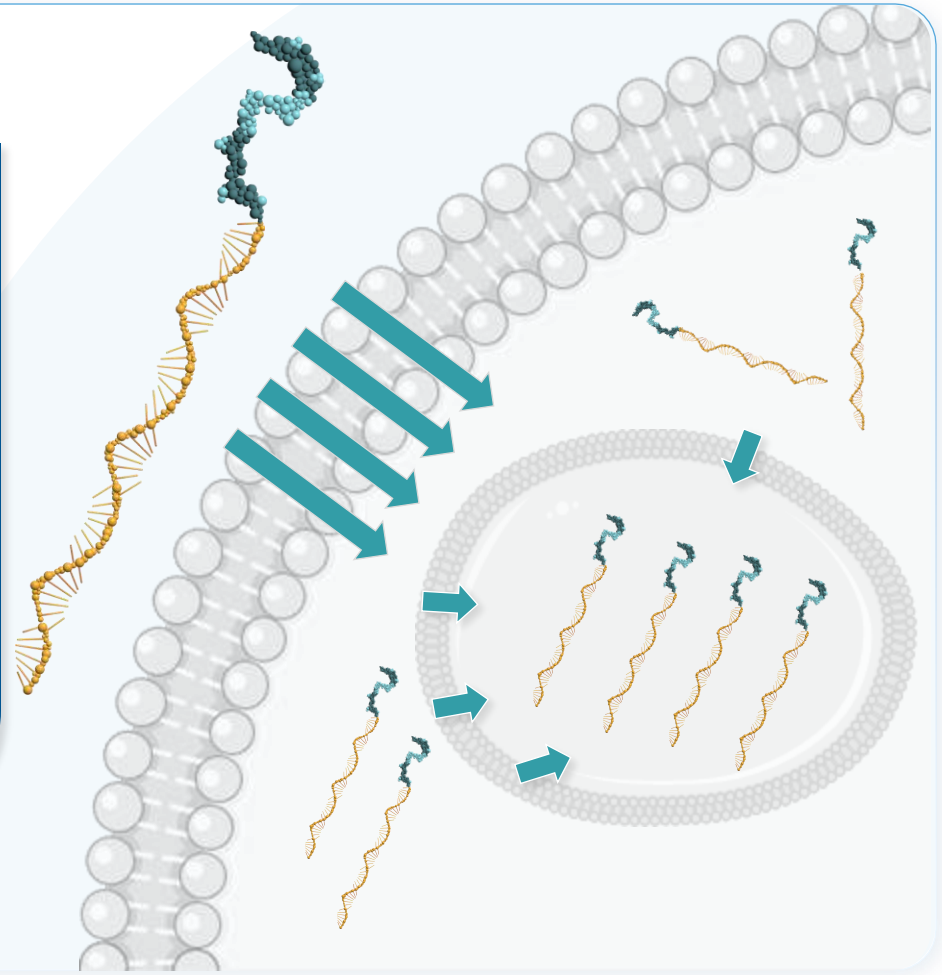
## Naked Oligonucleotide (PMO)



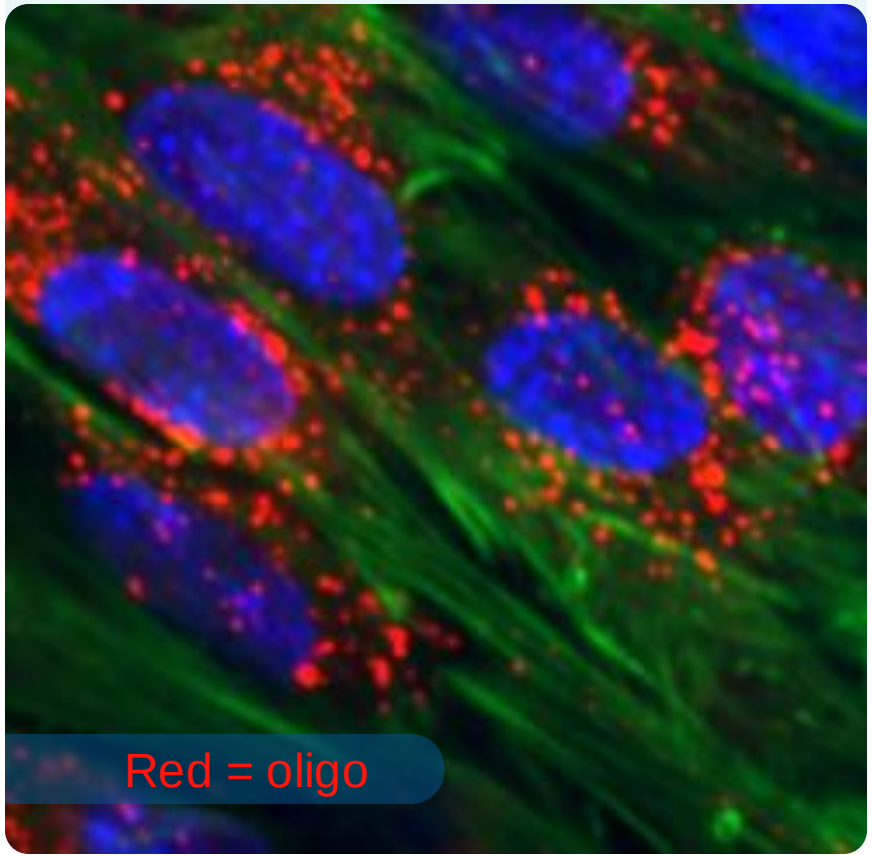

In vitro staining image is shown with 10µM concentration of PMO23 (naked oligonucleotide). C2C12 mouse cells were differentiated for 4 days into myotubes and treated with fluorescently tagged compounds for 24h. PMO: phosphorodiamidate morpholino oligonucleotide

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

**EDO platform results in nuclear delivery of oligonucleotide therapeutics**



**PepGen's EDO: Up to 25X Higher Nuclear Uptake of Oligonucleotide**




Note: 1. In vitro staining image is shown with 10µM conc. of EDO23; 2. C2C12 mouse cells were differentiated for 4 days into myotubes and treated with fluorescently tagged compounds for 24h.

# Latest Achieved Milestones

## DMD: PGN-EDO51

- CONNECT1-EDO51 (Phase 2) at 5 mg/kg
  - Encouraging levels of muscle adjusted (0.70%) and total dystrophin (0.26%) after 3 months and 4 doses
  - High levels of exon 51 skipping (2.15%)
  - Data demonstrates EDO technology delivers high levels of oligonucleotides to the nucleus
- CONNECT1 10 mg/kg dosing underway

## DM1: PGN-EDODM1

- FREEDOM-DM1 (Phase 1) open in US, Canada and UK
- FREEDOM2-DM1 (Phase 2) open in Canada and UK

# Anticipated Upcoming Milestones

| | 2H: 2024 | 1H: 2025 |
|---|---|---|
| **DM1** | • FREEDOM clinical results in Q4 2024<br>• Initiate dosing in FREEDOM2 in 2H:2024 | |
| **DMD** | • CONNECT2-EDO51 regulatory clearance in the US[1] | • CONNECT1 10 mg/kg dose cohort results in early 2025 |

1. Subject to regulatory clearance

# PGN-EDO51 for DMD

# DMD Presents with a Significant Unmet Medical Need

## Overview

- Caused by mutation in dystrophin gene resulting in progressive muscle damage
- Onset of symptoms in early childhood
  - Loss of ambulation by early adolescence
  - Loss of respiratory and cardiac function resulting in early adulthood mortality

## Market opportunity

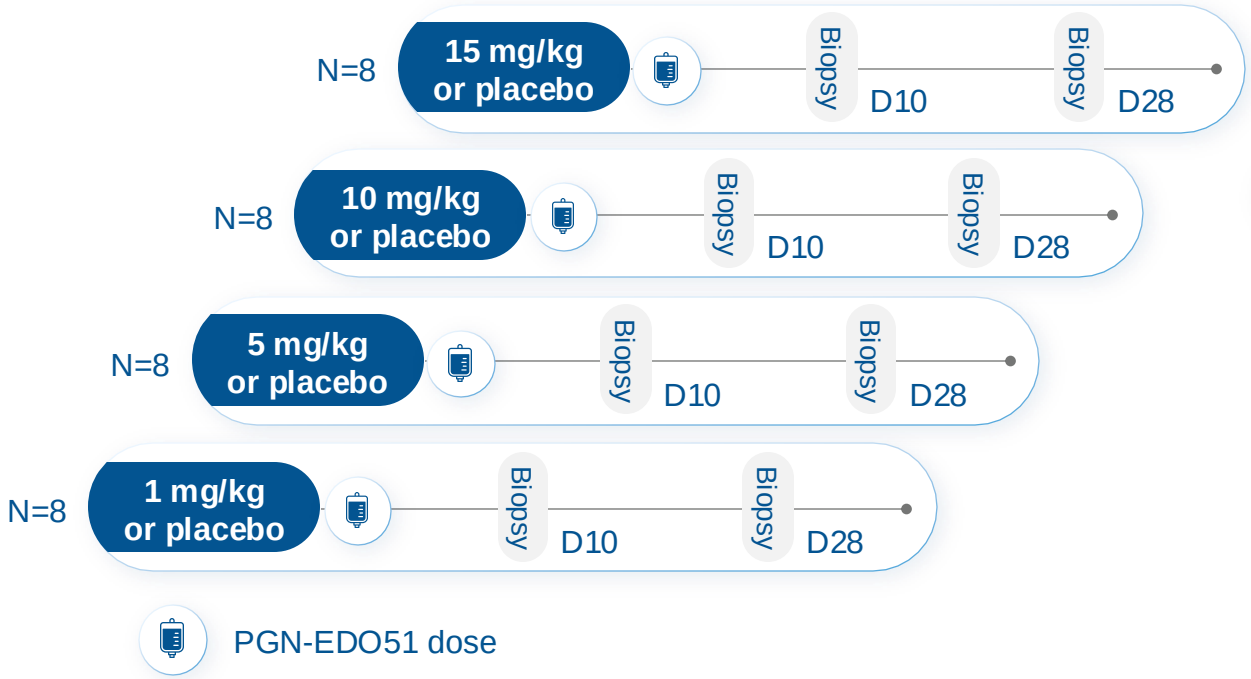
- US and EU ~40,000 patients
- ~21% patients amenable to:
  - PGN-EDO51: Phase 2 (exon 51)
  - PGN-EDO53: CTA/IND enabling studies advancing in 2024 (exon 53)
- Novel therapies needed to restore functional dystrophin and prevent loss of muscle function and early mortality

Source: https://www.cureduchenne.org/cure/exon-skipping/.

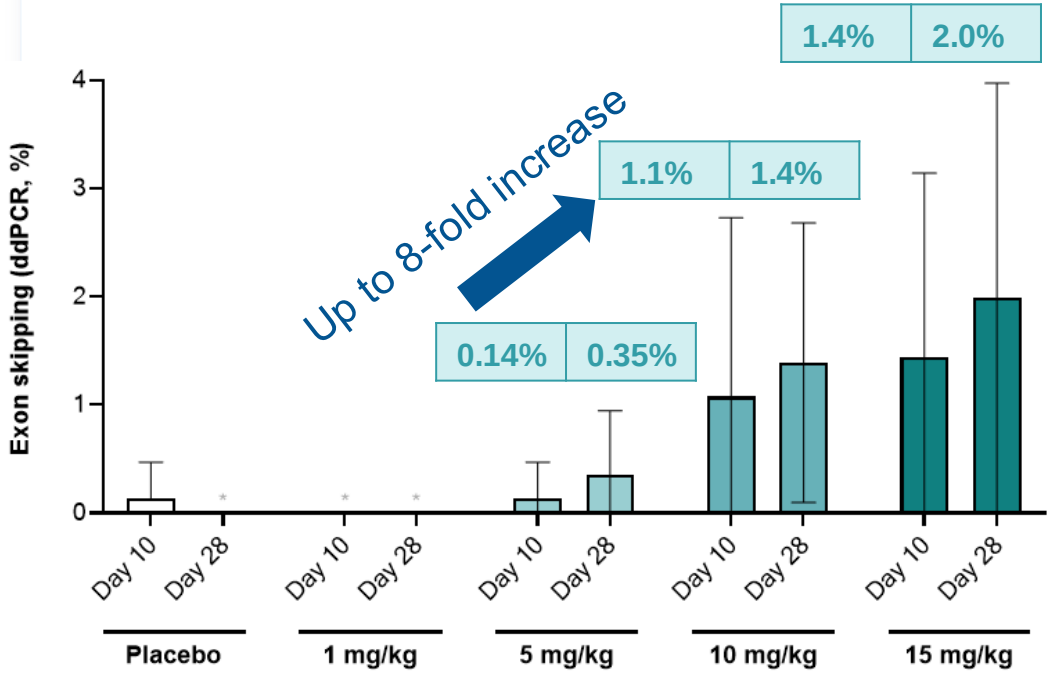
# Healthy Volunteer Study Results Led to CONNECT1: Highest Levels of Exon 51 Skipping in Humans Following Single Dose of PGN-EDO51[1]

## Phase 1 Healthy Volunteer (HV) Trial Design

- Study population: Healthy adult males (n = 32; 8 per cohort, 3:1 PGN-EDO51:placebo)
- Dosing: Single dose, IV administration
- Biceps biopsies conducted on Day 10 and Day 28




## Trial Results: Exon Skipping (Biceps)




Protocol PGN-EDO51-101: Phase 1, first in human, randomized double blind, placebo controlled single ascending dose study in healthy adult volunteers. Single dose of either PGN-EDO51 or placebo administered by IV infusion at doses indicated. Participants were followed for 28-day period following dose administration to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics. Needle biopsies of biceps muscle were taken on Days 10 and 28. Exon skipping measured by ddPCR. Shown as mean ± SD; n = 6 PGN-EDO51: 2 placebo per cohort (n = 5 for D10 at 15 mg/kg). Asterisk indicates values that were under the lower level of quantification

1.Comparative statement based on cross-trial comparison of Phase 1 HV data of single dose administration of EDO51 with publicly available Phase 1 HV data following a single dose of other exon skipping approaches (vesleteplirsen and eteplirsen).

# CONNECT1: Designed to Establish Proof-of-Concept and Inform CONNECT2 Clinical Trial Design


## Study Design and Population

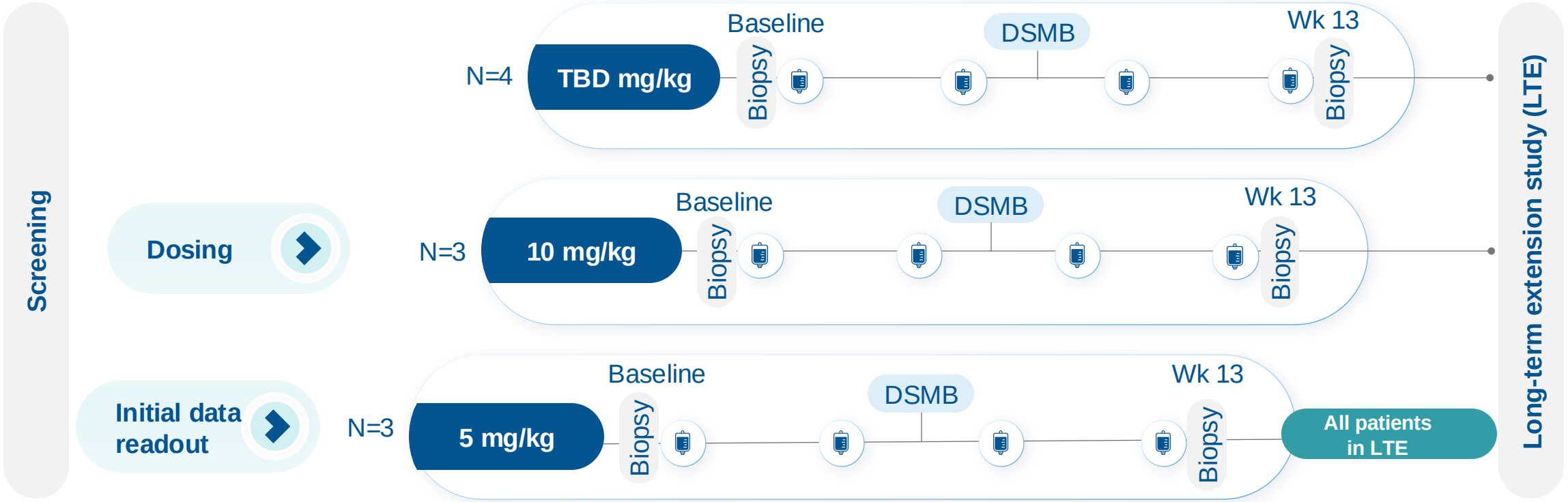
- Open label, multiple ascending dose (MAD) clinical trial in Canada
- DMD patients (n=10) with exon 51 skippable mutation
- Ages ≥ 8 years
- Ambulatory and non-ambulatory

## Endpoints

- Safety and tolerability
- Dystrophin production
- Muscle tissue concentration of PGN-EDO51
- Exon skipping

# CONNECT1 Trial Design

## Open Label Study in Patients with DMD Amenable to Exon 51 Skipping Therapy



# CONNECT1 5 mg/kg: Baseline Characteristics of Participants (n=3)

| | Mean (SD) |
|---|---|
| Age (years) | 11.7 (1.5) |
| BMI (kg/m$^2$) | 19.8 (2.7) |
| Height (cm) | 132.0 (9.9) |
| Weight (kg) | 34.4 (3.9) |
| Age of DMD genetic diagnosis (years) | 6.3 (1.5) |
| Number of patients on daily corticosteroid dosing regimen | 3 |
| Number of ambulatory patients | 3 |
| Number of patients previously on DMD therapy | 0 |

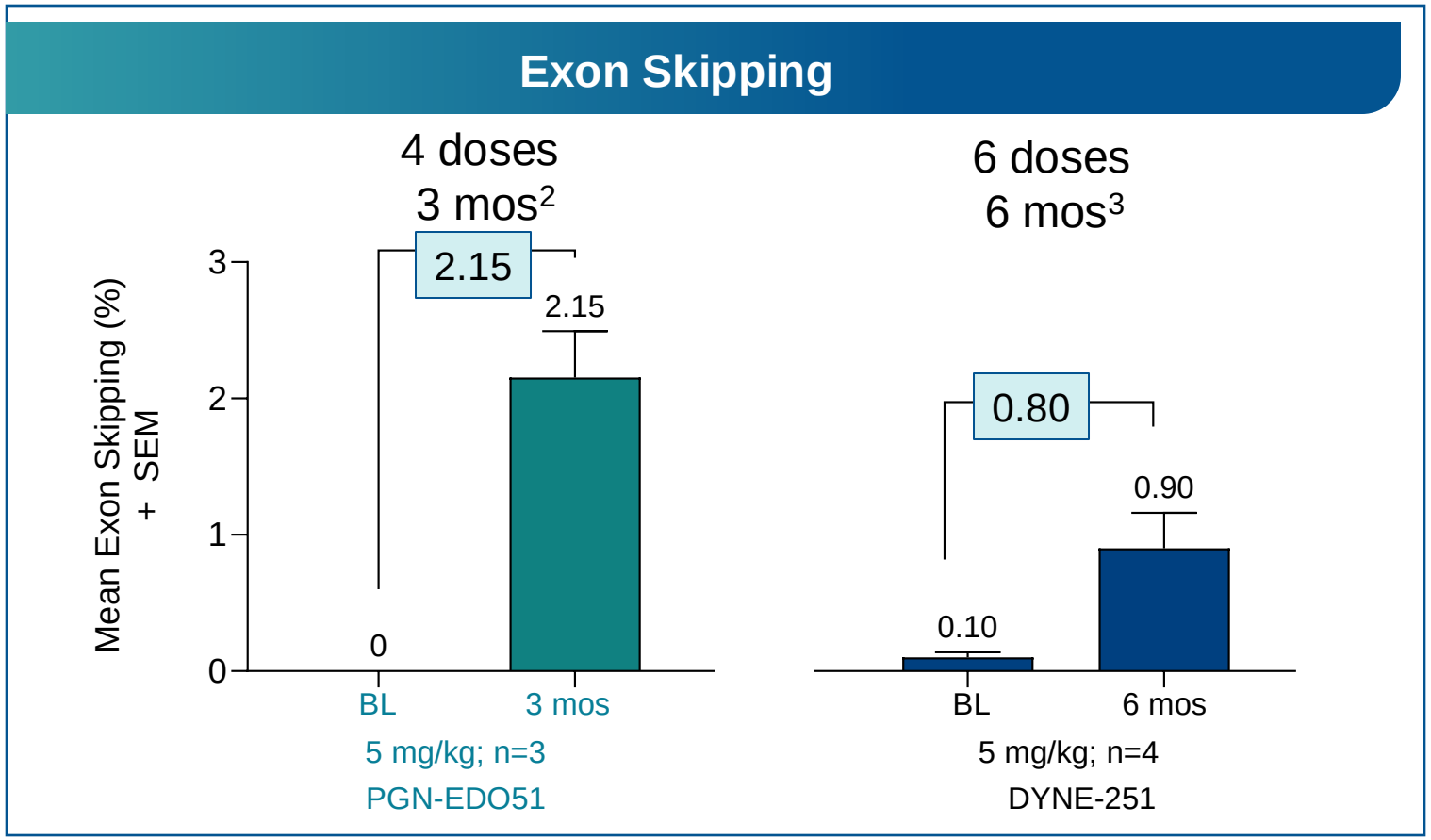
# CONNECT1 5 mg/kg: PGN-EDO51 Was Well Tolerated[1]

| | n (%) |
|---|---|
| Any TEAEs, n (%) | 3 (100) |
| Related to study drug | 1 (33.3) |
| • Mild<br>• Moderate<br>• Severe | 1 (33.3)<br>0<br>0 |
| Serious Adverse Events (AEs) | 0 |
| AEs leading to dose modification/ discontinuation/interruption | 0 |
| AEs leading to death | 0 |

- All treatment emergent adverse events (TEAEs) were mild and resolved
- Related TEAE was mild (abdominal pain, flatulence)
- No discontinuations, dose modifications or dose interruptions
  - All participants rolled over to the long-term extension study
- No sustained elevation in kidney biomarkers
- No changes in electrolytes
  - No hypomagnesemia or hypokalemia
- No changes in hepatic function
- No anemia or thrombocytopenia

1. As of May 31, 2024

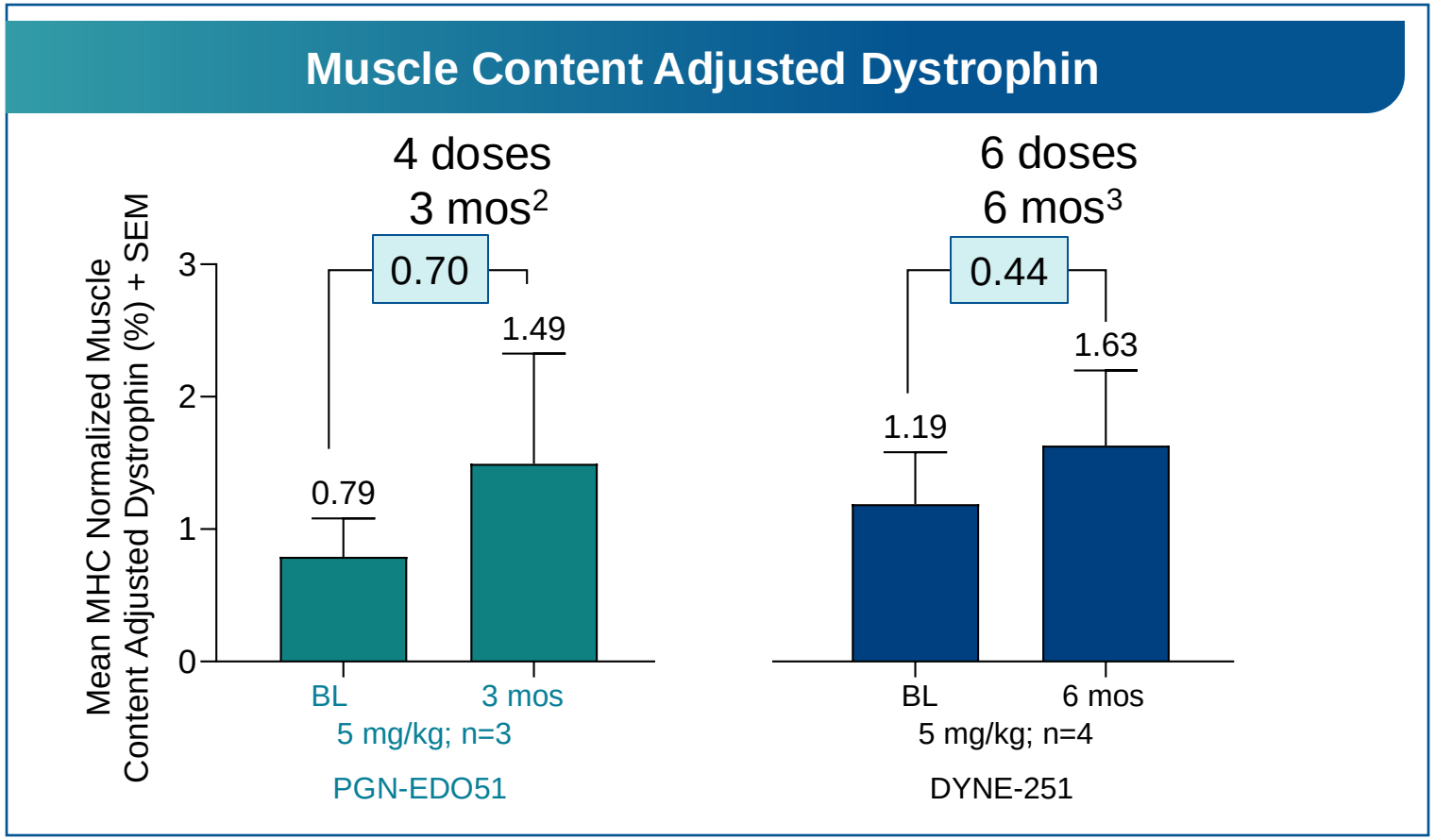
# PGN-EDO51 Showed High Levels of Mean Exon Skipping




2. PGN-EDO51 muscle biopsy taken approximately 7 days after last dose. 3. DYNE-251 muscle biopsy taken approximately 28 days after last dose.

1. No head-to-head trials have been conducted comparing PGN-EDO51 to DYNE-251. Data from studies of these clinical candidates may not be directly comparable due to differences in molecule composition, trial protocols, dosing regimens, and patient populations and characteristics. Accordingly, cross-trial comparisons may not be reliable.DYNE-251 DELIVER clinical Data update, May 20, 2024. Note: DYNE-251 error bars estimated based on public presentations.

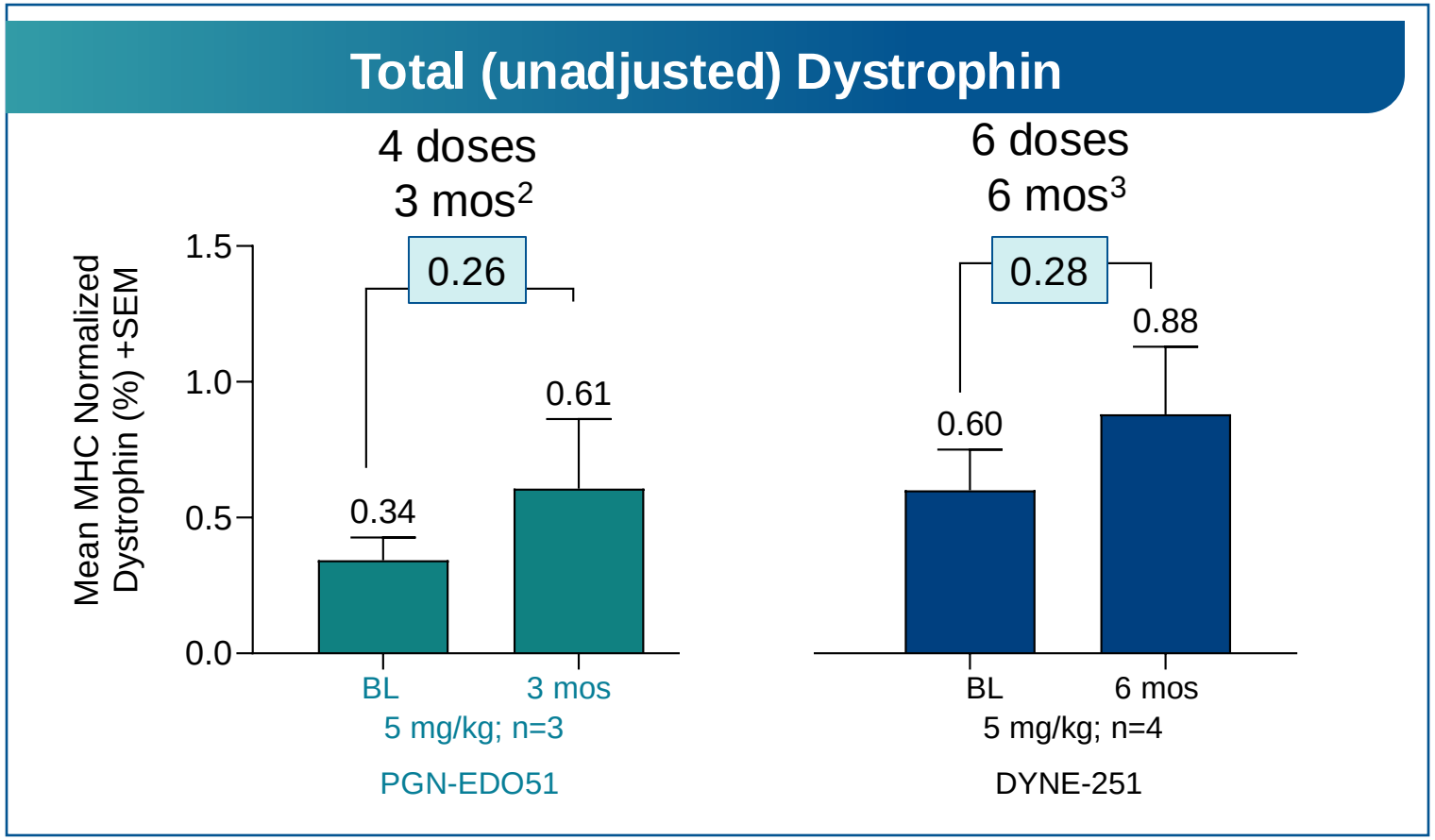
# PGN-EDO51 Produced Greater Muscle Content Adjusted Dystrophin Increase in Half the Treatment Duration and Fewer Doses[1]




2. PGN-EDO51 muscle biopsy taken approximately 7 days after last dose. 3. DYNE-251 muscle biopsy taken approximately 28 days after last dose.

1. No head-to-head trials have been conducted comparing PGN-EDO51 to DYNE-251. Data from studies of these clinical candidates may not be directly comparable due to differences in molecule composition, trial protocols, methodologies for calculating muscle content adjusted dystrophin, dosing regimens, and patient populations and characteristics. Accordingly, cross-trial comparisons may not be reliable.DYNE-251 DELIVER clinical Data update, May 20, 2024. Note: Dyne-251 error bars estimated based on public presentations.

# PGN-EDO51 Produced Similar Dystrophin Increase in Half the Treatment Duration[1]




2. PGN-EDO51 muscle biopsy taken approximately 7 days after last dose. 3. DYNE-251 muscle biopsy taken approximately 28 days after last dose.

1. No head-to-head trials have been conducted comparing PGN-EDO51 to DYNE-251. Data from studies of these clinical candidates may not be directly comparable due to differences in molecule composition, trial protocols, dosing regimens, and patient populations and characteristics. Accordingly, cross-trial comparisons may not be reliable.DYNE-251 DELIVER clinical Data update, May 20, 2024. Note: Dyne-251 error bars estimated based on public presentations.

# CONNECT1 Key Takeaways

- PGN-EDO51 was well tolerated at 5 mg/kg, currently dosing at 10 mg/kg
- All patients dosed at 5 mg/kg demonstrated increased exon skipping and dystrophin production and have continued into the long-term extension study
- PGN-EDO51 generated encouraging levels of muscle adjusted (0.70%) and total dystrophin (0.26%) after just 3 months and 4 doses of 5 mg/kg
- PGN-EDO51 produced high levels of mean exon 51 skipping (2.15%) after just 3 months and 4 doses of 5 mg/kg
- Initial results support that our EDO technology delivers high levels of oligonucleotides to the nucleus

Potentially higher levels of dystrophin production are expected with higher doses of PGN-EDO51 over longer treatment periods

# PGN-EDO51 Development Path to Support Registration


## Ongoing

Phase 2: Open-label MAD trial in patients

Open in Canada

Fast path to proof-of-concept: Dystrophin expression at 13 weeks

## Open

Phase 2: Randomized, double-blind, placebo-controlled MAD trial in patients

Multinational trial; open in United Kingdom

Potential to support accelerated approval[1]: Dystrophin expression at 25 weeks



1. Subject to alignment with regulatory authority feedback

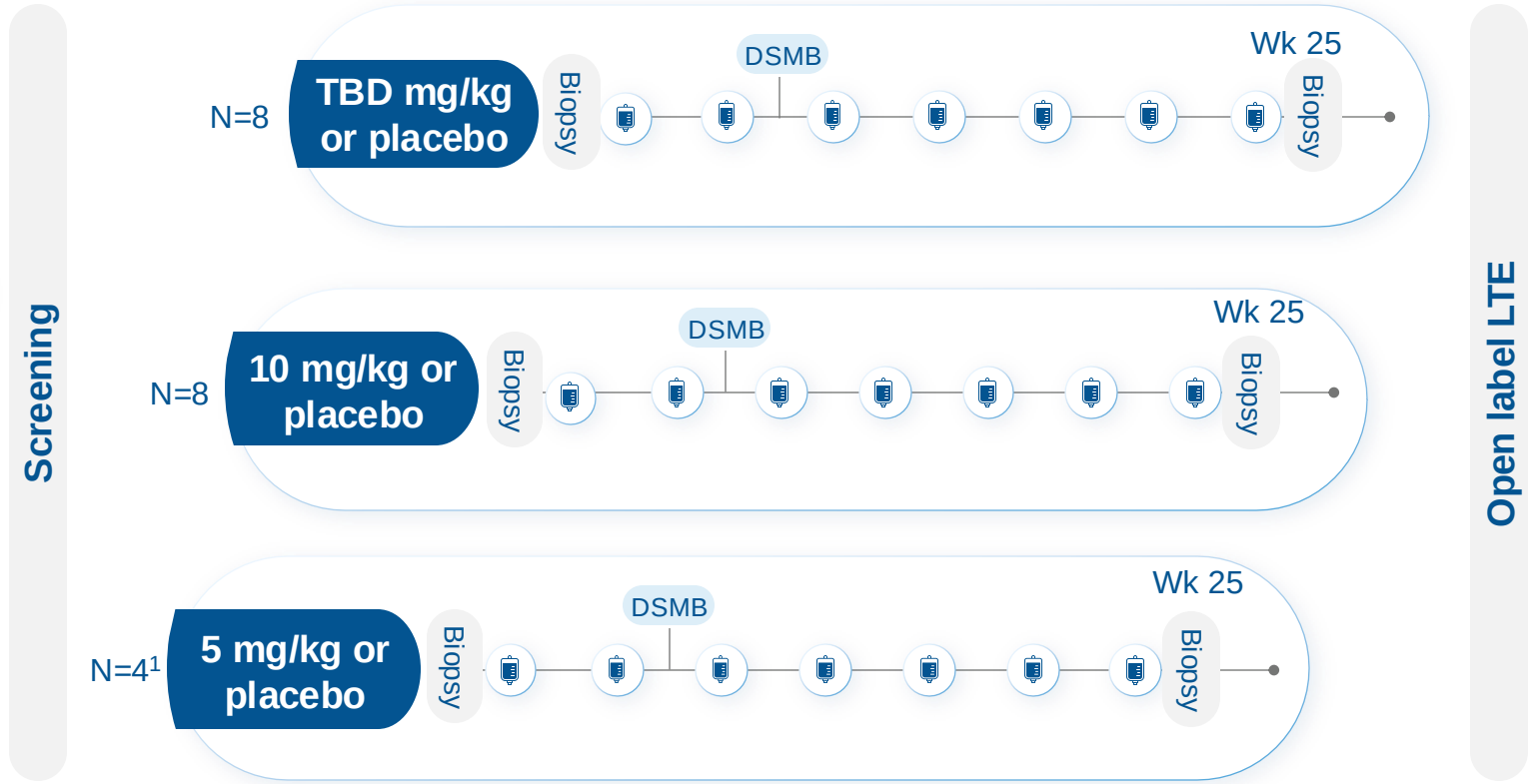
# CONNECT2: Phase 2 PGN-EDO51 MAD Trial

Connect 2
EDO51

## CONNECT2 Trial Overview

- Multinational, randomized, double-blind, placebo-controlled trial
- IV administration of PGN-EDO51 or placebo every 4 weeks
- Muscle biopsies in biceps at baseline and week 25
- Key endpoints: Safety biomarkers, dystrophin, exon skipping, North Star Ambulatory Assessment (NSAA), Time to stand from supine, Performance of Upper Limb

**PGN-EDO51 Dosing Q4W for Treatment Period of 24 weeks Prior to Rolling over into LTE Trial (randomized 3:1)**




1. Approved for n=8 in UK; amendment being submitted for the truncated cohort (n=4); truncated cohort planned for US and EU

# PGN-EDODM1 for DM1

# Myotonic Dystrophy Type 1 (DM1) Overview and Unmet Medical Need

## Overview

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

## Market opportunity

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

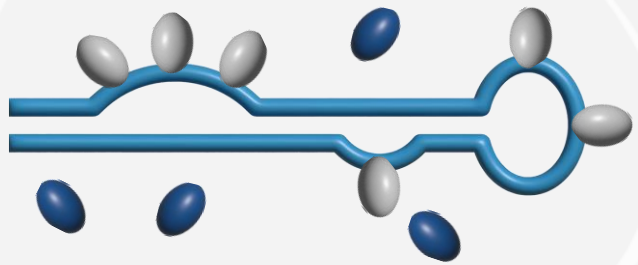


Sources: Neuroepidemiology (2022) 56 (3): 163–173., Neurology 2021 Feb 16;96(7):e1045-e1053

# Pathogenic DMPK Transcript is the Driver of Pathology in DM1

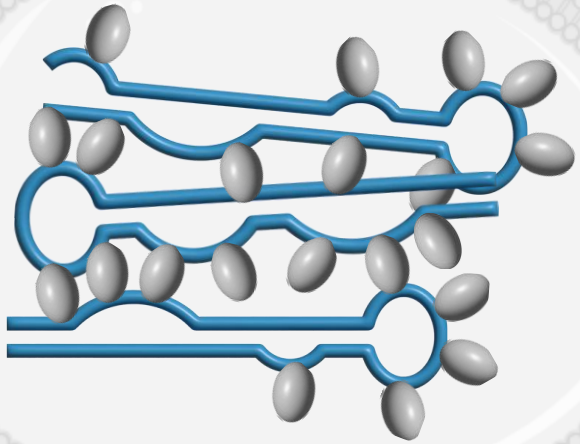
## DM1 CUG REPEAT

Pathogenic DMPK transcripts with CUG repeat expansion form hairpin loops that bind MBNL1



## DMPK PATHOLOGY

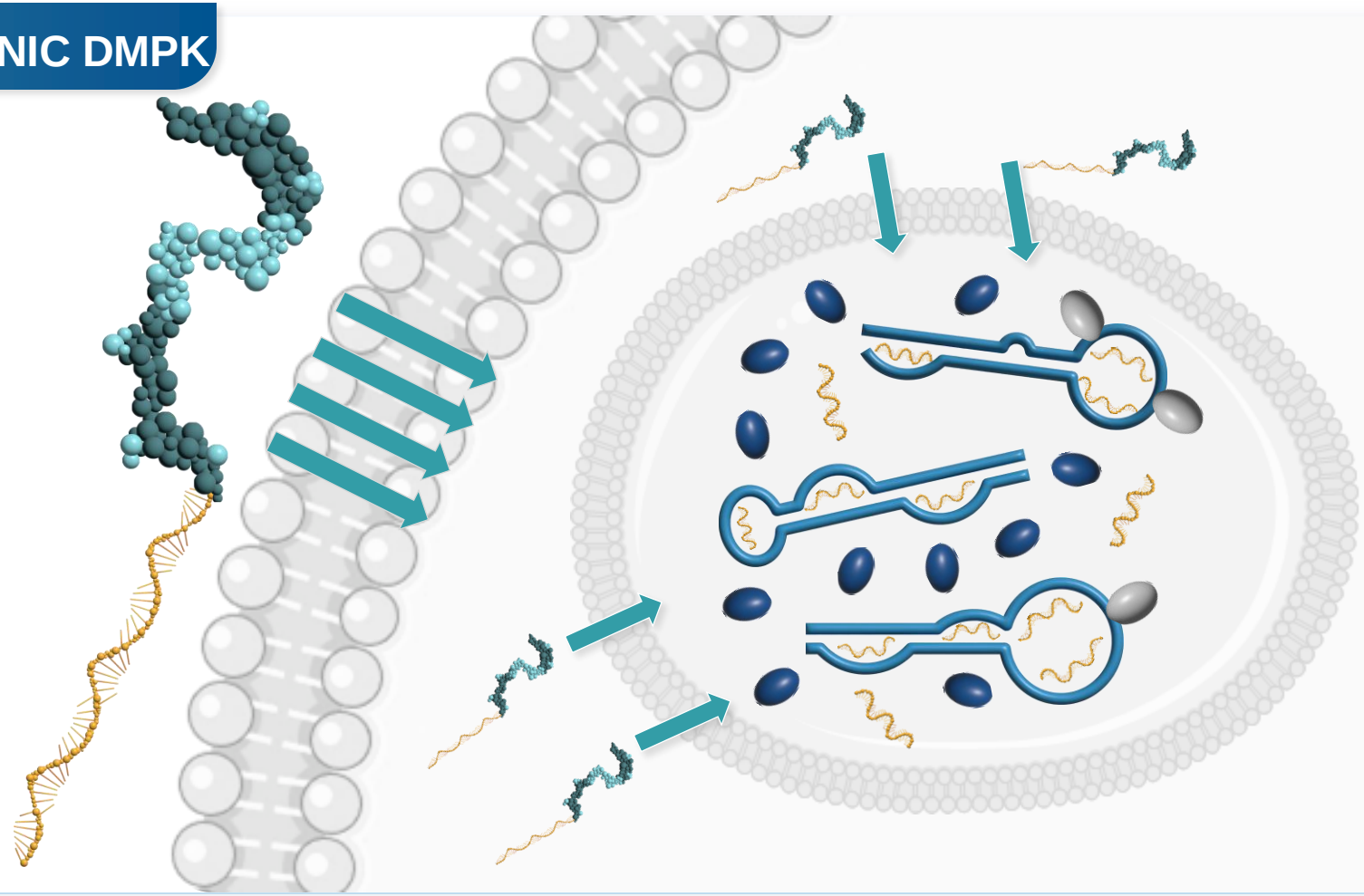
Pathogenic DMPK CUG repeat RNA accumulate and form foci that further traps MBNL1 protein causing extensive RNA mis-splicing



# PepGen's Novel Therapeutic Approach to Treating DM1

## PGN-EDODM1 TARGETS PATHOGENIC DMPK

PGN-EDODM1 binds pathogenic CUG *DMPK* transcript loops, reducing toxic foci, and liberating MBNL1 to restore normal splicing



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Free (active) MBNL1

Bound (inactive) MBNL1

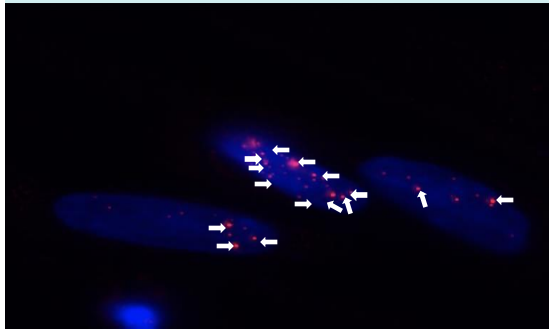
PGN-EDODM1 (EDO conjugated to oligonucleotide)

Oligonucleotide sequence only

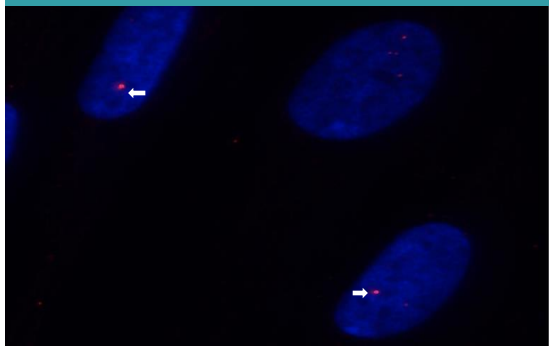
# PGN-EDODM1 Reduced Pathogenic Nuclear Foci, Liberated MBNL1 and Corrected Mis-Splicing in Patient Cells with Long CUG Repeats

## Foci Reduction

**Not Treated**



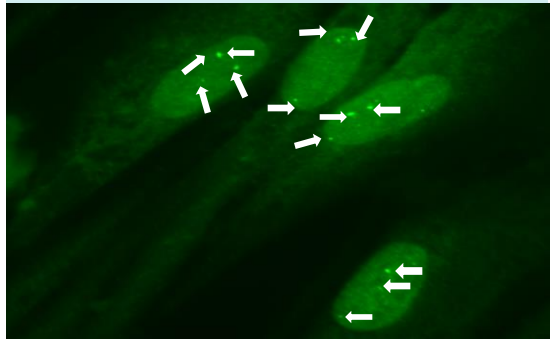
**PGN-EDODM1 Treated**



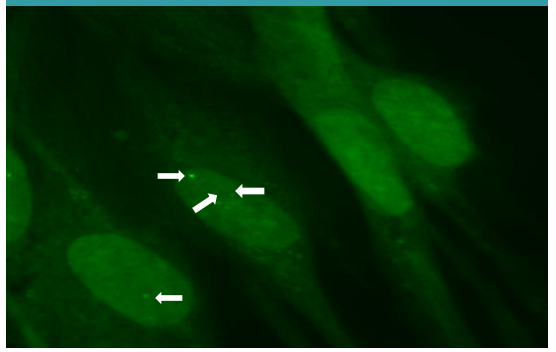
**54%**
reduction in toxic foci

## MBNL1 Liberation

**Not Treated**



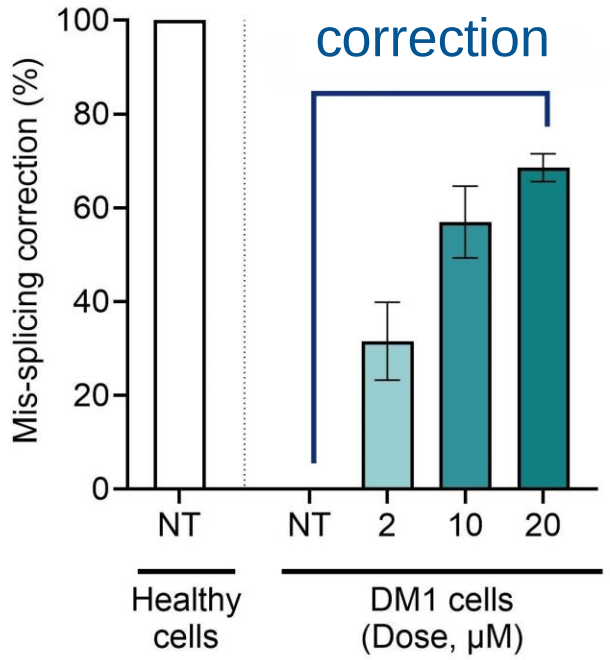
**PGN-EDODM1 Treated**



## Mis-Splicing Correction

***Across multiple transcripts***

**69%**
correction

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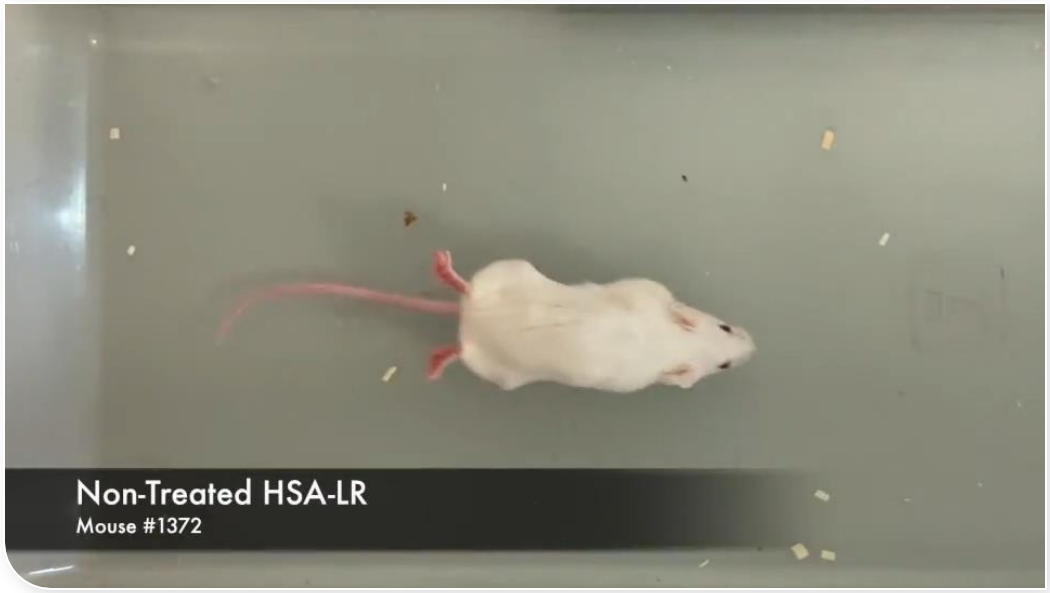
Immortalized myoblasts from healthy individual or DM1 patient with 2600 CTG repeats were cultured then differentiated for 4 days into myotubes. Treatment with peptide-PMO conjugates at concentrations given. Cells were harvested for analysis 24h after treatment. RNA isolation, RT-PCR and capillary electrophoresis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

# PGN-EDODM1 Corrected Movement Disorder of DM1 Mouse Model

## Non-Treated HSA$^{LR}$



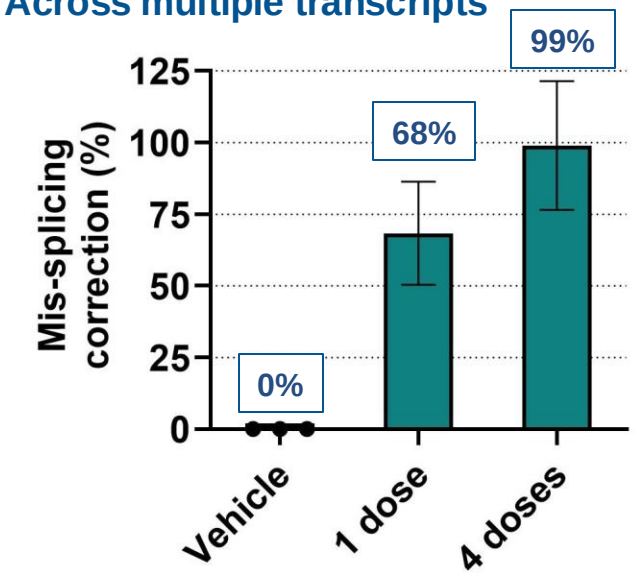

## Treated HSA$^{LR}$


Protocol: PGN-EDODM1 was administered intravenously (IV) to wild-type and HSA$^{LR}$ mice at 50 mg/kg (n=4-16); myotonia assessed two weeks post-administration. HAS: human skeletal actin.

# Resolution of Myotonia Correlated with Robust Correction of Splicing at Tissue Concentration Achieved in Single Dose Phase 1 Study of PGN-EDO51

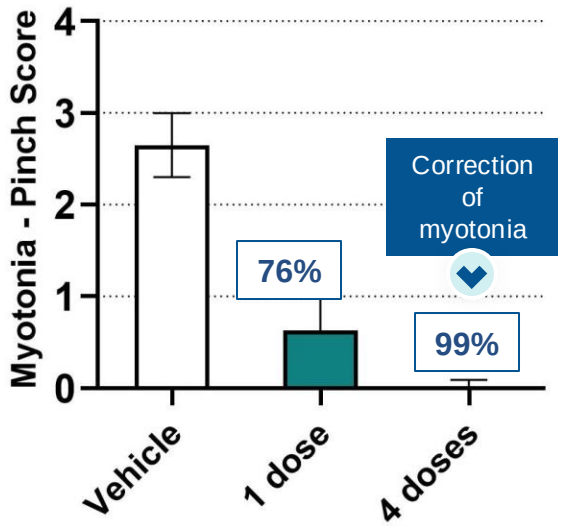
## Mis-Splicing Correction

**Across multiple transcripts**



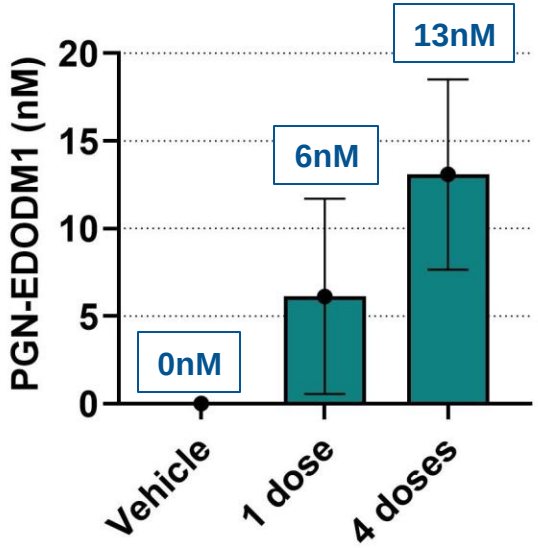

## Reversal of Myotonia

***Pinch test***




## Tissue Concentration

***Skeletal muscle***




**EDO technology (PGN-EDO51) resulted in activity in HVs while achieving PMO concentration >11nM with a single dose; therefore, we expect meaningful improvement in key biomarkers with a single dose of PGN-EDODM1 in FREEDOM**

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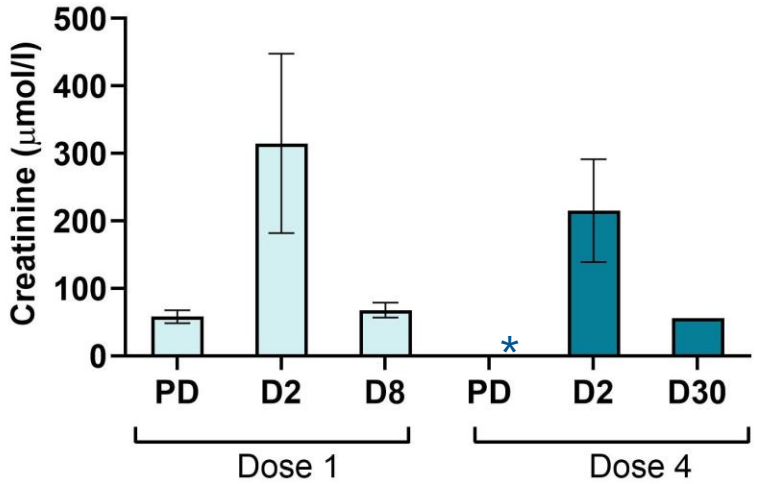
Protocol: HSA$^{LR}$ mice received 1 or 4 doses of PGN-EDODM1, with 4-week intervals between doses. Skeletal muscle tissues were collected 4 weeks post-final dose. Mis-splicing analysis considers multiple transcripts. Graph is presented as mean ± SD; n = 8-12 per cohort per transcript. Myotonia pinch 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. Graph is presented as mean ± SD; n = 12-43 per cohort. Skeletal muscle tissue concentration was measured by fluorescent based HPLC method. Graph is presented as mean ± SD; n = 8-12 per cohort.

# Preclinical Safety: Observed Changes in Creatinine are Transient and Not Associated with Adverse Kidney Findings

**We believe these results support the potential tolerability of PGN-EDODM1 with repeat dosing**

## PGN-EDODM1 REPEAT-DOSE SERUM CREATININE




Dosing schedule

| Month: | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| | ● | ● | ● | ● |

● PPMO dose- 60 mg/kg

- Transient increase in serum creatinine resolved within a week post-dose
- No adverse findings in the kidney even after 4 doses up to 60 mg/kg
- No notable hematologic, cardiovascular or hepatic effects in 13-week study

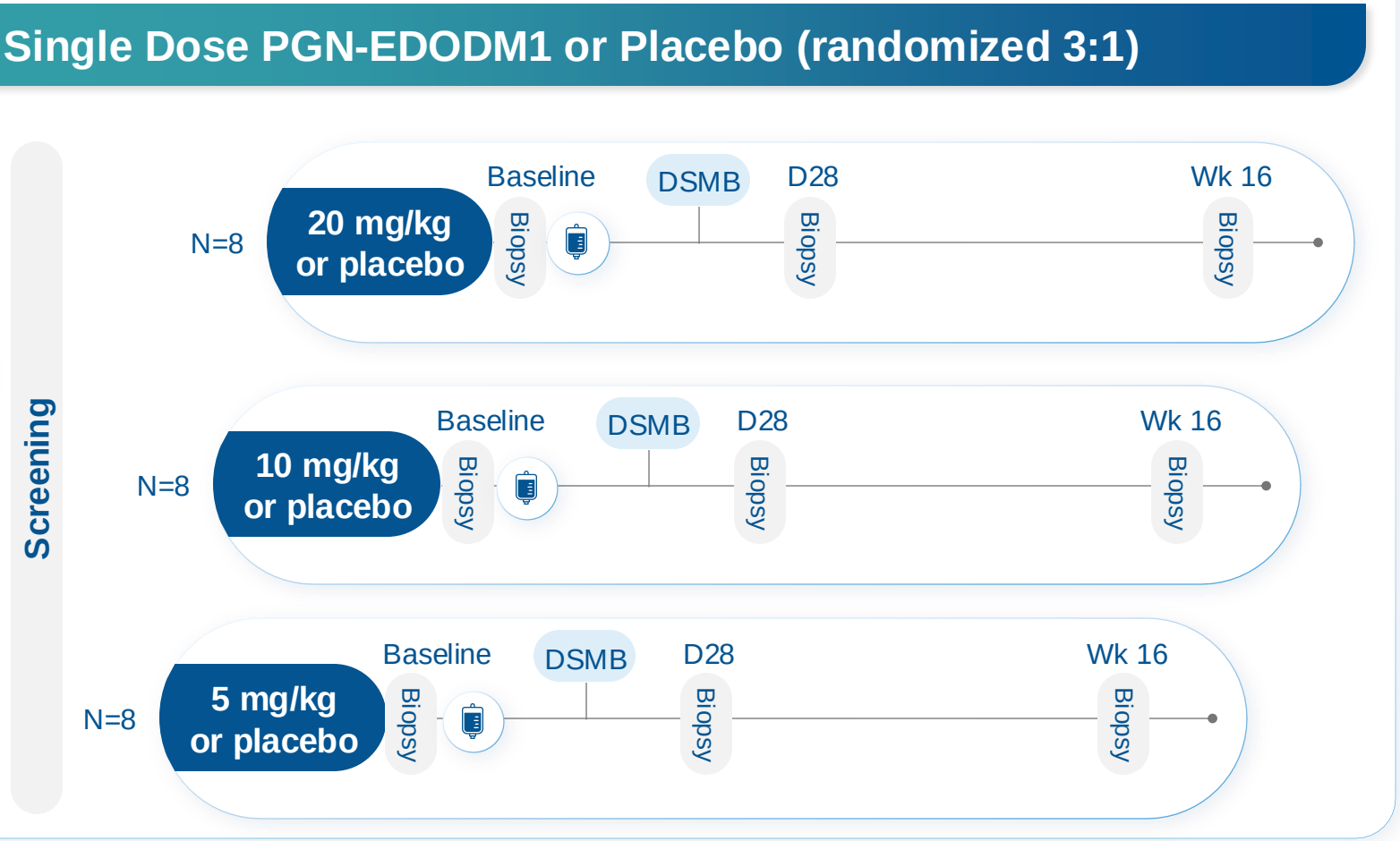
PD = pre-dose. * Data not collected. NHP protocol: PGN-EDODM1 was administered to NHP (males and females) by IV infusion at 60 mg/kg over 60 min (n=5/sex) for 4 doses. Dosing schedule was once every 28 days. Male and female results were comparable with male-only data presented. Shown as mean ± SD.

# FREEDOM: Phase 1 PGN-EDODM1 Single-Ascending Dose (SAD) Trial

Freedom
DM1

## FREEDOM study overview

- Multinational, randomized, double-blind, placebo-controlled SAD trial in patients
- Single IV administration of PGN-EDODM1
- Muscle biopsies in tibialis anterior at baseline, day 28, week 16
- Key endpoints: Safety, correction of mis-splicing, vHOT



# FREEDOM Informed Design of Phase 2 FREEDOM2 Trial

Freedom DM1

## Open in US, CANADA and UK

- Phase 1 Randomized, double-blind, placebo-controlled SAD study in patients
- Key anticipated readouts: Functional assessments, correction of mis-splicing, safety data

Freedom 2 DM1

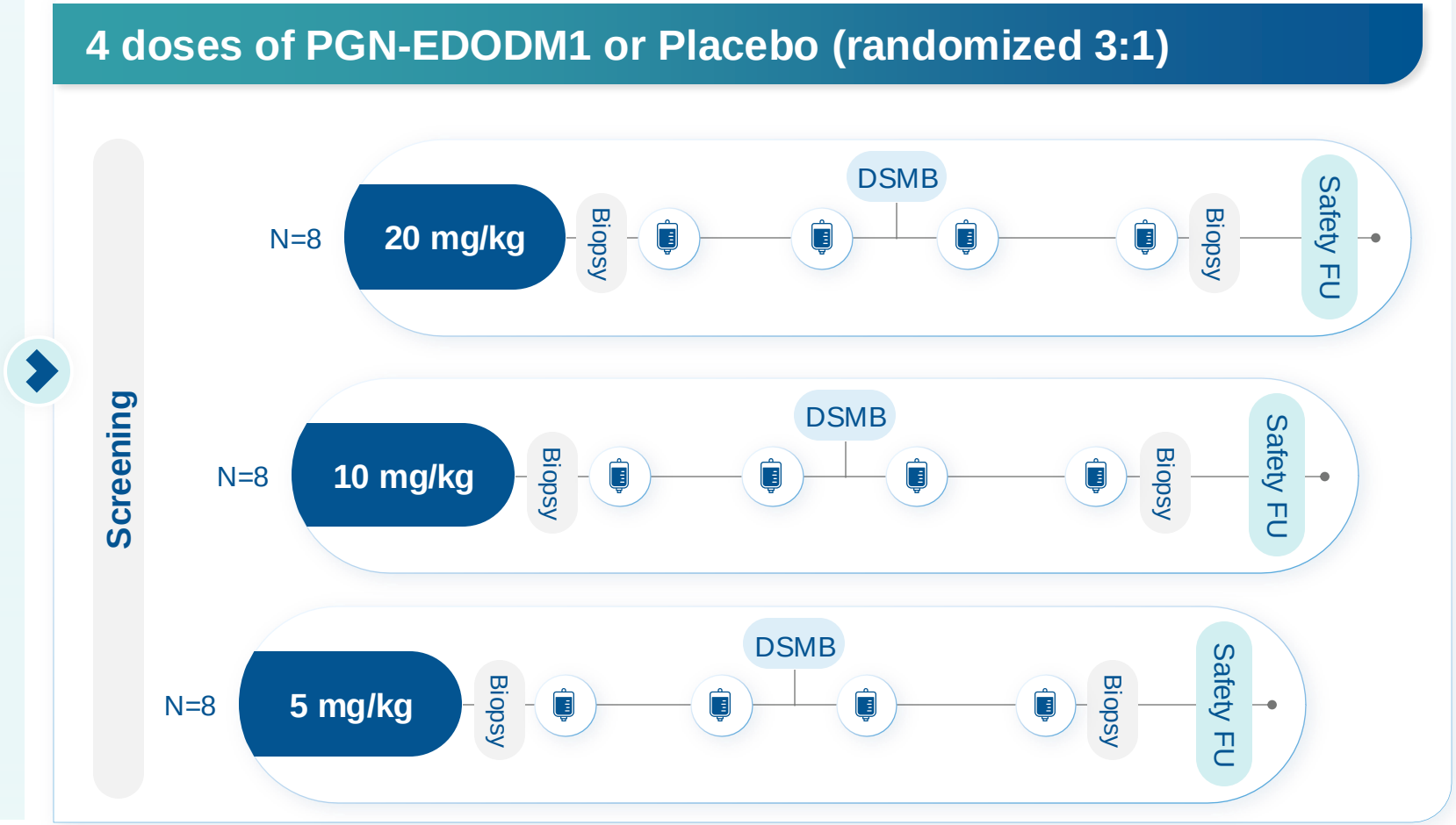
## Multinational Study Initiated

- Phase 2 Randomized, double-blind, placebo-controlled MAD study in patients
- Expect to initiate dosing of FREEDOM2 clinical trial in 2H:2024
  - IV administration of EDODM1 every 4 weeks up to 12 weeks
  - Key anticipated readouts: Functional assessments, correction of mis-splicing, safety data

# FREEDOM2-DM1 Phase 2 MAD study

## FREEDOM2 study overview

- Multinational, randomized, double-blind, placebo-controlled, MAD study
- 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




PepGen™

PGN-EDODM1 dose every 4 weeks

# Conclusion

# Continued Execution Toward Key Readouts Through Early 2025 with Existing Cash Funding Operations into 2026[1]

## Key expected data readouts/milestones

### PGN-EDO51
DMD Exon 51

- CONNECT1 10 mg/kg dose cohort results in early 2025
- CONNECT2
  - Currently open in UK
  - Engaging with EU regulators
  - Open in US by year-end, subject to regulatory clearance

### PGN-EDODM1
DM1

- FREEDOM clinical results in Q4 2024
- FREEDOM2 initial dosing in 2H:2024



1. Based on current operating plan