



Analysis of Individual Patient Mis-Splicing Data from PGN-EDODM1, an Investigational Therapy for Myotonic Dystrophy Type 1 (DM1)

James McArthur, PhD, President and CEO, PepGen

May 2026

J. Hamel, T. Wheeler, J. Brisson, H. Lochmuller, J. Sampson, N.A. Goyal, H. Phan, N. Johnson, J. Statland, J.B. Lilleker, C. Turner, G. Pfeffer, B. Garg, G. Song, P. Lonkar, S. Vacca, S. Babcock, S. Batra, S. Yu, P. Streck, A. Barbier, J. Larkindale, J. McArthur

Disclosures

- Dr. McArthur is an employee of and is paid by PepGen
- Dr. McArthur has PepGen stock and stock options
- Dr. McArthur is an inventor on patents or patent applications licensed to PepGen

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 promising trends and therapeutic potential and safety profile of PGN-EDODM1 based on data from the 5, 10 and 15 mg/kg cohorts of the FREEDOM study and 5 mg/kg cohort of the FREEDOM2 study, our expectations regarding the potential for significant correction of mis-splicing with more and higher 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 data readouts from our FREEDOM2 trial, 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.

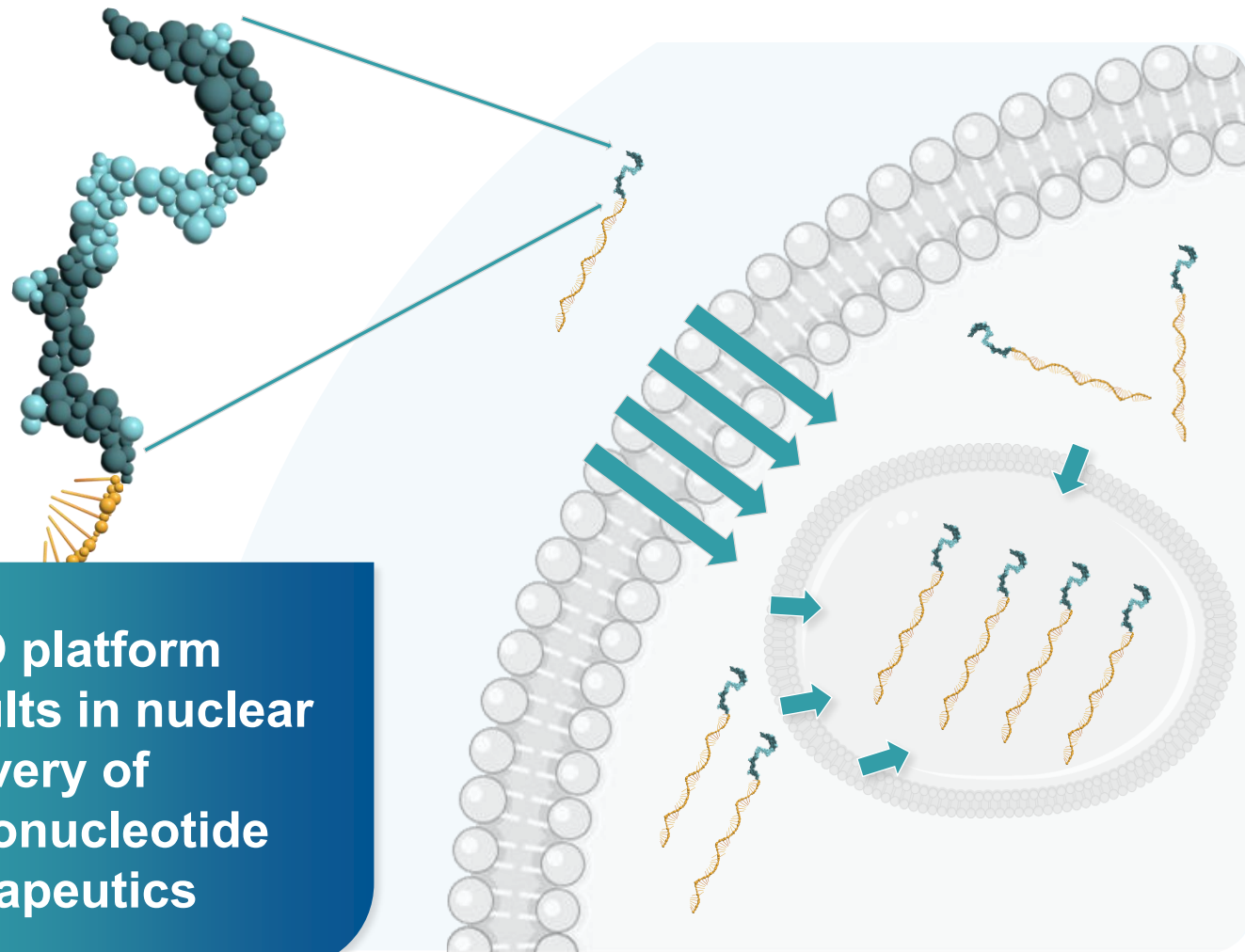
This presentation discusses PGN-EDODM1, an investigational therapy, that has not been approved for use in any country, and is not intended to convey conclusions about their efficacy or safety. There is no guarantee that PGN-EDODM1 or any other investigational therapy will successfully complete clinical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

Jubal, retired professor living with DM1

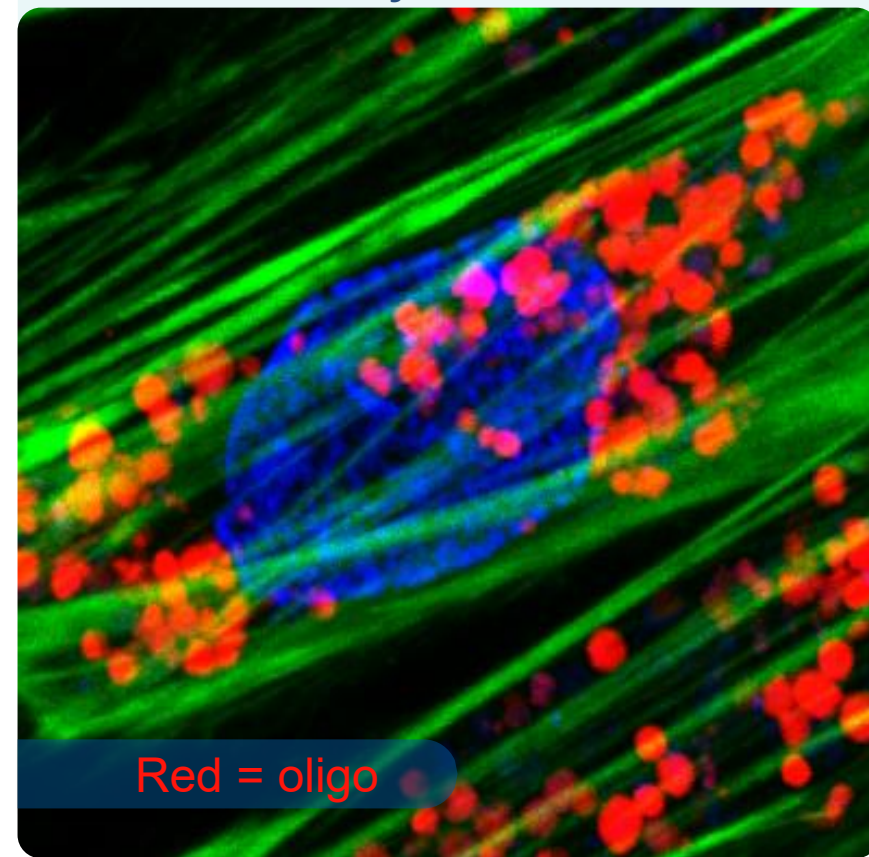


PepGen is committed to transforming the lives of people and families living with myotonic dystrophy type 1 (DM1).

PepGen's EDO Platform Has Been Designed and Developed to Solve the Delivery Challenge of Oligonucleotides



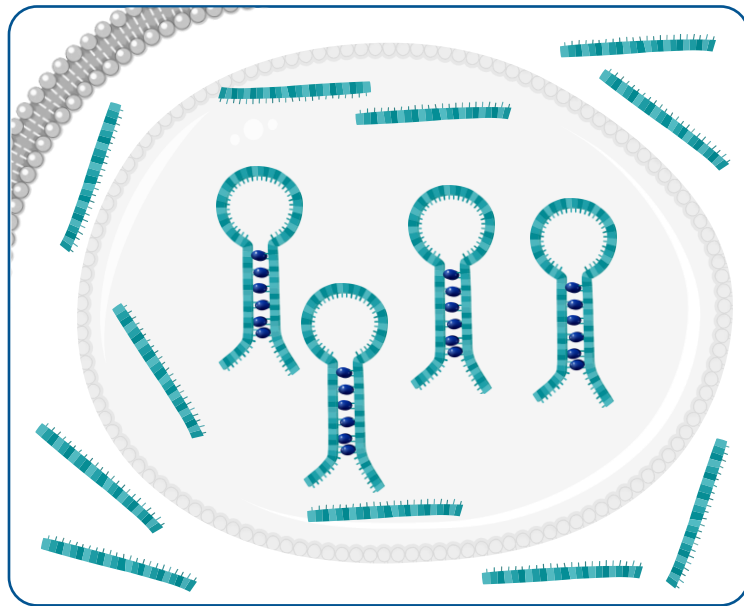
PGN-EDODM1 Delivery to DM1 Patient Myotubes



EDO platform results in nuclear delivery of oligonucleotide therapeutics

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

DM1 is caused by pathogenic *DMPK* transcripts

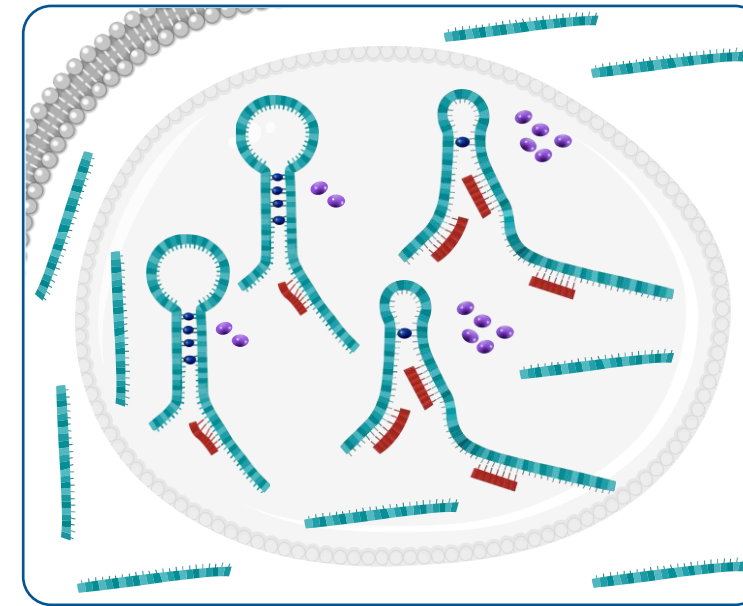


Trapped MBNL1 is inactive and results in mis-splicing



- 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



Liberated MBNL1 restores correct splicing



- 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

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



Freedom

DM1

FREEDOM Phase 1

Study Overview

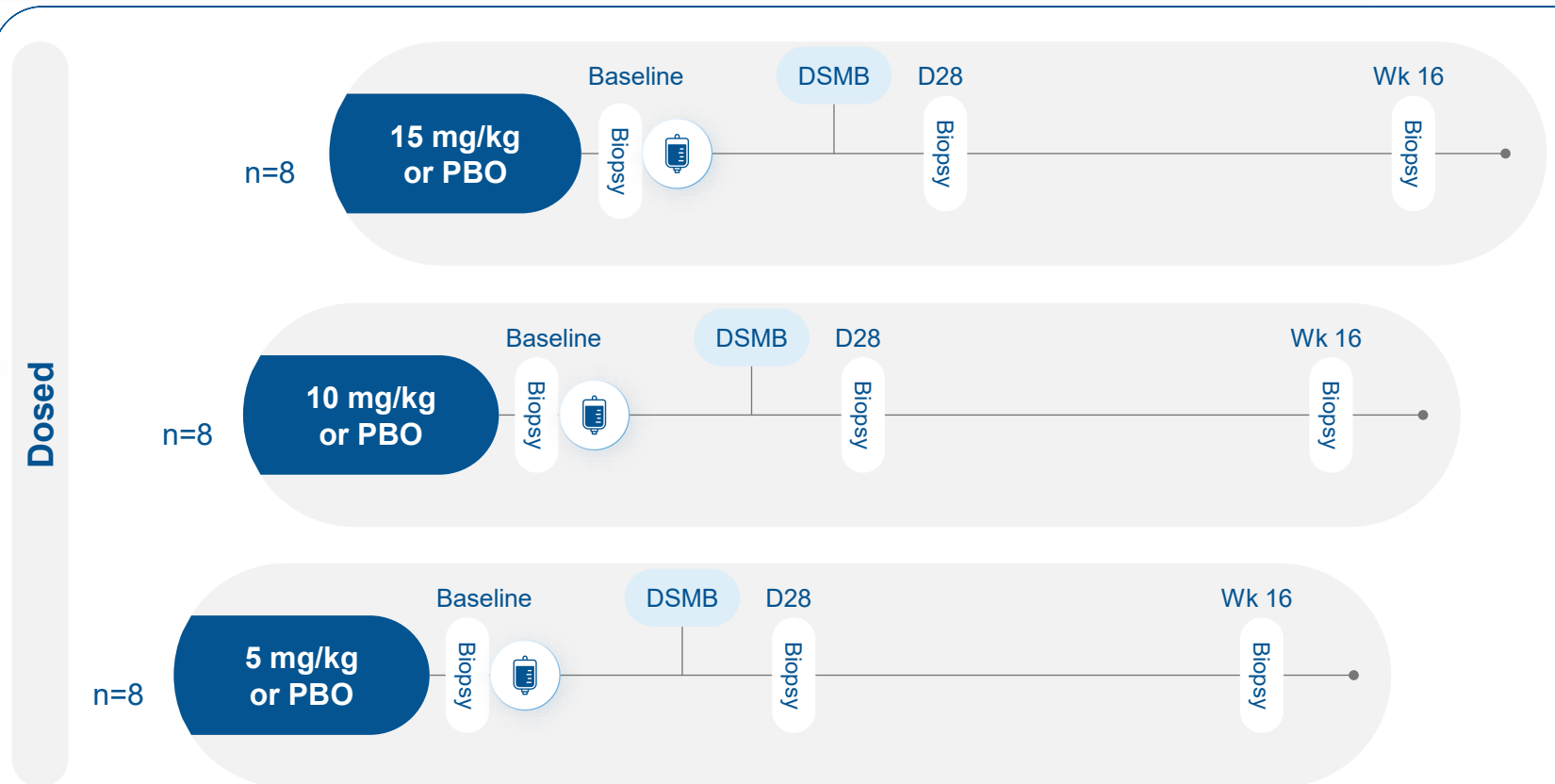
Multinational, randomized, double-blind, placebo-controlled SAD study in patients

Single IV administration of PGN-EDODM1

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

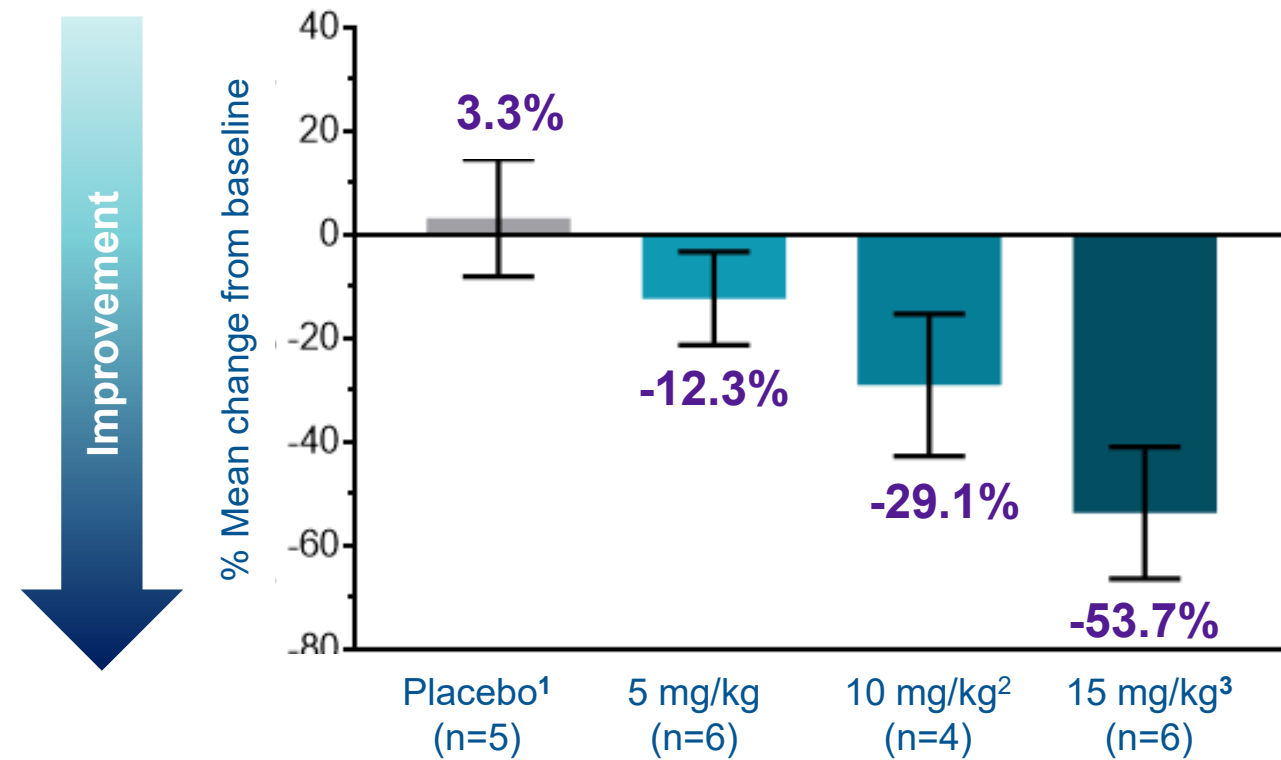
Safety, PK, correction of mis-splicing, initial functional assessments

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



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

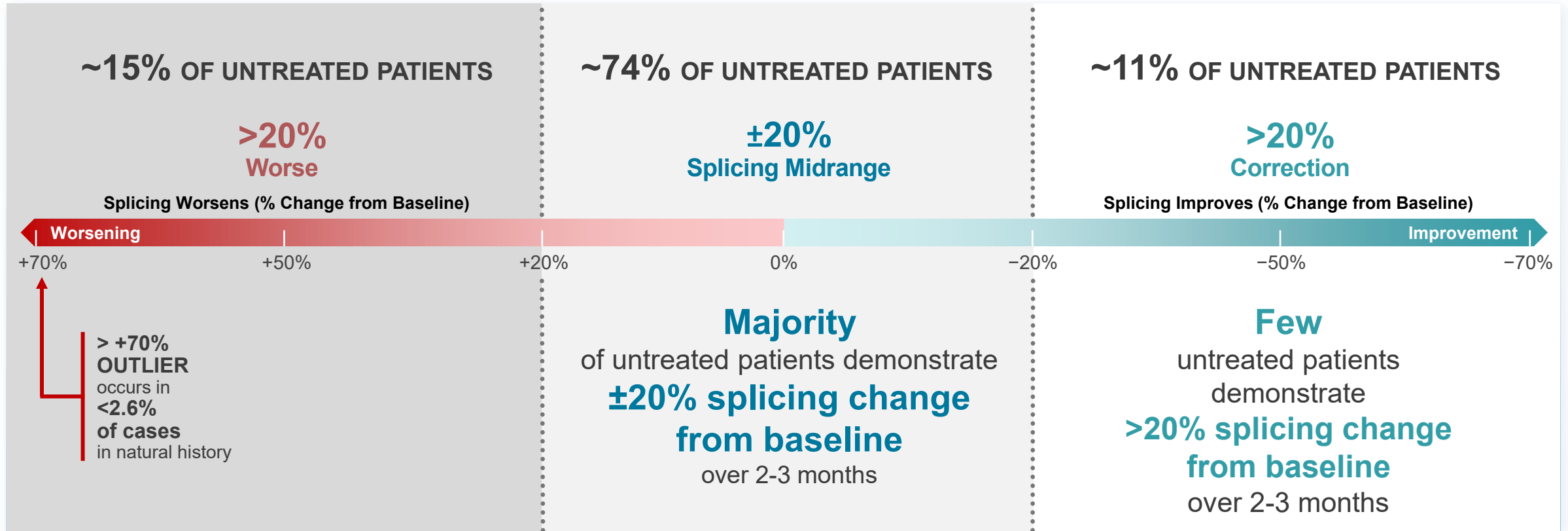
PGN-EDODM1 Was Generally Well Tolerated, with TEAEs Primarily Mild to Moderate Across Dose Cohorts

	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	5	2	2	5	14
Severe	0	1	2	0	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

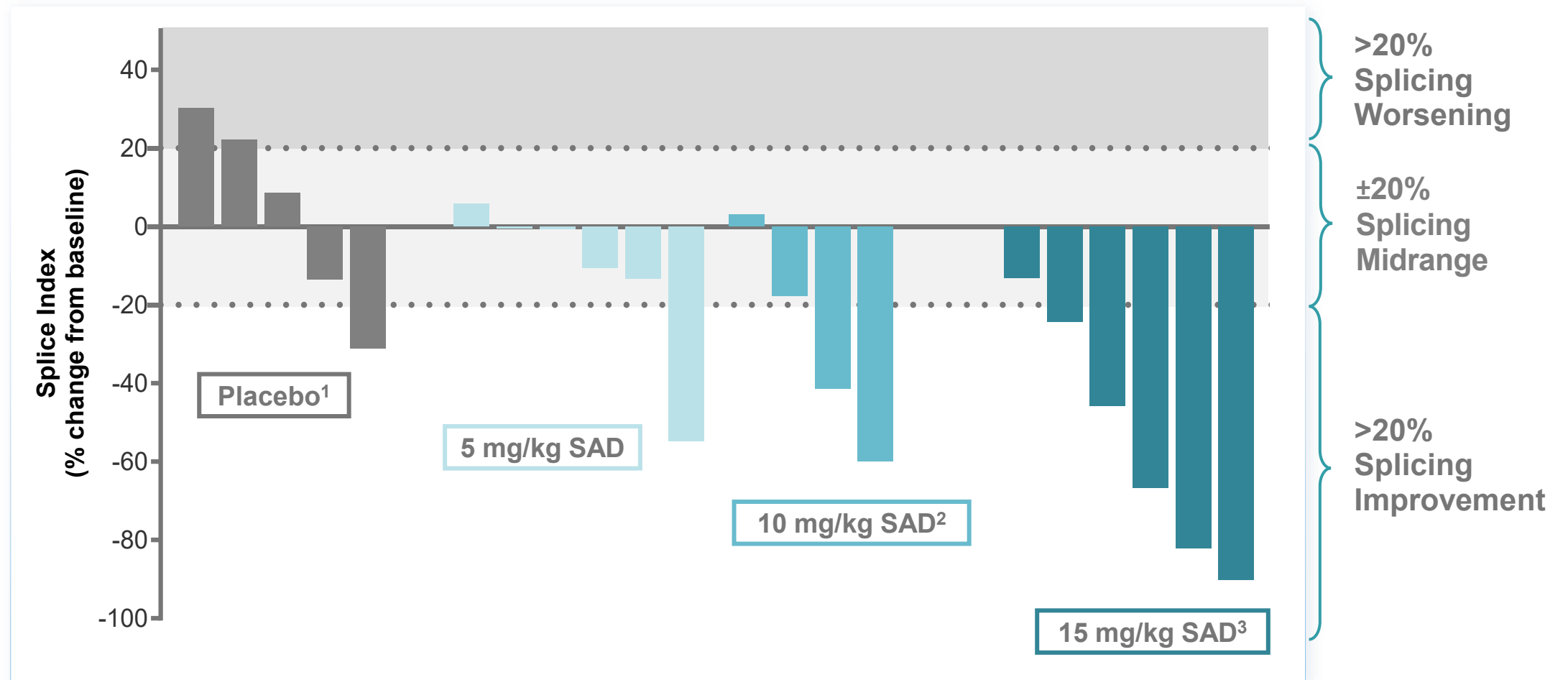
- Most frequent TEAEs: nausea, nasopharyngitis, and headache
- No electrolyte-related TEAEs or hypomagnesemia observed across dose cohorts
- No renal-related TEAEs observed at 5 and 10 mg/kg; DLT at 15 mg/kg involving a transient decrease in eGFR(cys), resolving without intervention
- Transient moderate 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

~11% of Untreated DM1 Patients Demonstrate >20% Splicing Improvement over a 2 to 3 Month Time Period

Natural History Data in Untreated DM1 Patients*



Higher PGN-EDODM1 Doses Associated with Increased Number of Patients Achieving >20% Splicing Improvement⁴



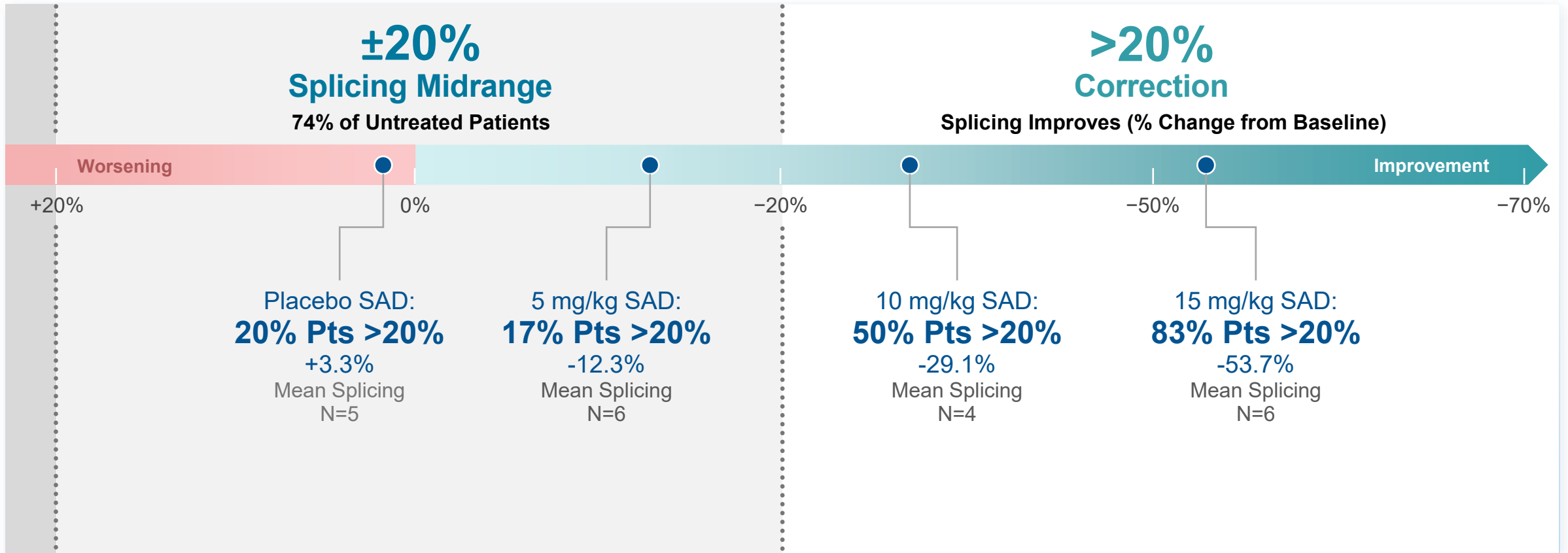
1. Missing samples due to unavailability of biopsy tissue or sample outside of assay window

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

4. Day 28 analysis from FREEDOM-DM1 clinical study

PGN-EDODM1 Demonstrated >20% Splicing Correction in a Majority of DM1 Patients after a Single Dose ≥ 10 mg/kg



FREEDOM2: Phase 2 MAD Study Design



Freedom 2

DM1

FREEDOM2 Phase 2 Study Overview

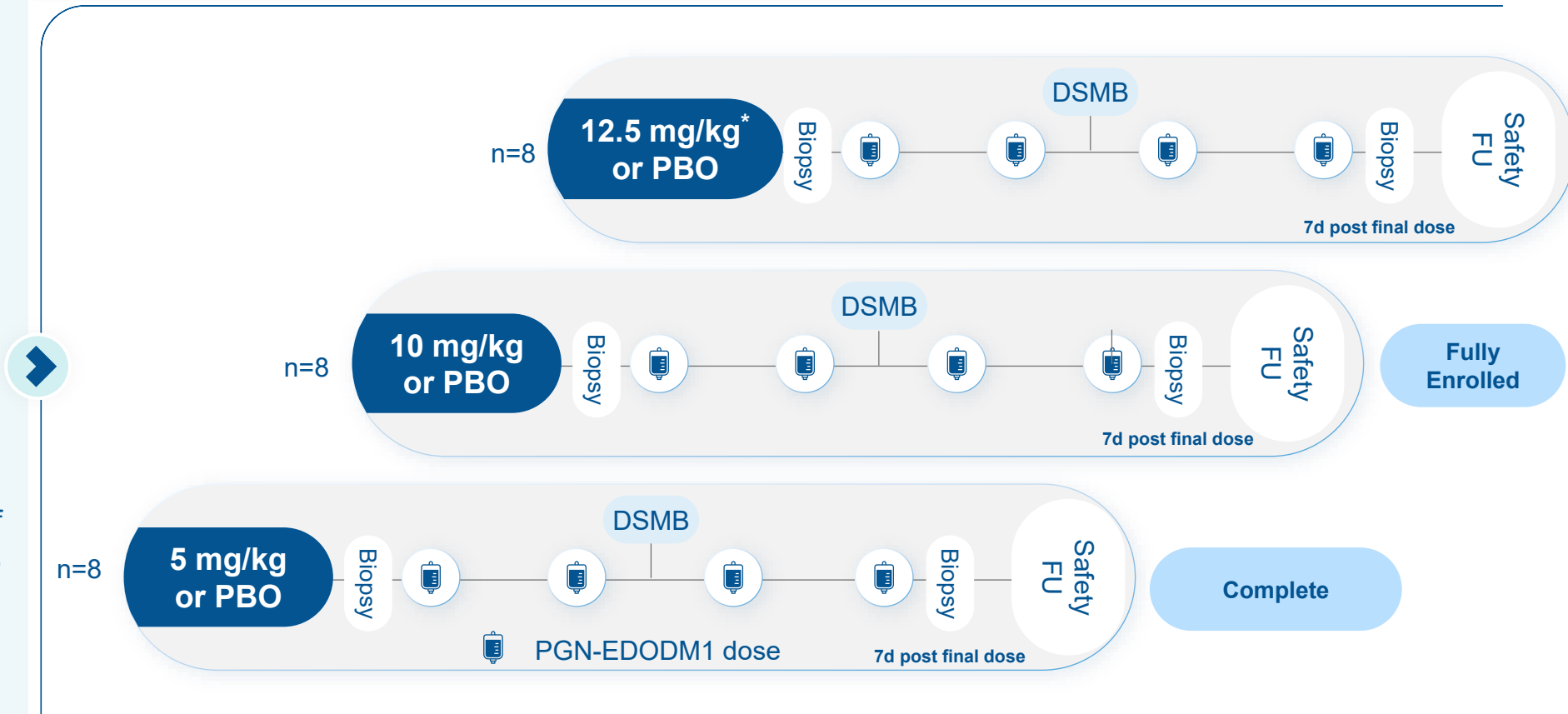
Multinational, randomized, double-blind, placebo-controlled, MAD study open in Canada, UK, NZ, Australia and South Korea**

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

FREEDOM-OLE open for patients in FREEDOM & FREEDOM2

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



Favorable Emerging Safety Profile of PGN-EDODM1; No Increase in Toxicity with Multiple Doses at 5 mg/kg

Summary of Treatment Emergent Adverse Events (TEAEs)¹

5 mg/kg (n=8)
n(%)

Any TEAE	7 (87.5)
Mild	4 (50.0)
Moderate	3 (37.5)
Severe	0 (0.0)
Any SAE	0
Any related SAE	0
Any AESI or dose-limiting toxicities	0
Any TEAE leading to study withdrawal	0
Any TEAE leading to death	0

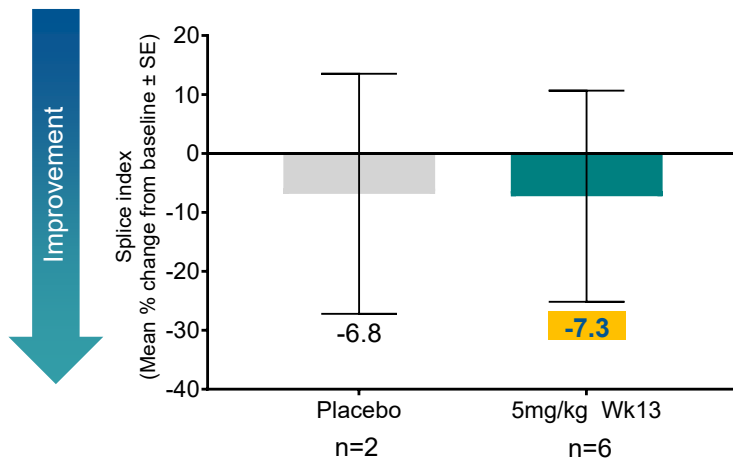
PGN-EDODM1 was Generally Well-Tolerated, with All AEs Mild or Moderate in Severity¹

- All participants completed all 4 doses, with no evidence of cumulative AEs
- The overall AE profile of MAD 5 mg/kg is consistent with that observed in SAD 5 mg/kg
- Nausea was the most common AE
- No SAEs, AESIs, or DLTs and no signs of hypersensitivity
- eGFR and creatinine measurements within the normal range
- No hypomagnesemia
- Transient albuminuria observed – did not increase with repeat dosing

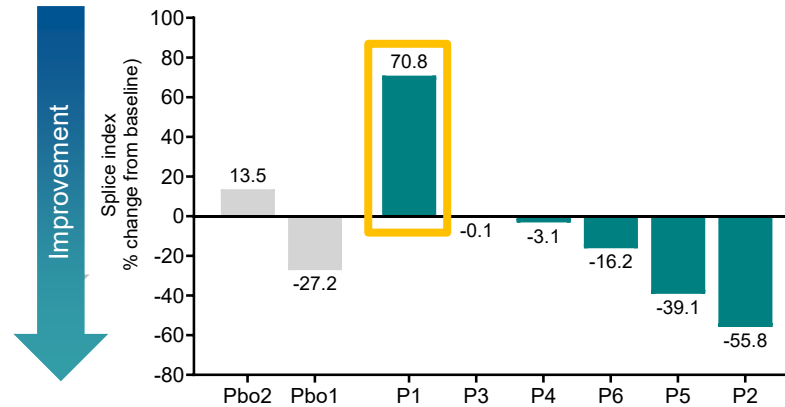
FREEDOM2 5 mg/kg Splicing Correction

5 mg/kg Collective Splicing Data

Splicing Analysis



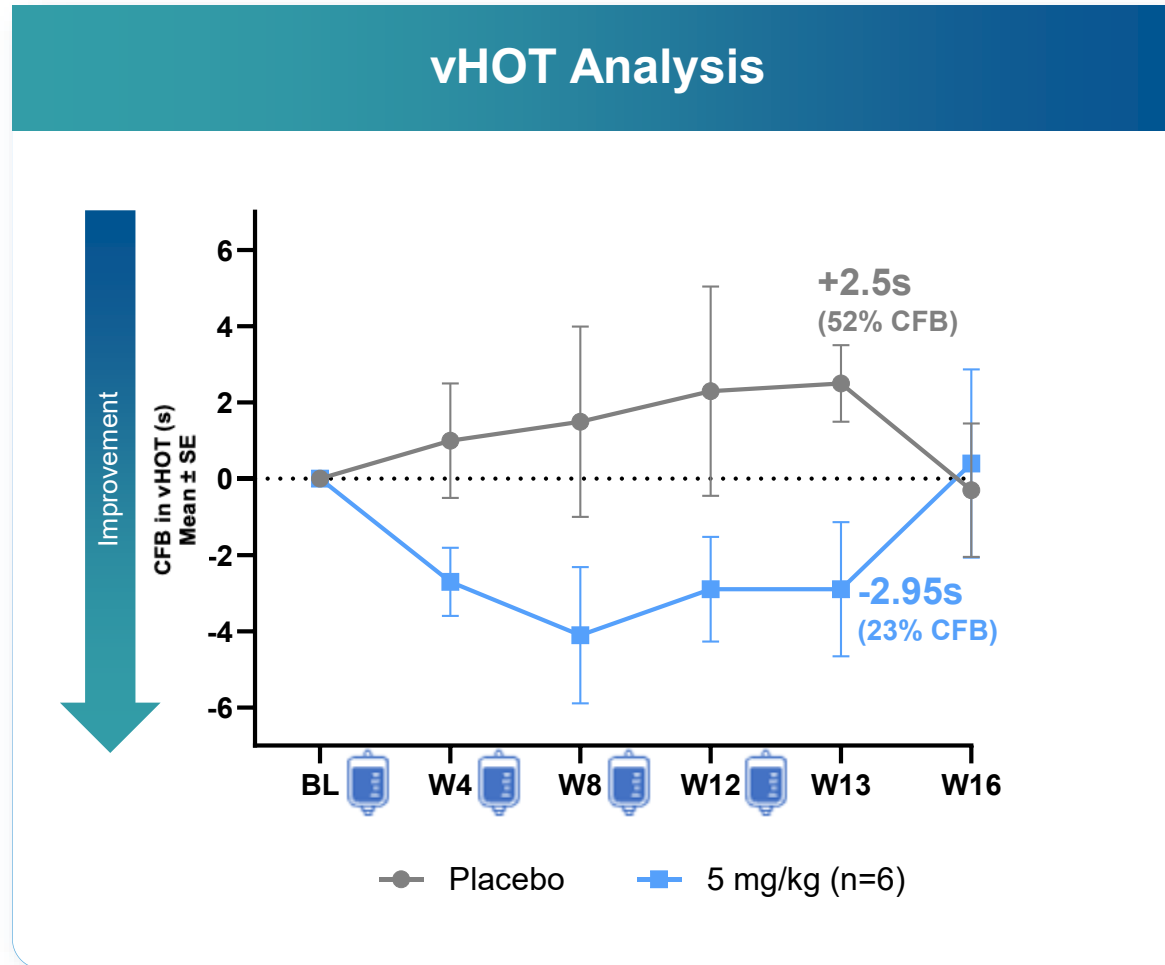
5 mg/kg Individual Splicing Data



Excluding notable splicing outlier mean splicing correction of 22.9% (n=5)

High mean muscle tissue concentration of PGN-EDODM1 of 158 ng/g at Day 7 post-dose (n=5)**

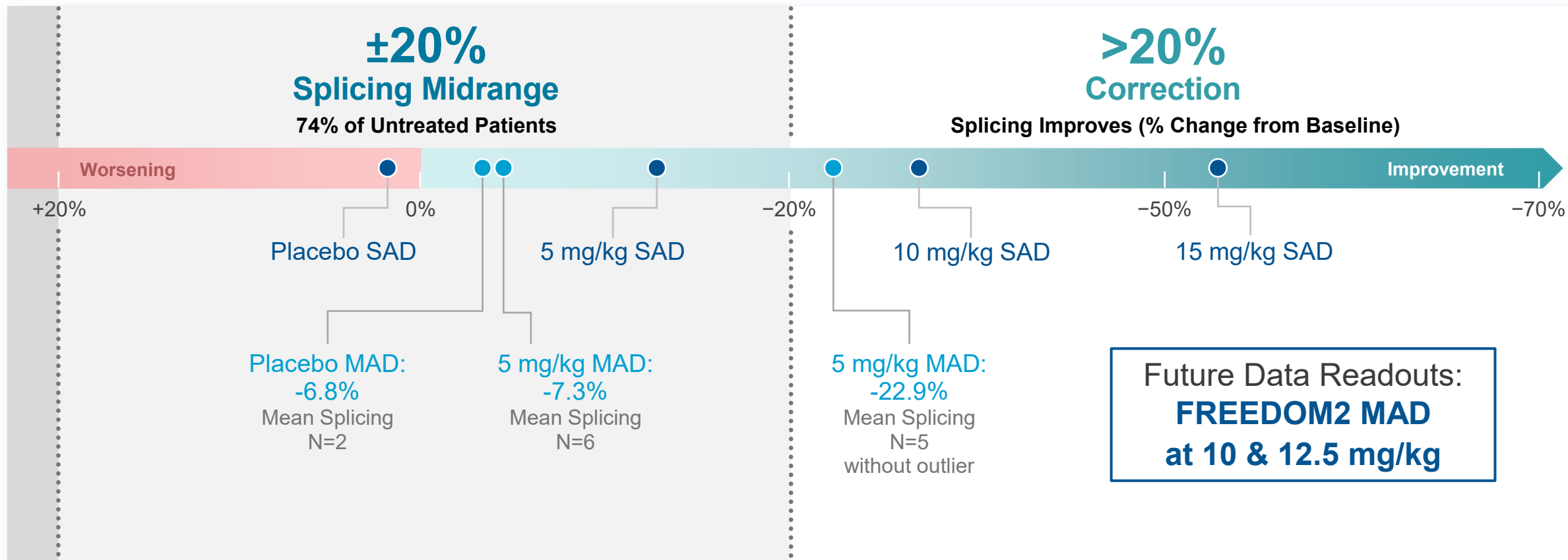
FREEDOM2 5 mg/kg Myotonia (vHOT): PGN-EDODM1 Shows Promising Middle Finger vHOT Trends at Lowest Dose



Excluding notable splicing outlier, the active group did not return to baseline (n=5)

Splicing outlier demonstrated 22 sec difference between nadir and week 16

FREEDOM2 MAD at 10 & 12.5 mg/kg has Potential to Build Upon Robust Single-Dose Splicing Correction



Summary of PGN-EDODM1 and FREEDOM Trials

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 & OLE

Promising Safety, Splicing and vHOT Data in FREEDOM2 Lowest Dose – Supports Ongoing 10 mg/kg MAD Cohort

- Company has **completed enrollment** in the 10 mg/kg MAD cohort of FREEDOM2
- **13 patients** have enrolled in the FREEDOM-OLE at 5 mg/kg, including 6 patients from FREEDOM2

ANTICIPATED READOUTS:

- **2H 2026:** FREEDOM2 10 mg/kg clinical results
- **2027:** FREEDOM2 12.5 mg/kg clinical results

Thank you



**Clinical trial
participants and
their families**



**Clinical site staff
and investigators**



**Community and
clinical advisors**