

The FREEDOM-DM1 clinical trial demonstrated strong splicing correction with single doses of PGN-EDODM1, with an acceptable safety profile



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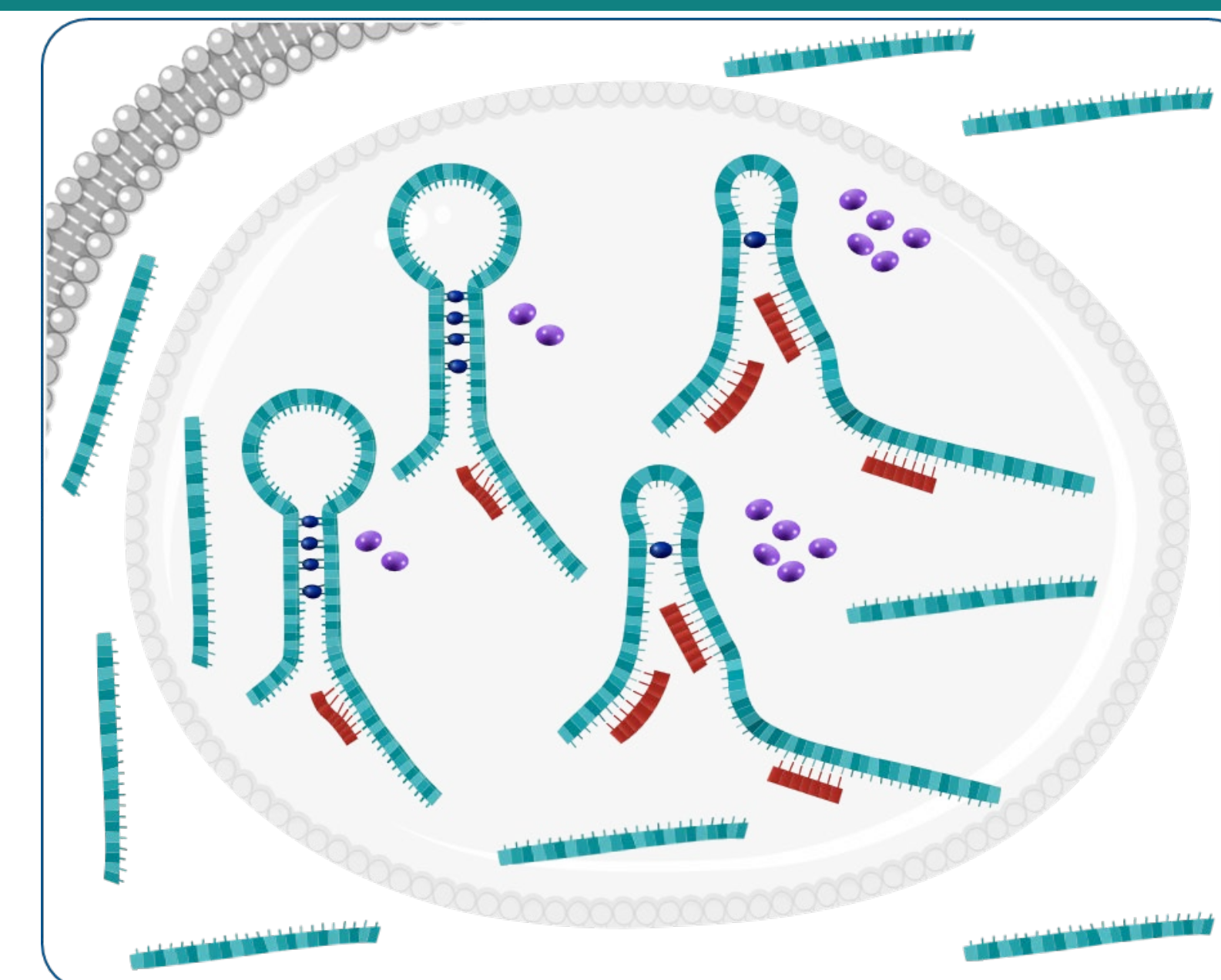
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INTRODUCTION

- PepGen's enhanced delivery oligonucleotide (EDO) cell-penetrating peptide technology is engineered to optimize tissue delivery and nuclear uptake of therapeutic oligonucleotides.
- PGN-EDODM1 is being evaluated for the treatment of myotonic dystrophy type 1 (DM1).
- The PGN-EDODM1 clinical development program includes:
 - FREEDOM-DM1 (NCT06204809), a completed randomized, double-blind placebo-controlled single ascending dose study.
 - FREEDOM2-DM1 (NCT06667453), an ongoing randomized, double-blind placebo-controlled multiple ascending dose study testing 4 monthly doses of PGN-EDODM1.
 - FREEDOM-OLE (NCT07220603), an ongoing open label extension study for participants having completed the FREEDOM-DM1 or FREEDOM2-DM1 trial.

MECHANISM OF PGN-EDODM1

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

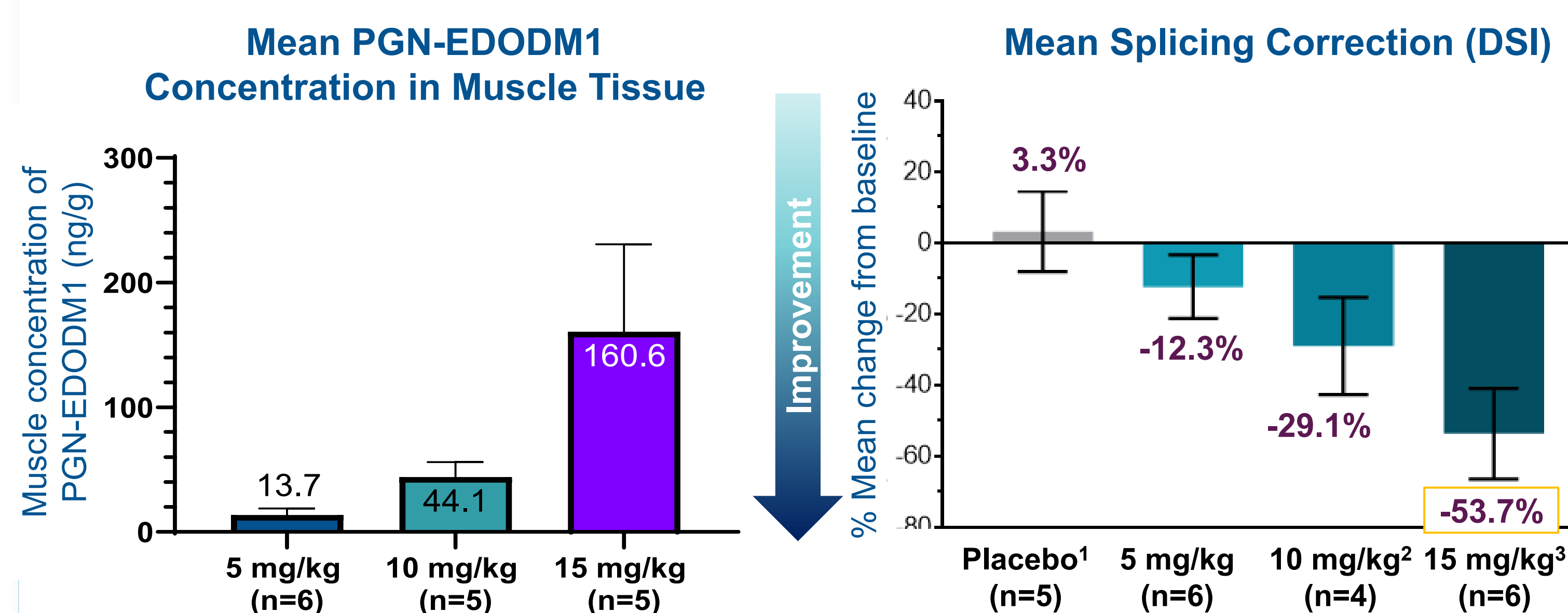


FREEDOM-DM1 BASELINE AND DEMOGRAPHIC CHARACTERISTICS

Mean (SD)	Placebo (N=6)	5mg/kg PGN-EDODM1 (N=6)	10 mg/kg PGN-EDODM1 (N=6)	15 mg/kg PGN-EDODM1 (N=6)
Age (years)	35.5 (10.4)	36.3 (9.0)	34.7 (8.2)	28.5 (9.0)
Sex (female)	5 (83)	3 (50)	3 (50)	2 (33)
Weight (kg)	59.2 (12.2)	67.3 (19.7)	65.8 (16.6)	71.5 (14.1)
BMI (kg/m ²)	21.0 (3.4)	22.8 (5.0)	22.8 (5.7)	23.6 (5.5)
vHOT (s) (mean, middle finger)	12.6 (5.9)	12.6 (7.3)	9.3 (2.8)	9.5 (5.8)
Grip strength max PPN (R)	43.49 (19.14)	36.97 (15.03)	28.71 (15.19)	47.24 (13.04)
Grip strength max PPN (L)	43.28 (20.25)	44.92 (18.12)	32.27 (14.29)	54.44 (16.23)
Splicing Index	69.6 (15.3)*	73.7 (15.2)	62.4 (19.6)*	51.6 (24.0)
DM1-ACTIVc	42.8 (8.6)	40.7 (6.7)	47.3 (3.7)	45.0 (5.1)
10MWRT (s)	4.0 (1.3)	3.9 (1.5)	4.4 (1.5)	3.8 (1.2)

*n=5 for placebo and n=4 for 10 mg/kg at baseline. SD: standard deviation; BMI: body mass index; PBO: placebo; vHOT: video hand opening time; sec: second; 10MWRT: 10-meter walk run test

DOSE-DEPENDENT INCREASES IN DRUG CONCENTRATION AND SPLICING CORRECTION 28 DAYS POST- SINGLE DOSE



1. Placebo n=5 as biopsies were not obtained from one of the placebo patients due to biopsy associated complications on day 0.
 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. Error bars are standard error of the mean; DSI: Myotonic dystrophy splicing index.

SINGLE DOSES OF PGN-EDODM1 WERE GENERALLY WELL TOLERATED¹

	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	2	1	2	3	8
Moderate	3	1	0	2	6
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 AESI	0	0	1(1)	2 (2)	3
Any DLT	0	0	0	1	1
Any TEAE leading to study withdrawal	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0

Overall

- 22 TEAEs considered related to PGN-EDODM1 or placebo in 8 participants
- TEAEs: mainly mild to moderate, 3 severe (abdominal pain, complicated appendicitis, pseudoaneurysm)
- Most frequent AEs overall: nausea, nasopharyngitis and headache
- One hypersensitivity reaction (rash) during infusion of one person with 15 mg/kg; resolved in less than 2 hours after oral antihistamines
- Transient moderate albuminuria observed at 15 mg/kg and mild albuminuria at 10 mg/kg; Normalized within 2-7 days without intervention

Serious adverse events related to PGN-EDODM1

- One SAE at 10 mg/kg: severe abdominal pain (confounded by use of an off-label medication on the morning of dosing)

Serious adverse events not related to PGN-EDODM1

- 2 SAEs of pseudoaneurysm and AV fistula in one person who received placebo, related to muscle biopsy procedure
- SAE of complicated appendicitis in one person at 5 mg/kg
- SAE of pseudoaneurysm in one person at 10 mg/kg

Dose limiting toxicity

- One person at 15 mg/kg had a DLT related to a transient decrease in eGFR(cys) that resolved without intervention by 48 hours post-dose

1. As of database lock on December 23, 2025. TEAE: treatment related adverse event, SAE: serious adverse event, AESI: adverse event of special interest, DLT: dose limiting toxicity, eGFR(cys): estimated glomerular filtration rate (cystatin equation)

FREEDOM2-DM1: 4 MONTHLY DOSES OF PGN-EDODM1 AT 5 MG/KG OR PLACEBO SHOW NO CHANGE IN SAFETY PROFILE; TRENDS TOWARDS IMPROVEMENT IN SPLICING AND MYOTONIA OBSERVED

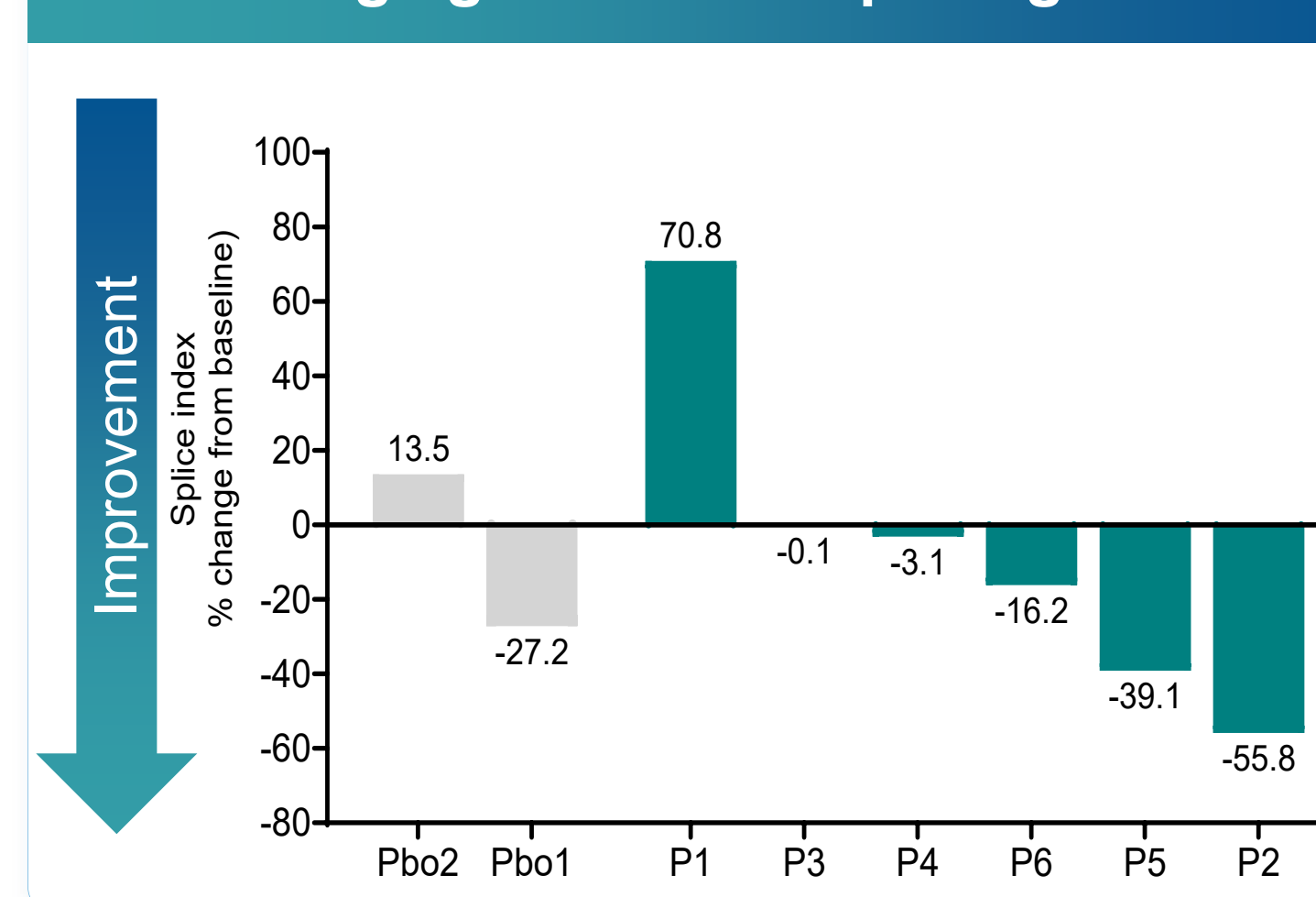
Summary of Treatment Emergent Adverse Events (TEAEs) ¹	5 mg/kg or PBO (n=8) n(%)
Any TEAE	7 (87.5)
Mild	4 (50.0)
Moderate	3 (37.5)
Severe	0 (0.0)
Any SAE	0
Any related SAE	0
Any AESI or dose-limiting toxicities	0
Any TEAE leading to study withdrawal	0
Any TEAE leading to death	0

PGN-EDODM1 was Generally Well-Tolerated, with All AEs Mild or Moderate in Severity in the 5 mg/kg cohort¹

- All participants completed all 4 doses, with no evidence of cumulative toxicity
- The overall AE profile of MAD 5 mg/kg is consistent with that observed in SAD 5 mg/kg
- Nausea was the most common treatment-related AE
- No SAEs, AESIs, or DLTs and no signs of hypersensitivity
- No kidney-related TEAEs
- No notable changes in eGFR/creatinine/BUN
 - Transient albuminuria observed – did not increase with repeat dosing

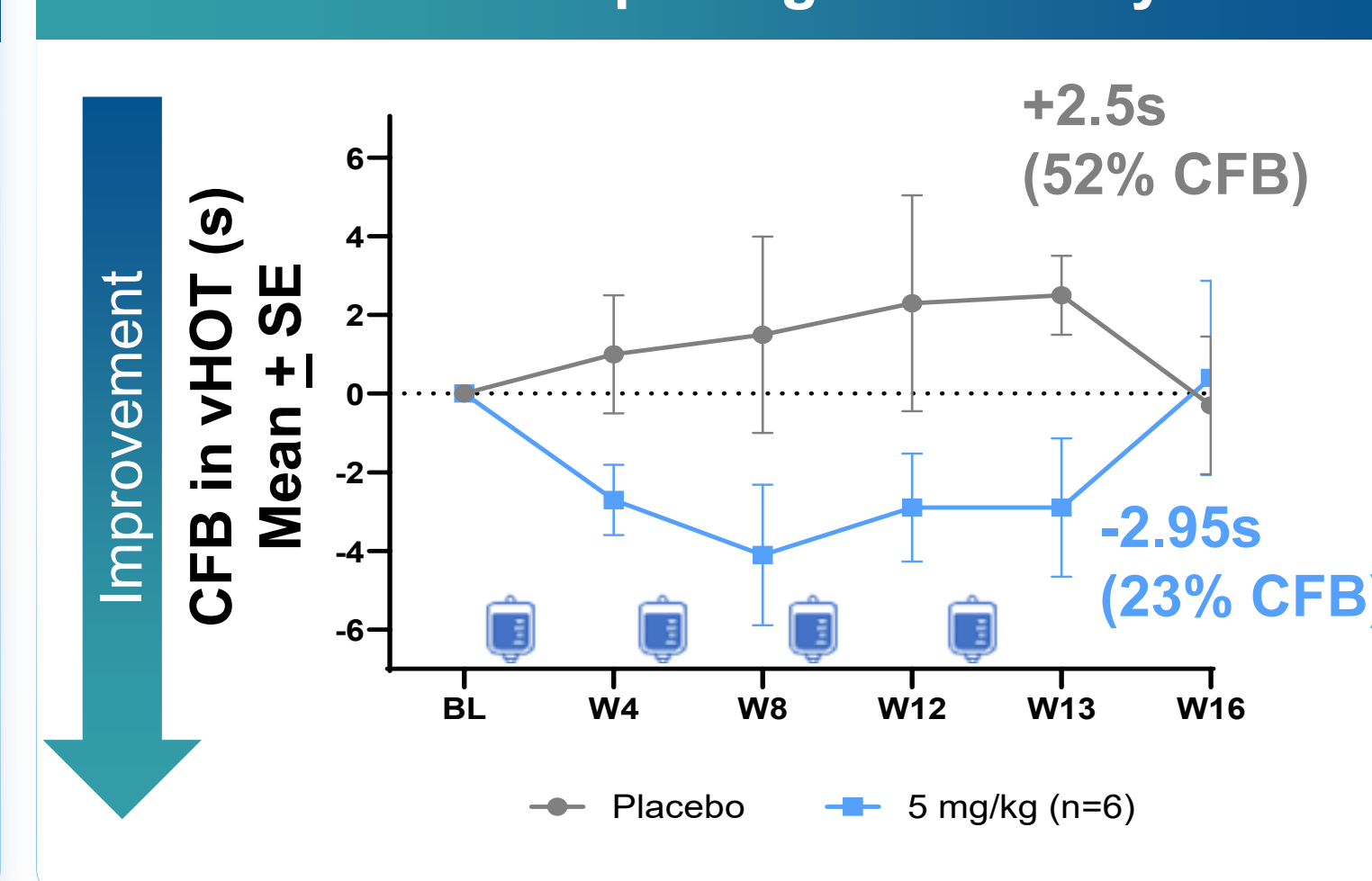
1. Data cutoff date: 04 March 2026

5 mg/kg Individual Splicing Data



Mean splicing correction of 7.3% with PGN-EDODM1 (n=6)

Video Hand Opening Time Analysis



Positive trends in vHOT observed, returned to baseline at week 16

CONCLUSIONS

- PGN-EDODM1 was generally well-tolerated in people with DM1 at doses showing pharmacodynamic activity; no changes in safety profile on repeat dosing.
 - Dose dependent increases in mean splicing correction following single doses of PGN-EDODM1; 5 mg/kg MAD data confirms 5mg/kg SAD results.
 - Study results support the continued development of PGN-EDODM1 at higher doses in the repeat dose study, FREEDOM2-DM1, which is ongoing.