



FREEDOM-DM1: Final results from a Phase 1, placebo-controlled SAD study to evaluate PGN-EDODM1 in people with myotonic dystrophy type 1 (DM1)

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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 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 for PGN-EDODM1; 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 FREEDOM and FREEDOM2 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 filings with the SEC. PepGen explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

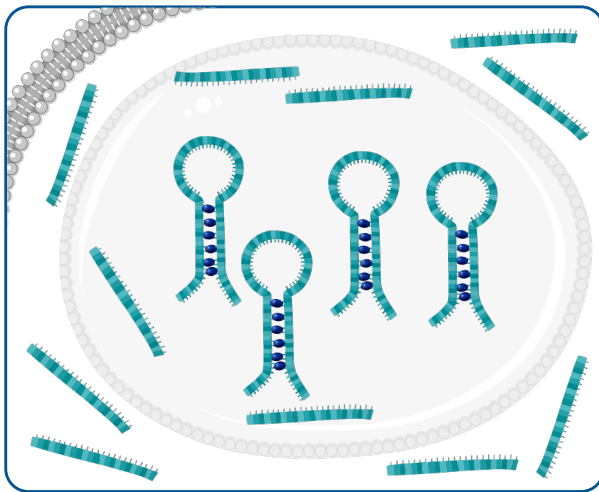
This presentation discusses PGN-EDODM1, an investigational therapy, that has not been approved for use in any country and is not intended to convey conclusions about their efficacy or safety. There is no guarantee that PGN-EDODM1 or any other investigational therapy will successfully complete clinical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

Disclosures

- Dr. Hamel is a principal investigator for the FREEDOM-DM1 clinical trial
- Dr. Hamel is a consultant to Design Therapeutics

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

DM1 is caused by pathogenic *DMPK* transcripts

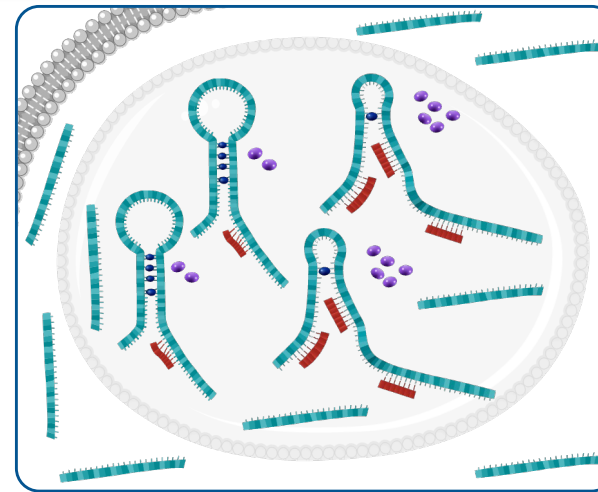


Trapped MBNL1 is inactive and results in mis-splicing



- 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

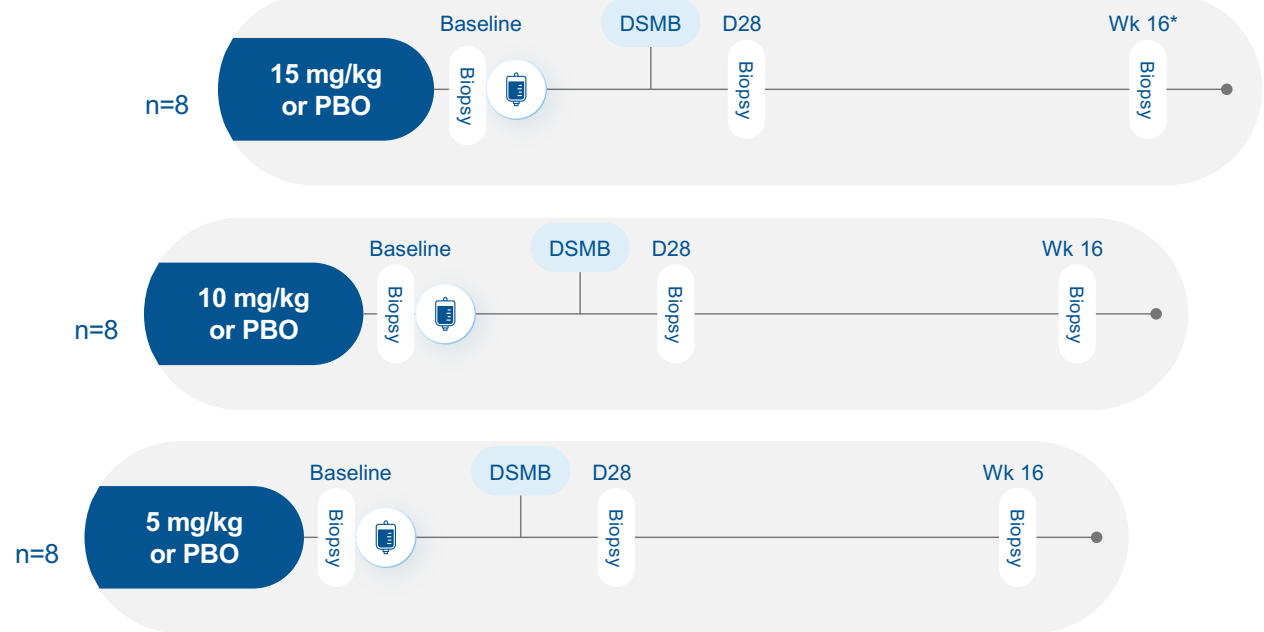
Single IV administration of PGN-EDODM1

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)



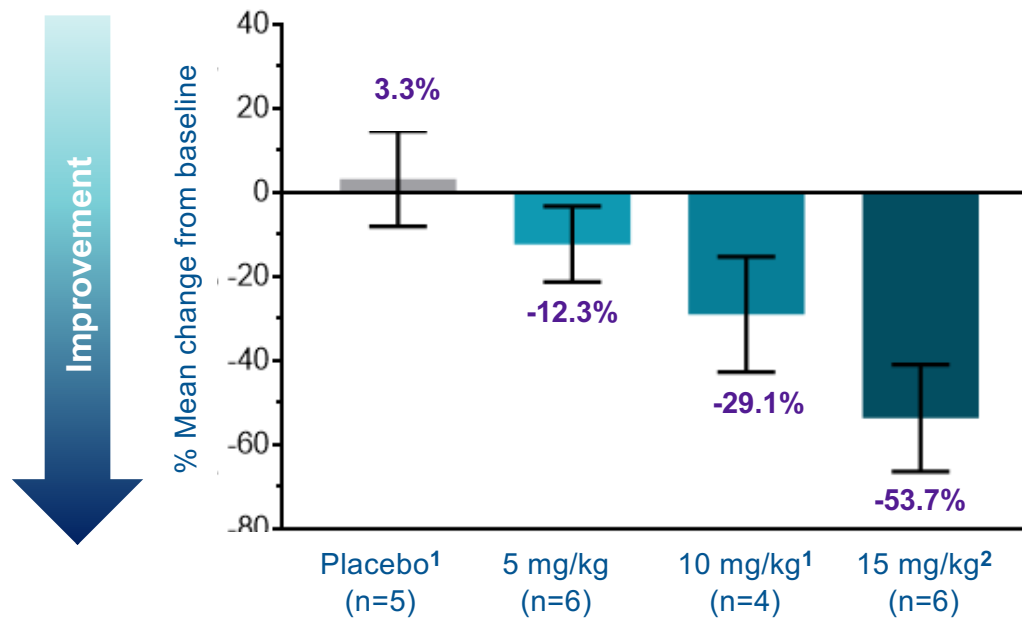
DSMB: data safety monitoring board; IV: intravenous; PBO: placebo; SAD: single-ascending dose; PK: pharmacokinetics



PGN-EDODM1 dose

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

Splicing Index Changes: 22-Gene Panel* at D28



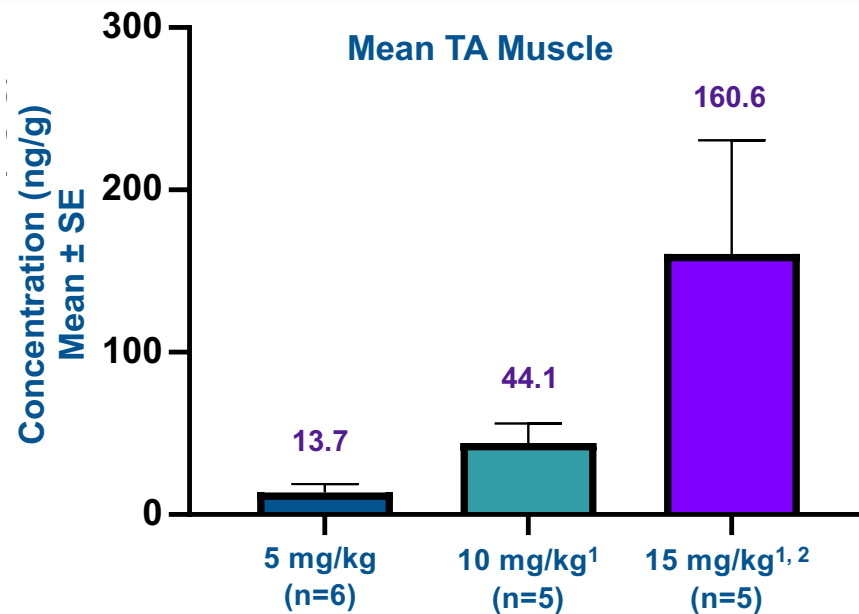
1. Missing samples due to unavailability of biopsy tissue or sample outside of assay window.

2. 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



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

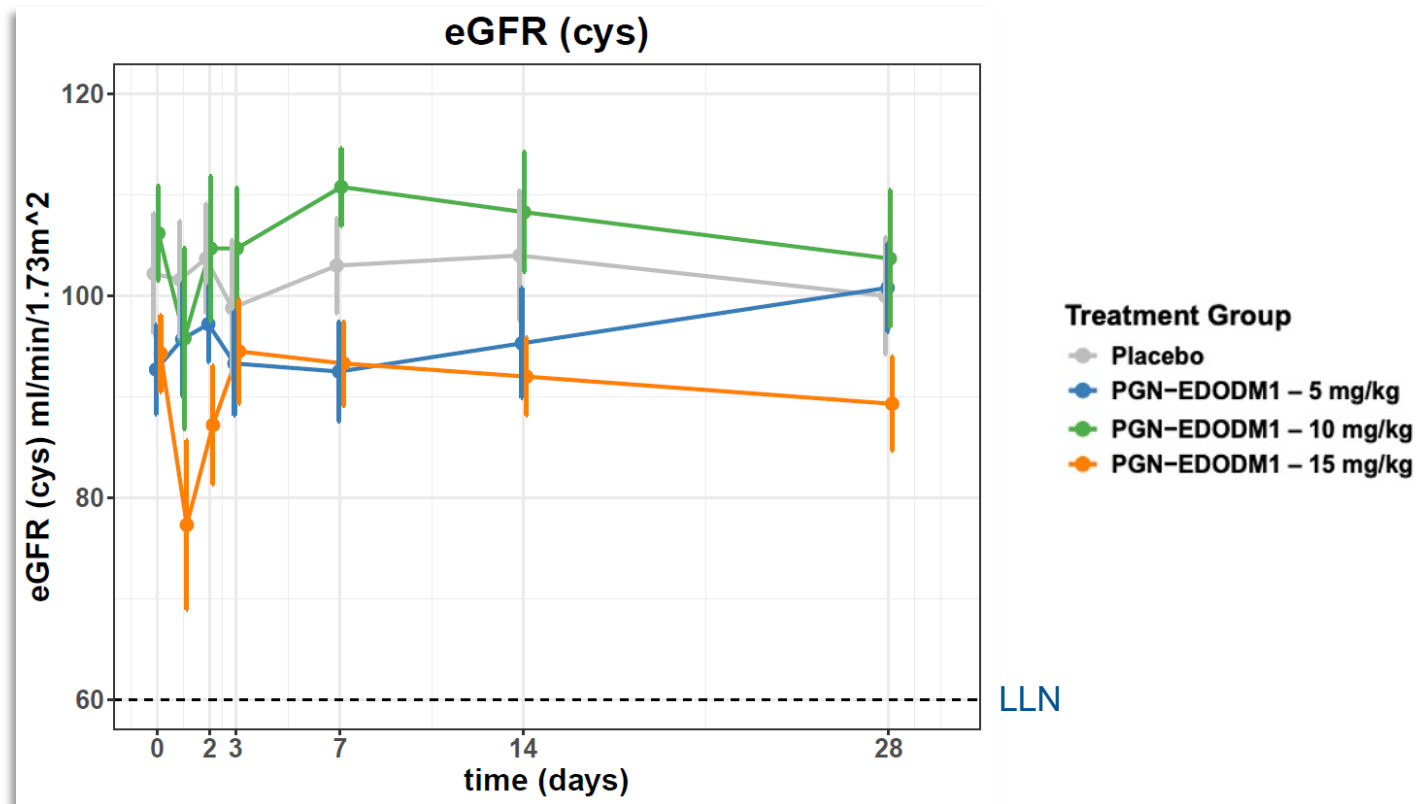
- Most frequent TEAEs: nausea, nasopharyngitis, and headache
- No electrolyte-related TEAEs or hypomagnesemia observed across dose cohorts
- No renal-related TEAEs observed at 5 and 10 mg/kg; DLT at 15 mg/kg involving a transient decrease in eGFR(cys), resolving without intervention
- One drug-related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



*As of database lock on December 23, 2025.

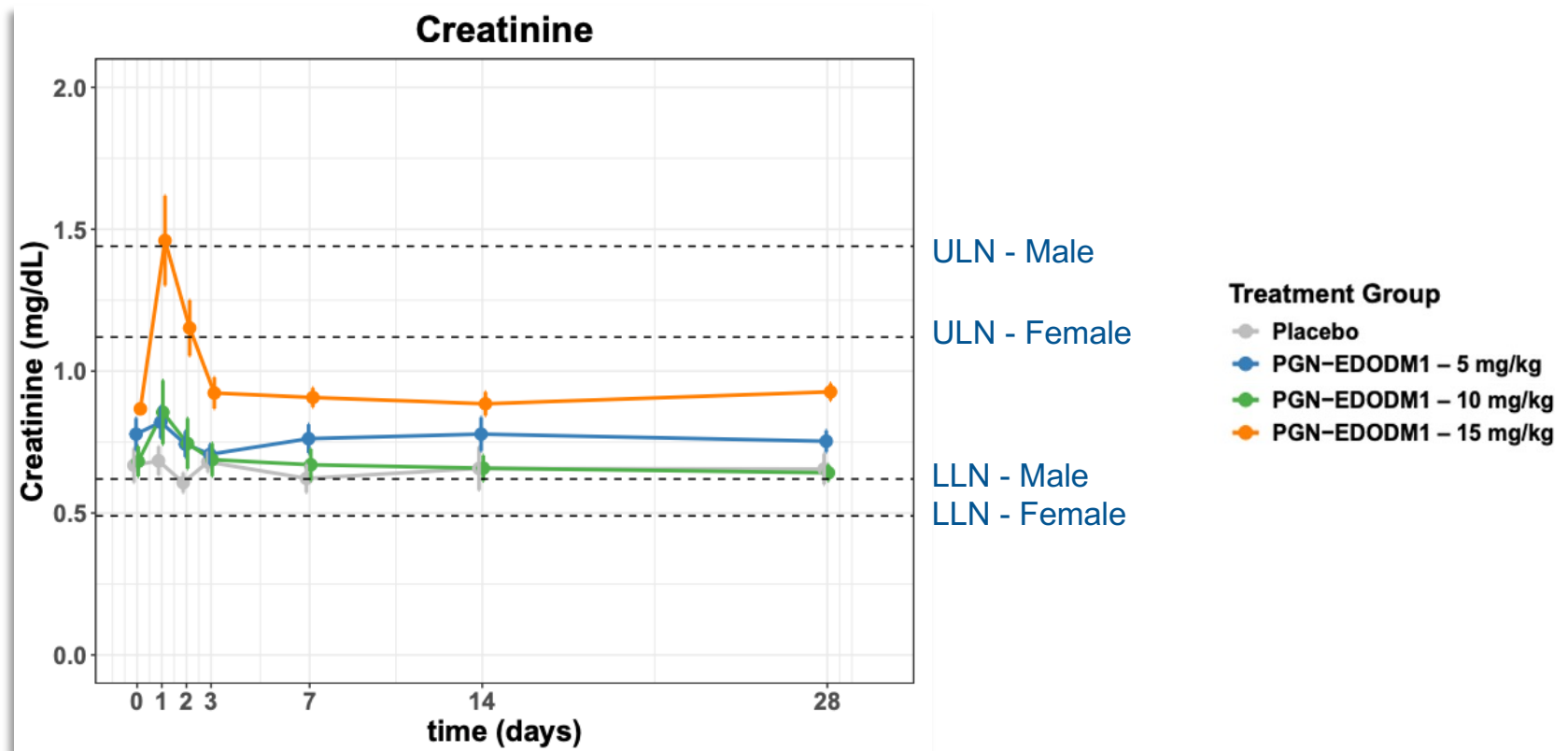
TEAE: treatment-emergent adverse event, SAE: serious adverse event, DLT: Dose limiting toxicity, eGFR(cys): estimated glomerular filtration rate (cystatin equation)

eGFR Remained Within Normal Range Across All Cohorts; Transient Decrease at 15 mg/kg Resolved Without Intervention



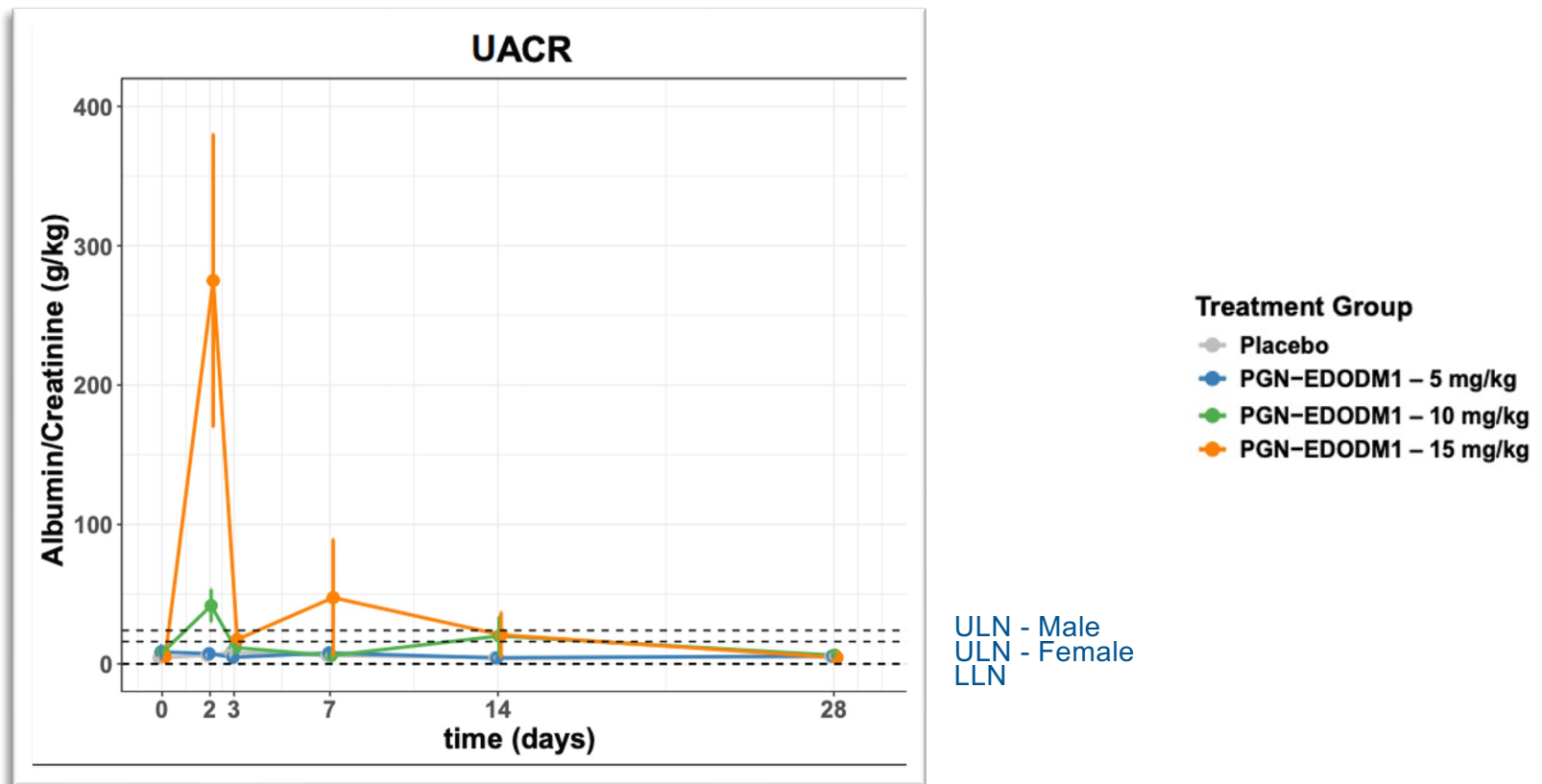
Note : Week 16 data excluded for reasons of clarity; error bars shown here are SE
LLN: lower limit of normal, eGFR: estimated glomerular filtration rate

Minimal Creatinine Movement at 5 and 10 mg/kg; Transient Elevation at 15 mg/kg Resolved Within 48 Hours Without Intervention



Note : Week 16 data excluded for reasons of clarity; error bars shown here are SE
ULN: upper limit of normal, LLN: lower limit of normal

Transient Moderate Albuminuria Observed at 15 mg/kg Dose; Normalized Within 2 to 7 Days Without Intervention



ULN - Male
ULN - Female
LLN



Note : Week 16 data excluded for reasons of clarity; error bars shown here are SE
ULN: upper limit of normal, LLN: lower limit of normal, UACR: Urine Albumin-Creatinine Ratio

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 correction 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

FREEDOM2 Phase 2 MAD Study Underway



FREEDOM2 Study Overview

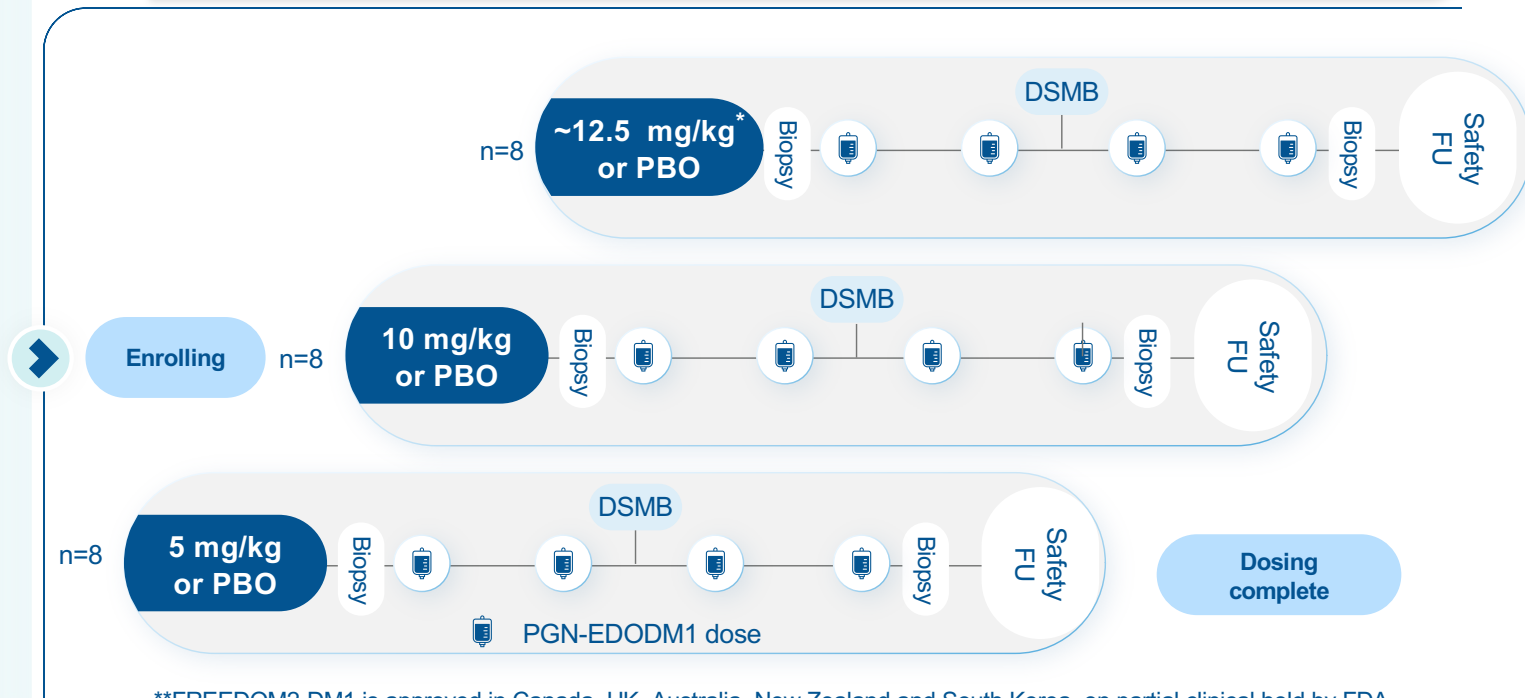
Multinational, randomized, double-blind, placebo-controlled, MAD study open in Canada, UK, NZ, Australia and South Korea

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

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



**FREEDOM2-DM1 is approved in Canada, UK, Australia, New Zealand and South Korea, on partial clinical hold by FDA



DSMB: data safety monitoring board; FU: follow-up; IV: intravenous; MAD: multiple-ascending dose; PBO: placebo; PK: pharmacokinetics; vHOT: video hand opening time; OLE: open label extension
 * Dose dependent on recommendations of DSMB.



Thank you
