

FREEDOM-DM1: Phase 1 Study Design to Assess Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of PGN-EDODM1 for Myotonic Dystrophy Type 1



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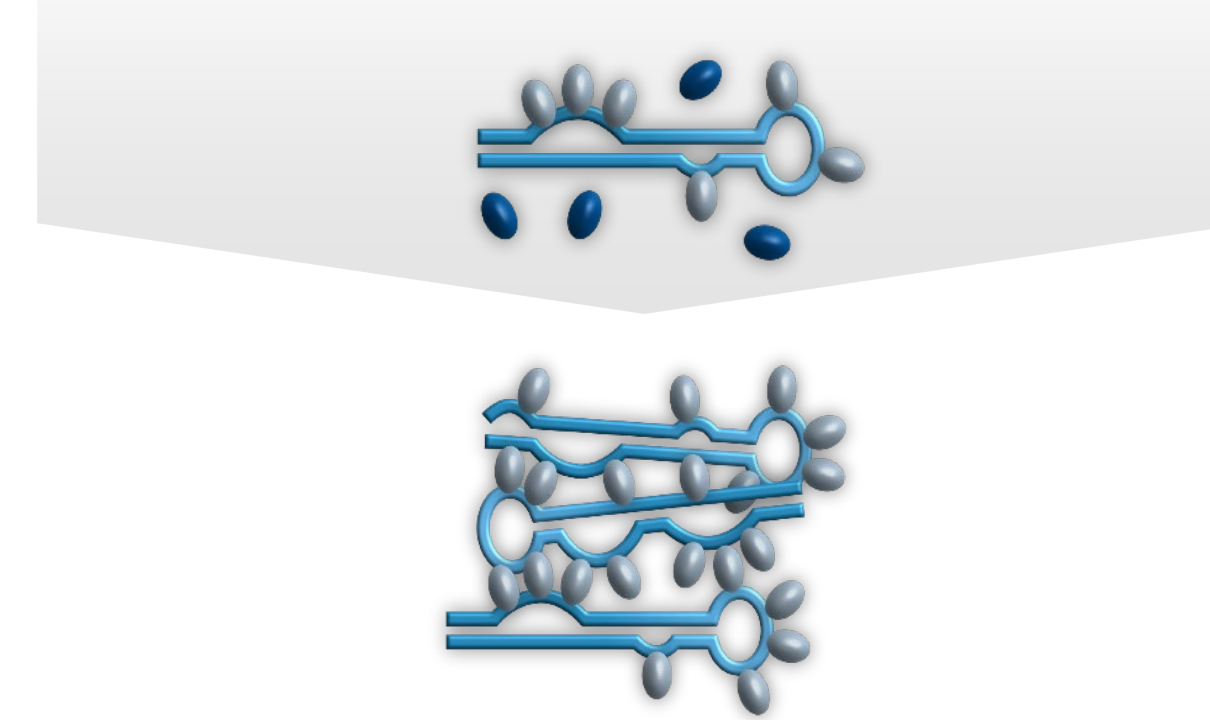


INTRODUCTION

PEPGEN'S NOVEL APPROACH TO DM1

DM1 PATHOLOGY

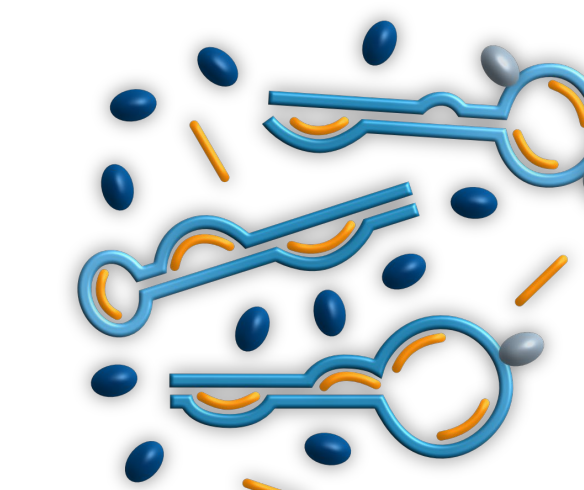
DMPK transcript CUG repeat hairpin loops bind MBNL1 and form foci



Expanding foci trap more MBNL1

MBNL1 COMPETITION

PGN-EDODM1 binds to the CUG repeats in the DMPK transcript, reducing toxic foci



- Binding of PGN-EDODM1 liberates MBNL1, restoring physiological splicing
- DMPK transcript retained; role in cellular processes uninterrupted

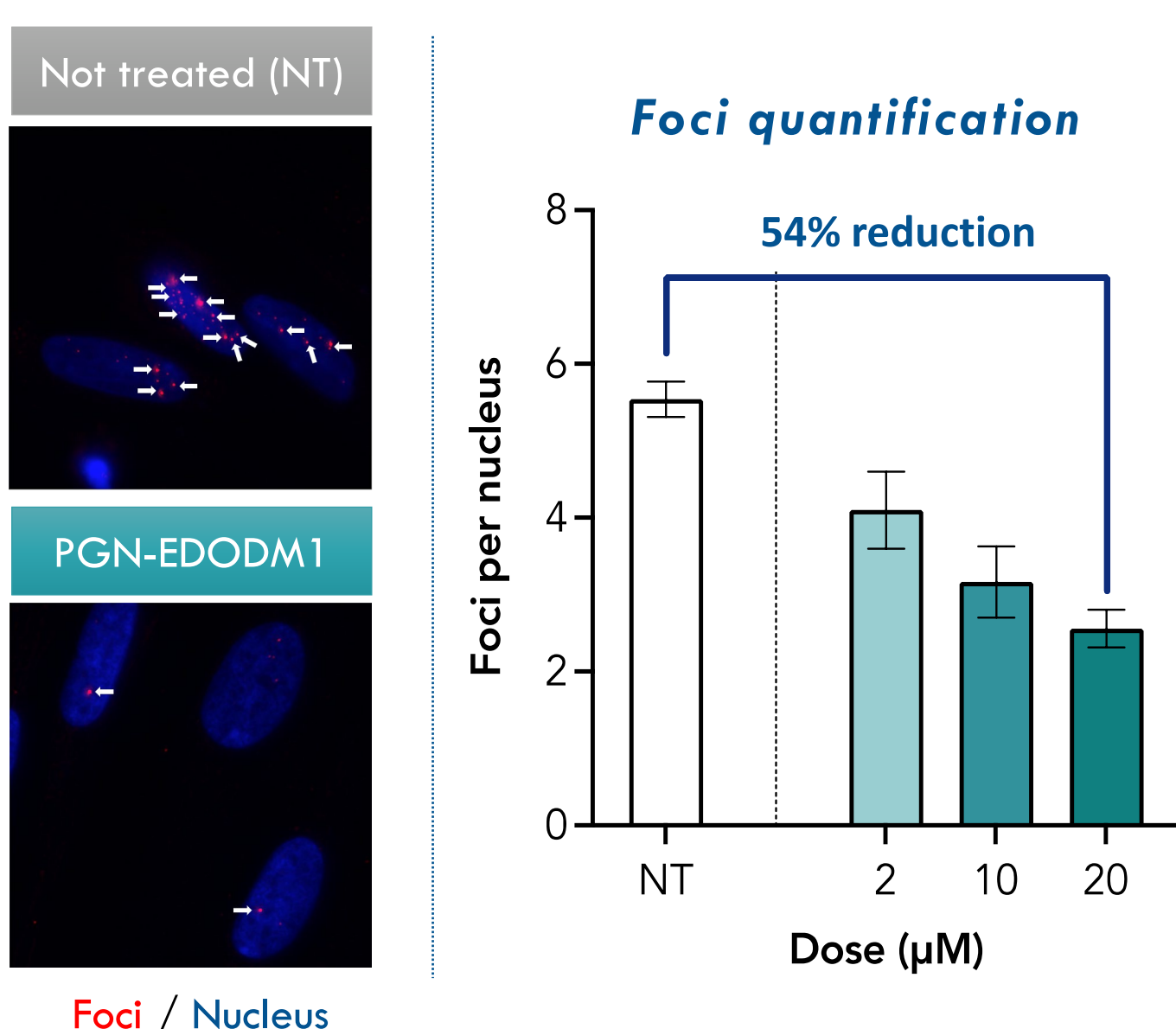
● denotes free (active) MBNL1 ○ denotes bound (inactive) MBNL1 ▲ denotes PGN-EDODM1

ROBUST PRECLINICAL EVALUATION OF PGN-EDODM1

PGN-EDODM1 REDUCED TOXIC FOCI, LIBERATED MBNL1 AND CORRECTED MIS-SPLICING IN DM1 CELLS

PGN-EDODM1 DM1 cells (2,600 CTG repeats) Hour: 0 24 PGN-EDODM1 dose Analysis

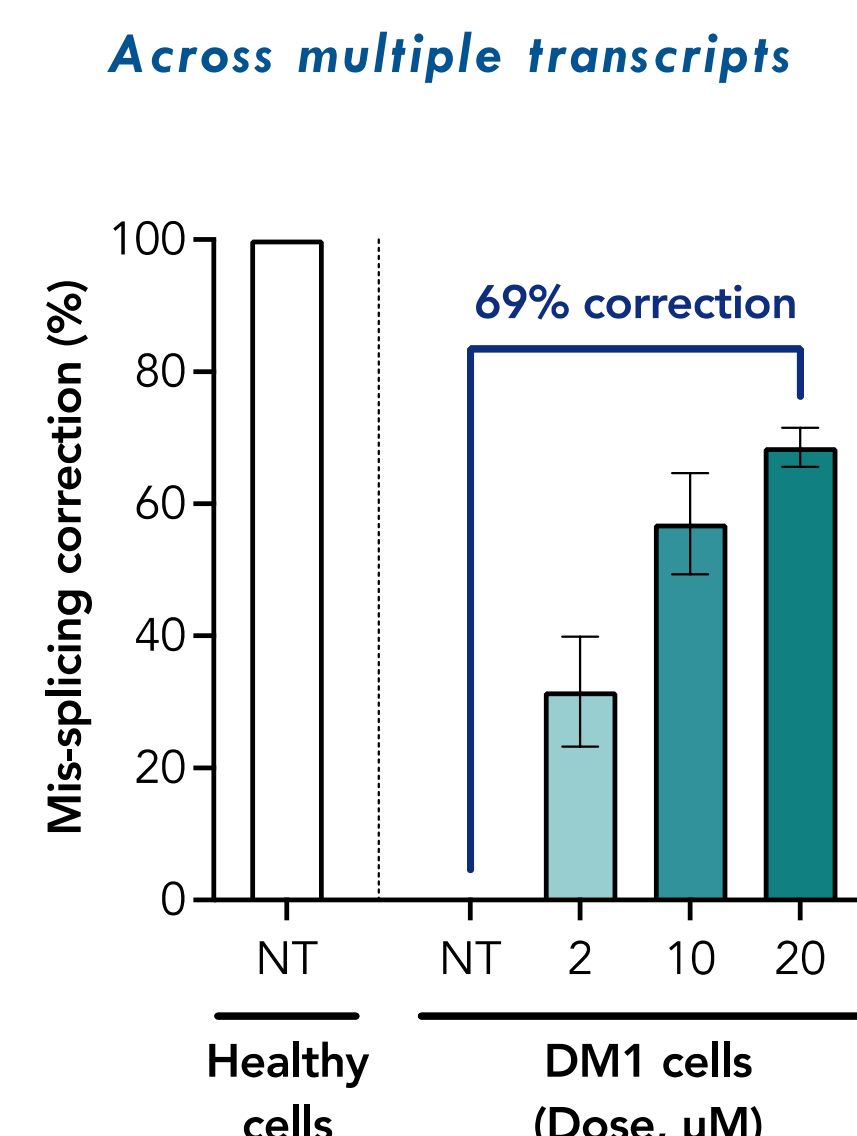
TOXIC FOCI REDUCTION



MBNL1 LIBERATION



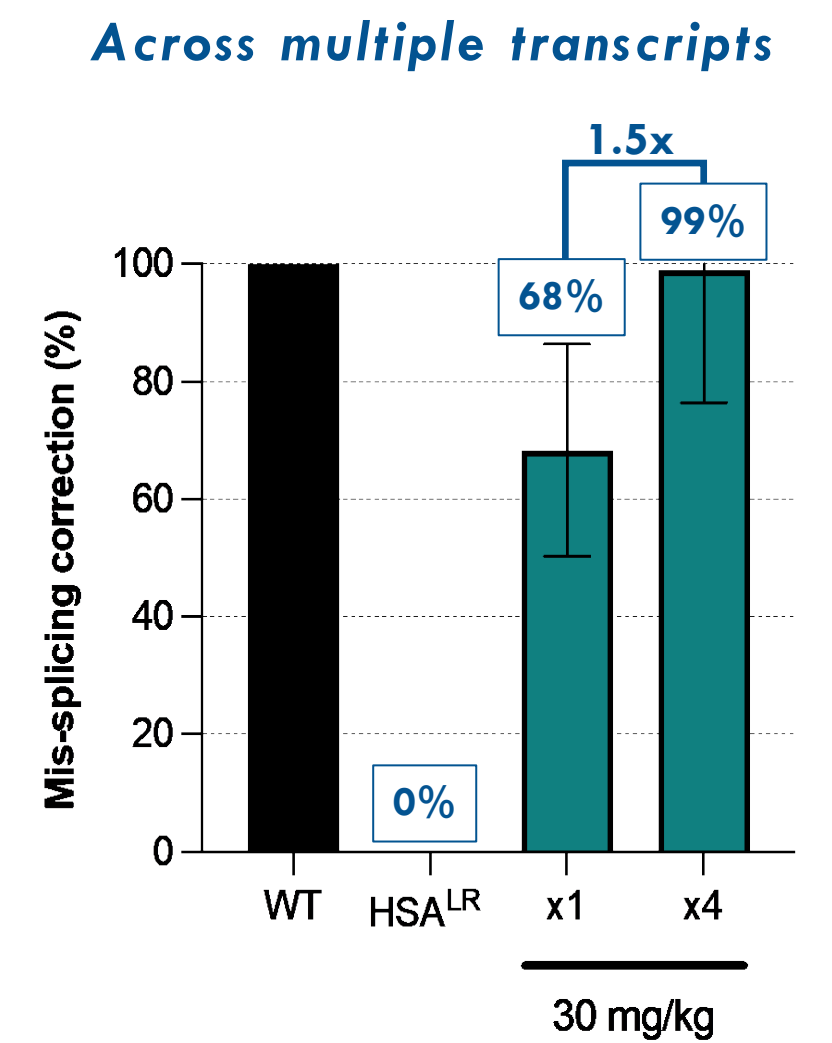
MIS-SPLICING CORRECTION



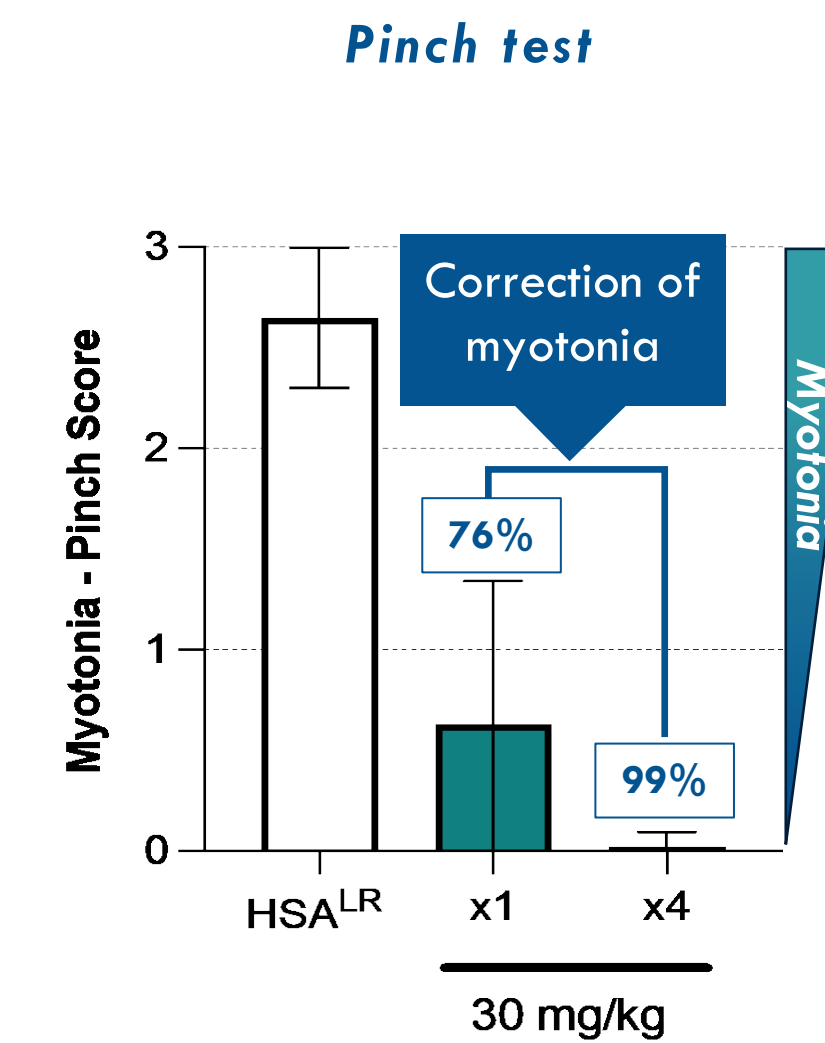
REPEAT DOSING OF PGN-EDODM1 IN HSA^{LR} MICE ENHANCED CORRECTION OF MIS-SPLICING, REVERSED MYOTONIA AND INCREASED MUSCLE DELIVERY

PGN-EDODM1 HSA^{LR} Week: 0 4 8 12 16 PGN-EDODM1 dose Tissue/myotonia analysis

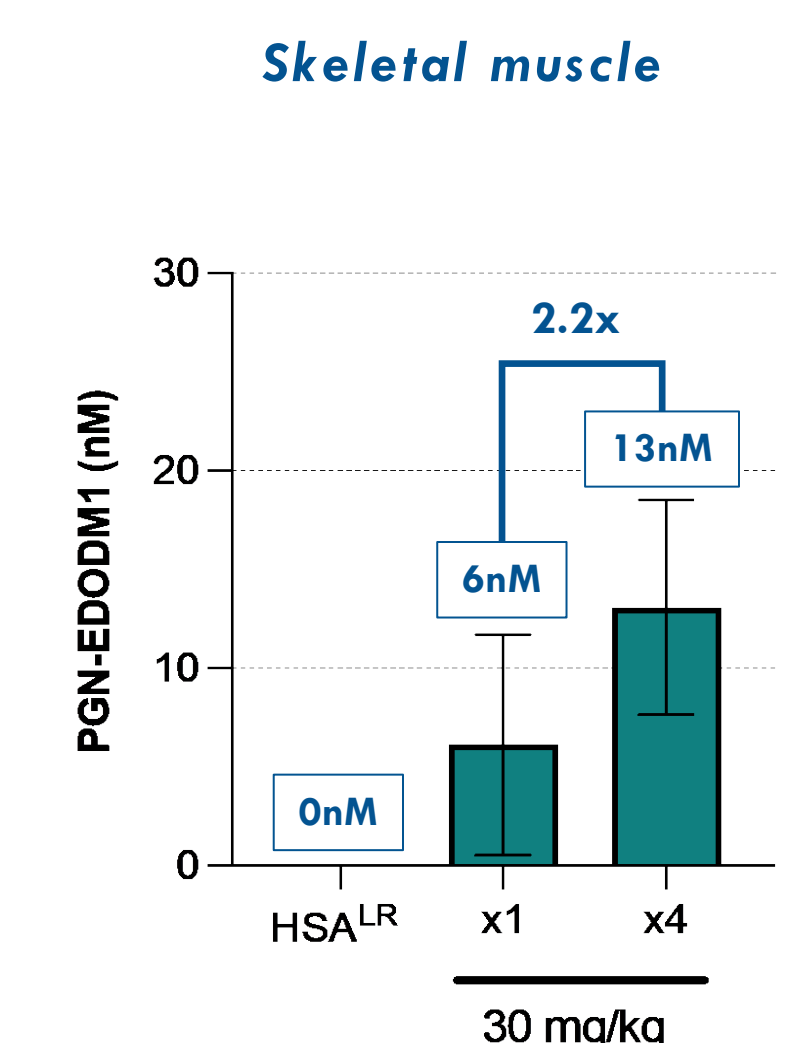
MIS-SPLICING CORRECTION



REVERSAL OF MYOTONIA



TISSUE CONCENTRATION



99% correction across multiple transcripts | Correction of myotonia observed after repeat dose | Increased levels of PGN-EDODM1 in tissue with repeat dose

PHASE 1 STUDY (FREEDOM-DM1) CLINICAL DESIGN

OPEN in USA, CANADA & UK

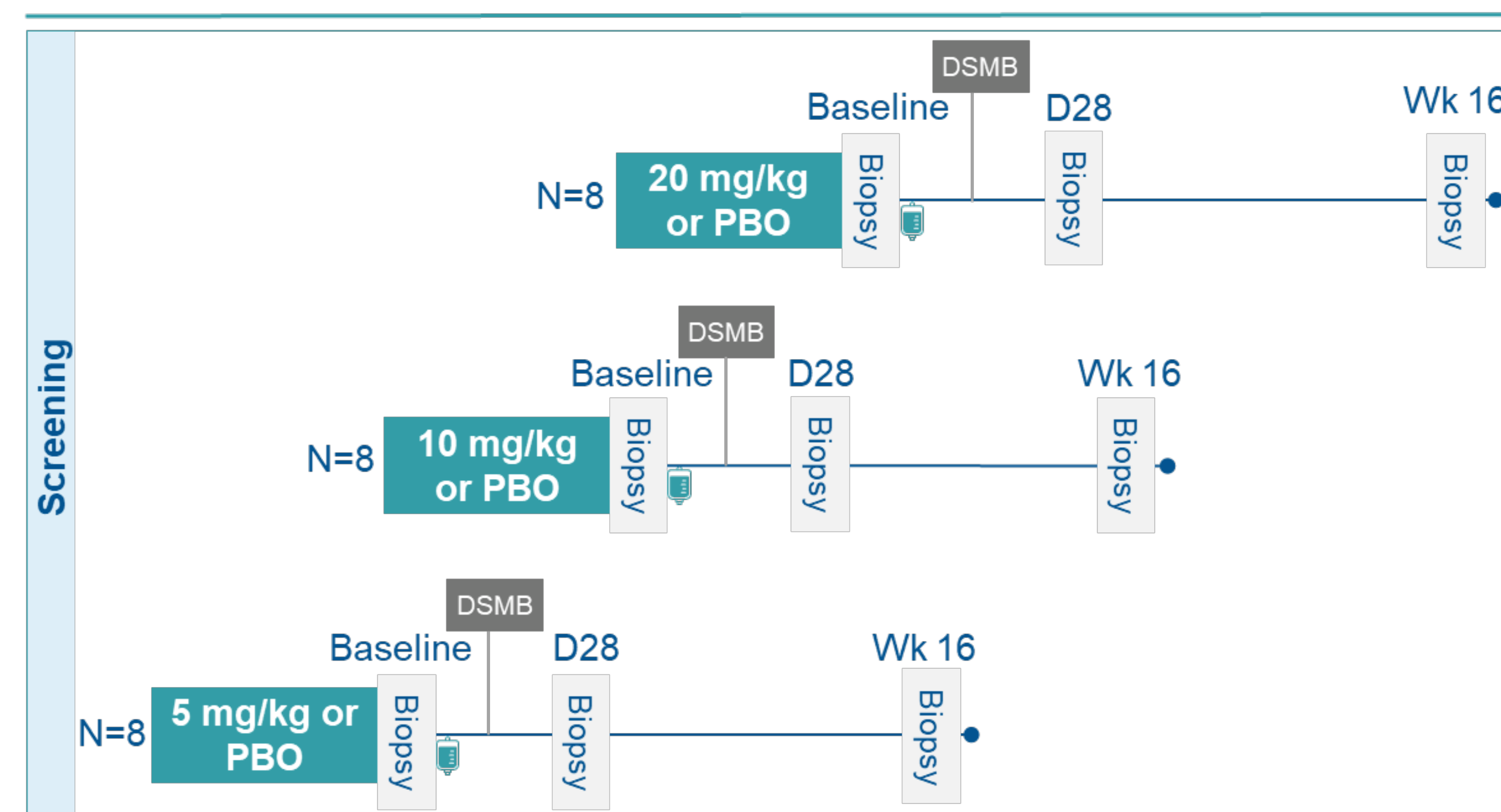
FREEDOM-DM1: PHASE 1 Single ascending dose (SAD)

Preliminary data expected in second half of 2024

- Being conducted in people with DM1
- Randomized, double-blind, placebo-controlled trial
- Key anticipated readouts: **Functional assessments, correction of mis-splicing, safety data**



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



STUDY OBJECTIVES

- **PRIMARY:** To evaluate the safety and tolerability of PGN-EDODM1 after a single dose
- **SECONDARY:** To evaluate the pharmacokinetics (PK) of PGN-EDODM1 after a single dose
- **SELECT KEY EXPLORATORY:**
 - Correction of mis-splicing
 - Functional assessments

KEY INCLUSION

- Male or female between the ages of 18 and 50 years, inclusive
- Confirmed diagnosis of DM1, defined as having a repeat sequence in the DMPK gene with at least 100 CTG repeats
- Medical Research Council (MRC) score of ≥Grade 4 in bilateral tibialis anterior (TA) muscles at Screening

KEY EXCLUSION

- Congenital DM1
- Known history or presence of any clinically significant conditions that may interfere with study safety assessments

CONCLUSION

- Robust nonclinical data in DM1 cells, HSA^{LR} mice and NHP support further development of PGN-EDODM1 in clinical studies
- The Phase 1 FREEDOM-DM1 study is designed to assess the safety and tolerability of PGN-EDODM1 and provide an initial assessment of the effect of PGN-EDODM1 on functional assessments and mis-splicing