T206

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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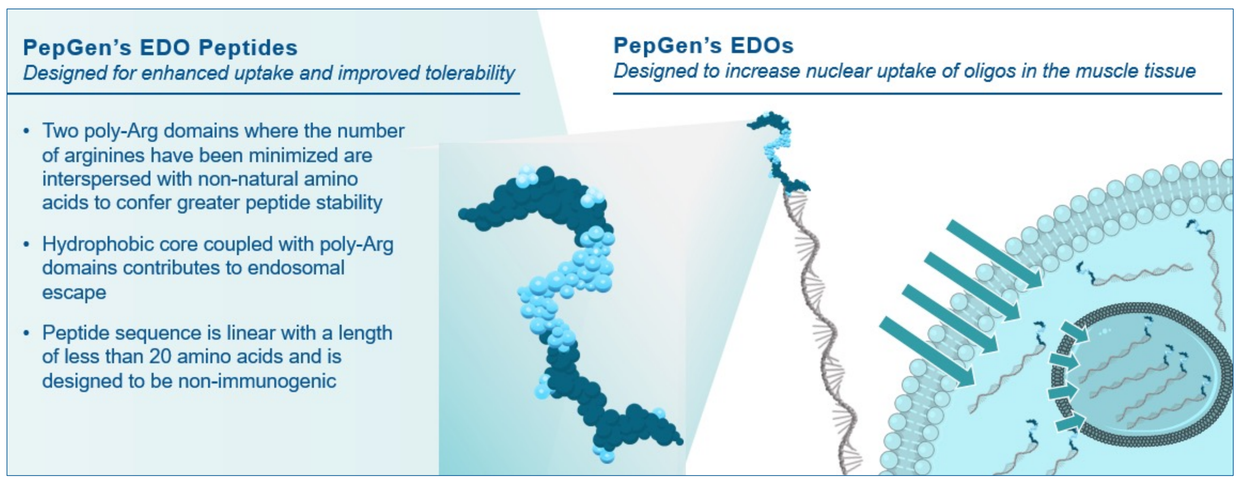
PepGen

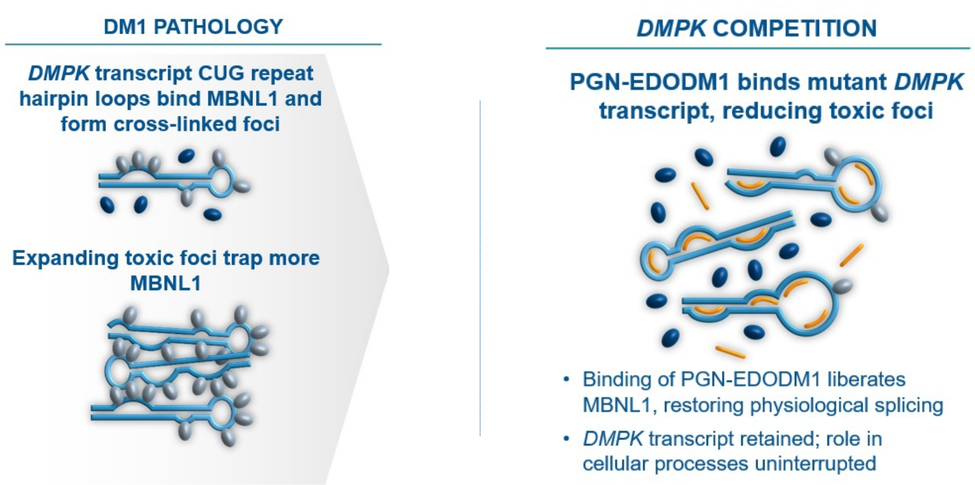
INTRODUCTION

- The **Enhanced Delivery Oligonucleotide (EDO)** platform is **engineered to optimize the tissue penetration, cellular uptake and nuclear delivery** of oligonucleotide therapeutic candidates.
  - Limited delivery and distribution of unconjugated oligonucleotides to affected tissues limits their activity in DM1.
- **PGN-EDODM1** is an EDO under investigation for the **treatment of people with Myotonic Dystrophy Type 1 (DM1)**.
- DM1 is a multi-systemic disease that has a **significant impact on physical function and quality of life.**
- PGN-EDODM1 was evaluated in multiple nonclinical models including DM1 human derived muscle cells, the HSA^{LR} mouse model of DM1 and in wild-type (WT) mice and non-human primates (NHPs)



PGN-EDODM1

PEPGEN'S NOVEL APPROACH TO DM1



DMPK: Myotonic Dystrophy Protein Kinase Gene; MBNL1: Muscleblind Like Splicing Regulator Protein 1

SUMMARY OF NONCLINICAL DATA

- PGN-EDODM1 resulted in reduction of toxic foci and liberation of MBNL1 in DM1 human muscle cells
- In the HSA^{LR} DM1 mouse model, robust mis-splicing correction and reversal of myotonia was observed with a single dose; durable mis-splicing corrections observed through 24 weeks
- Enhanced mis-splicing correction, reversal of myotonia and increased levels of tissue delivery observed with repeat dosing in DM1 mouse
- PGN-EDODM1 is not designed to degrade *DMPK*, the transcript where the pathogenic CUG expansion is located
- Observed to be well-tolerated through 90 mg/kg in single dose NHP GLP toxicology studies
- **See poster T309: "PGN-EDODM1 Single- and Repeat-Dose Nonclinical Data Indicated Mechanistic and Meaningful Activity for Potential Treatment of Myotonic Dystrophy Type 1"**

PHASE 1 STUDY (FREEDOM-DM1) CLINICAL DESIGN

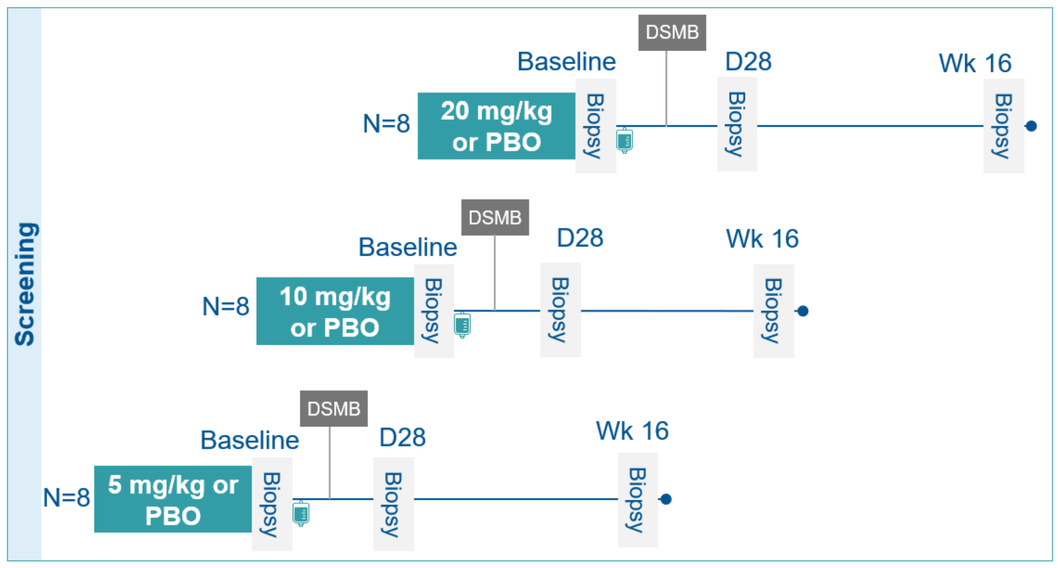
Freedom
DM1

OPEN in USA, CANADA & UK

FREEDOM-DM1: PHASE 1
Single ascending dose (SAD): Interim data readout expected in 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)



PBO: Placebo; Study drug dose

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 ELIGIBILITY CRITERIA

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

- 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