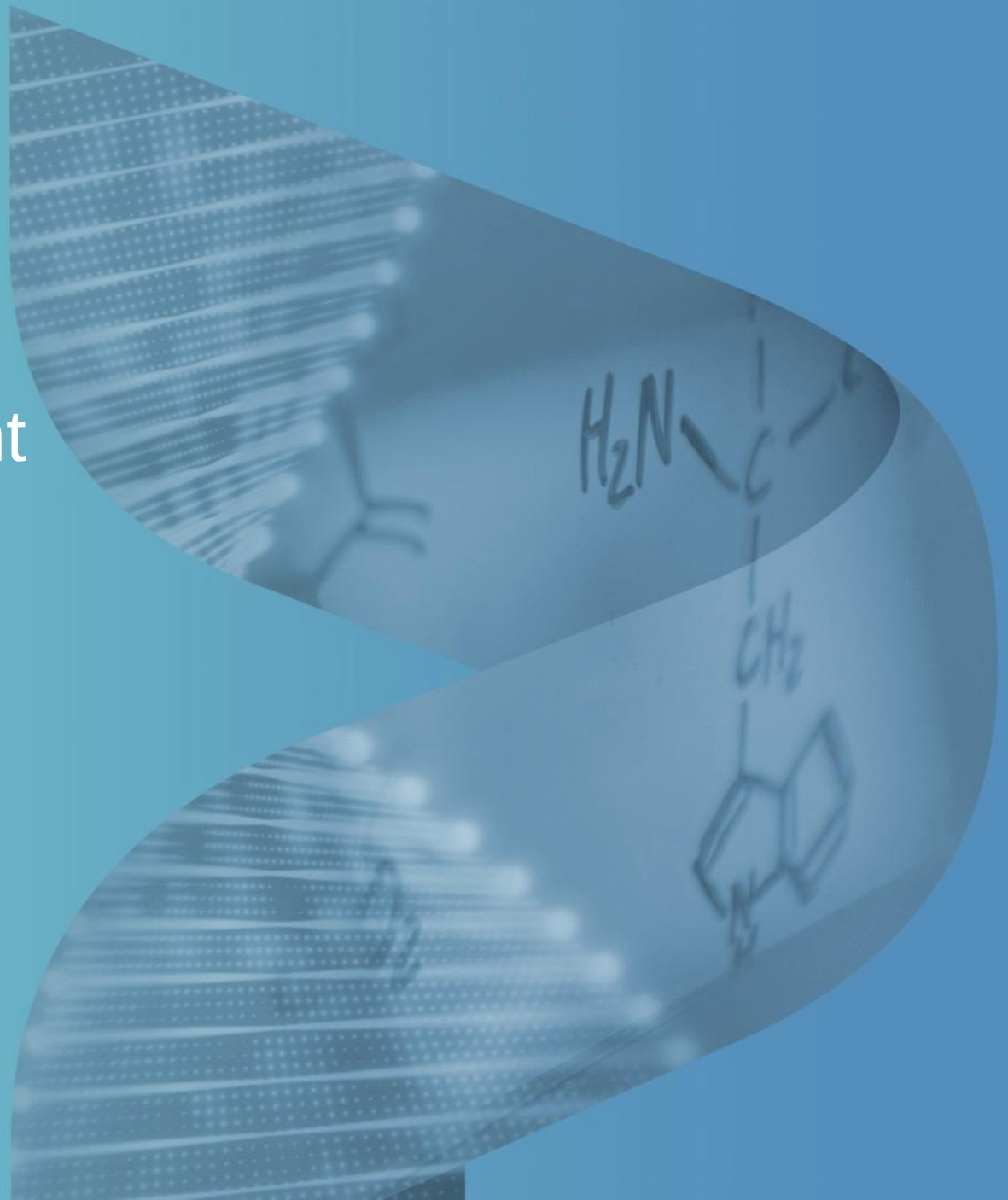
PepGen

PGN-EDODM1 in Development for Myotonic Dystrophy Type 1



Jenny Shoskes, PharmD
Associate Director, Clinical Development

MDF Conference, May 2-3, 2025

PepGen is committed to transforming the lives of people with severe neuromuscular and neurological disorders with our Enhanced Delivery Oligonucleotides (EDOs)

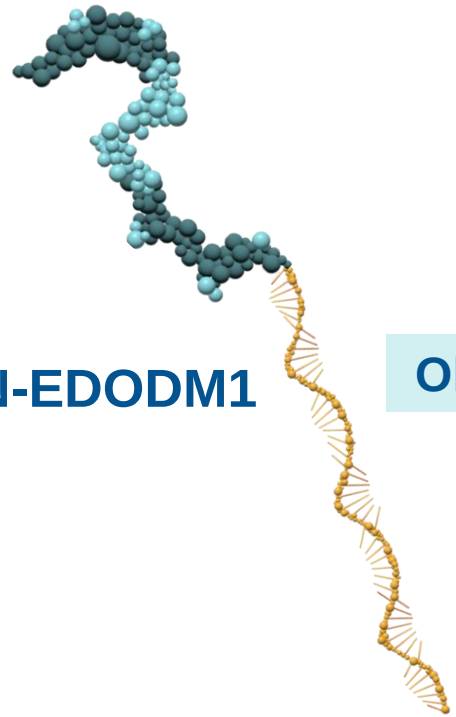
Jubal and family

What is an Enhanced Delivery Oligonucleotide?

Enhanced **D**elivery **O**ligonucleotide

EDO peptide

A peptide is a small piece of a protein
EDO peptides are designed to deliver the active part of the drug into the cell



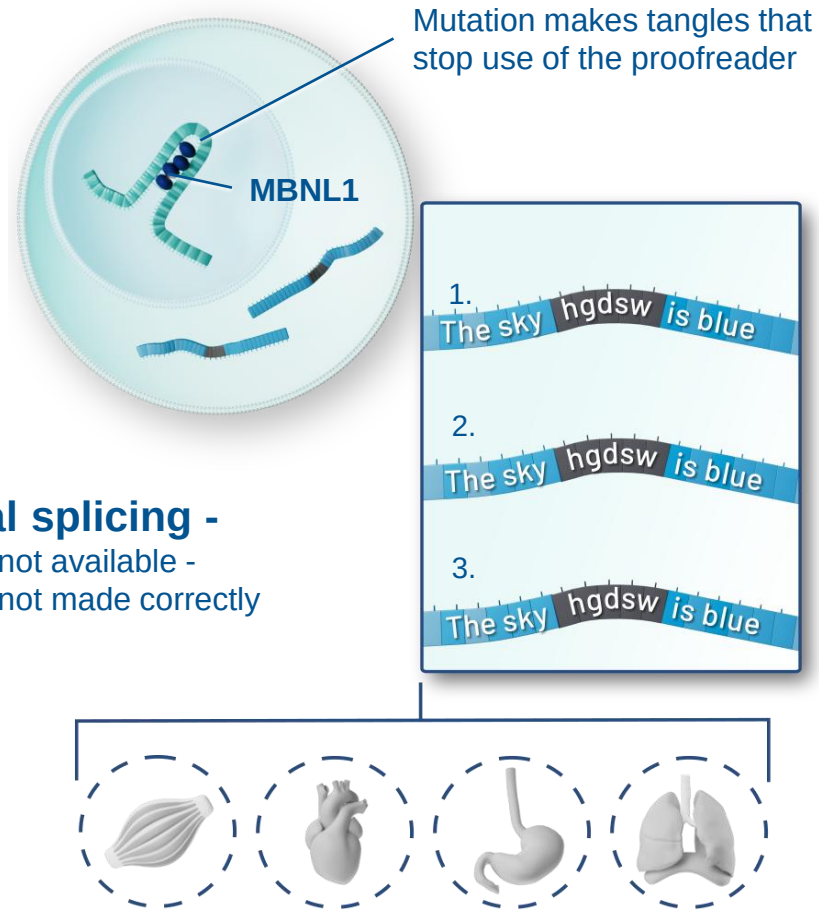
PGN-EDODM1

Oligonucleotide

An oligonucleotide is a small piece of genetic material
This is the active part of the drug

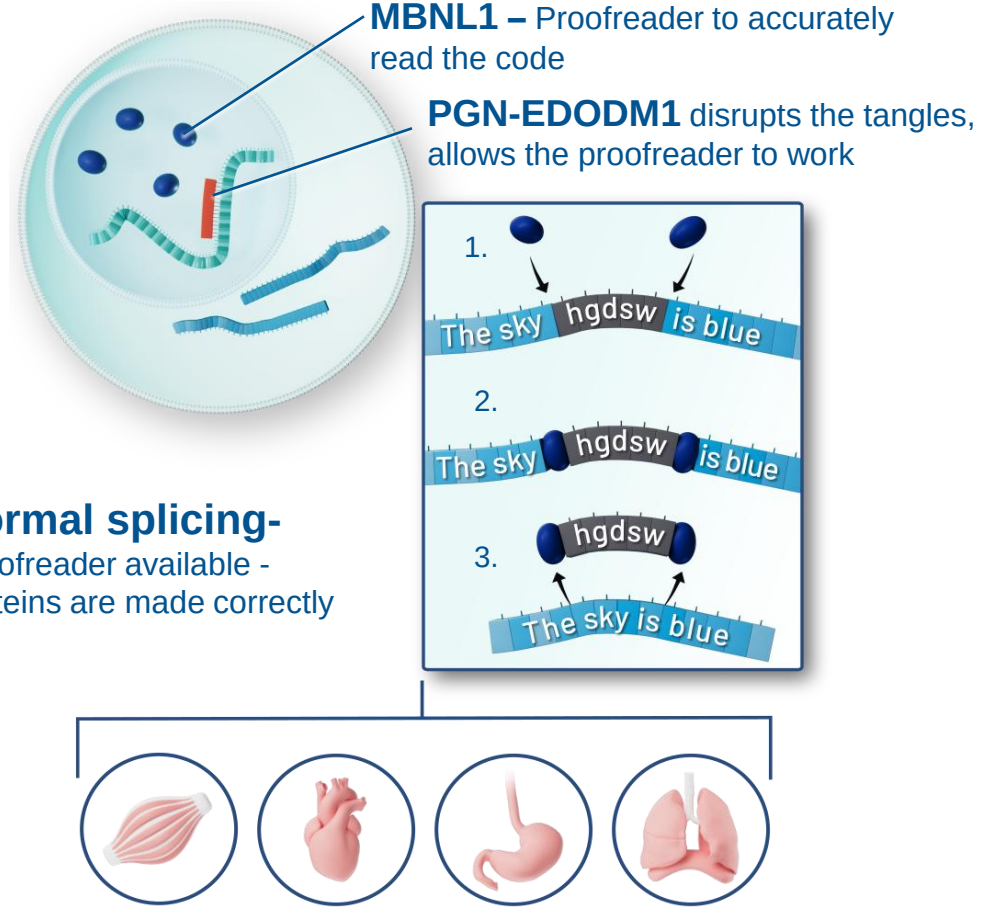
PGN-EDODM1 Mechanism of Action - Approach in DM1

DM1



Abnormal splicing -
Proofreader not available - proteins are not made correctly

DM1 + PGN-EDODM1



Normal splicing-
Proofreader available - proteins are made correctly

The DM1 Community Helps to Inform our Clinical Trials

Sharing perspectives on **inclusion and exclusion criteria**

Advising us on the **preferred order of the assessments** and **time in clinic to help reduce fatigue**

Guiding us on which **symptoms** matter most to them

Helping us understand ways to **reduce travel and planning burdens**

Overview of FREEDOM-DM1 and FREEDOM2-DM1 Trials

Freedom DM1

Open in US, Canada and UK

- Phase 1 Randomized, double-blind, placebo-controlled single ascending dose study in people with DM1
- Key anticipated readouts: functional assessments, correction of mis-splicing, safety data

Freedom 2 DM1

Multinational Study Initiated

- Phase 2 randomized, double-blind, placebo-controlled multiple ascending dose study in people with DM1
- Dosing initiated in FREEDOM2 in Q4 2024
  - IV administration of PGN-EDODM1 every 4 weeks up to 12 weeks
  - Key anticipated readouts: functional assessments, correction of mis-splicing, safety data

IV= intravenous

Select Inclusion and Exclusion Criteria for FREEDOM and FREEDOM2

Inclusion Criteria:

- Ages 18-60 (FREEDOM), 16-60 (FREEDOM2)
- Confirmed genetic testing of DM1
- Must meet a certain level of strength in both legs, as measured by a physical therapist
- Presence of hand myotonia

Exclusion Criteria:

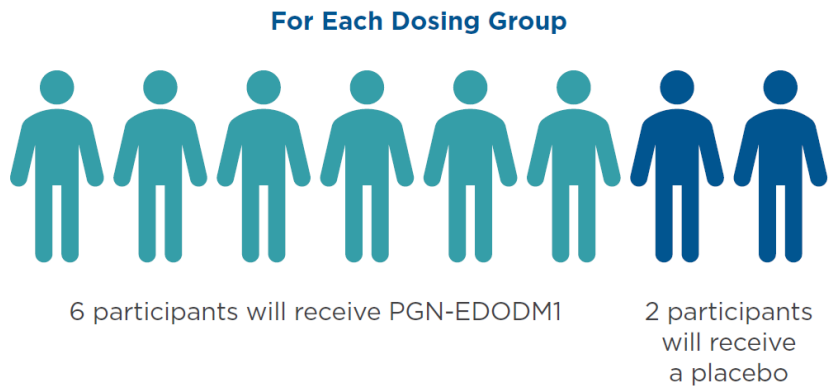
- Congenital DM1
- Known history or presence of any clinically significant conditions that may interfere with study safety assessments
- Medications specific for the treatment of myotonia within 2 weeks prior to screening
- Percent predicted forced vital capacity (FVC) <40%

Additional inclusion and exclusion criteria exist.

FREEDOM-DM1 Information

- **Phase 1 study** to explore if a single intravenous dose of the investigational drug, PGN-EDODM1, is safe and tolerable for people with DM1 compared to a placebo (a substance that has no active drug).

- Planning to enroll **32 people with DM1 in US, Canada, and UK**
  - Randomized 3:1 (drug: placebo)



- **Measuring:**
  1. Safety and tolerability
  2. Splicing, myotonia, muscle concentration of drug
  3. Exploring other endpoints

PGN-EDODM1 Selectively Targets Only Pathogenic *DMPK* to Correct RNA Mis-Splicing

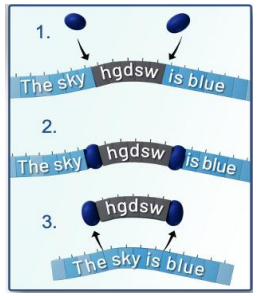
Favorable emerging safety profile[1] in people with myotonic dystrophy type 1

Dose-dependent increase in drug **tissue concentration** observed in first two cohorts

Dose-dependent increases in evaluable people[2] in mean **splicing correction** following single dose

~29% at 10 mg/kg

~12% at 5 mg/kg

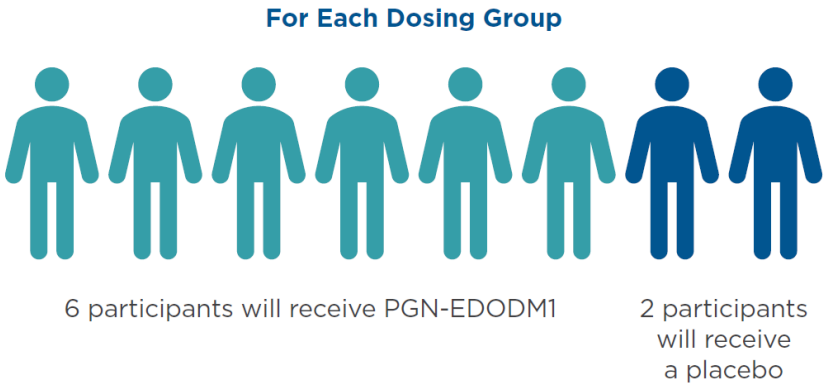


1. Through February 24, 2025
2. Two participants in the 10 mg/kg cohort were excluded from the splicing correction assay. One participant's biopsy was not collected at Day 28 and the other participant's splicing index values were outside of the pre-specified assay range, both at Baseline and at Day 28.

FREEDOM2-DM1 Information

- **Phase 2 study** to explore if **multiple,** intravenous doses of PGN-EDODM1 every 4 weeks is safe and tolerable for people with DM1 compared to a placebo (a substance that has no active drug) at different dose levels

- Planning to enroll **24 people with DM1. Currently open in Canada and the UK**
  - Randomized 3:1 (drug: placebo)



- **Measuring:**
  1. Safety and tolerability
  2. Splicing, myotonia, muscle concentration, hand grip, walking
  3. Exploring other endpoints for other body systems

Enrolling FREEDOM-DM1 and FREEDOM2-DM1 Sites

Canada

- CIUSSS du Saguenay-Lac-Saint-Jean* – Dr. Jean-Denis Brisson
- University of Ottawa* – Dr. Hanns Lochmuller
- University of Calgary – Dr. Gerald Pfeffer

United States

- Stanford University – Dr. Jacinda Sampson
- University of California-Irvine – Dr. Namita Goyal
- University of Rochester – Dr. Johanna Hamel
- Rare Disease Research – Dr. Han Phan
- Virginia Commonwealth University – Dr. Nick Johnson
- University of Kansas Medical Center - Dr. Jeff Statland
- Massachusetts General Hospital – Dr. Thurman Wheeler

United Kingdom

- Salford Royal Hospital – Dr. James Lilleker
- University College London Hospital* – Dr. Chris Turner

*All listed sites enrolling for FREEDOM, * = enrolling for FREEDOM and FREEDOM2*

Thank You and To Learn More

Clinical study participants and their families

Community and clinical advisors

Clinical site staff and researchers and investigators

Freedom DM1

www.freedom-dm1.com

clinicaltrials.gov: NCT06204809

Freedom 2 DM1

www.freedom-dm2.com

clinicaltrials.gov: NCT06667453

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General inquiries and ideas: community@pepgen.com