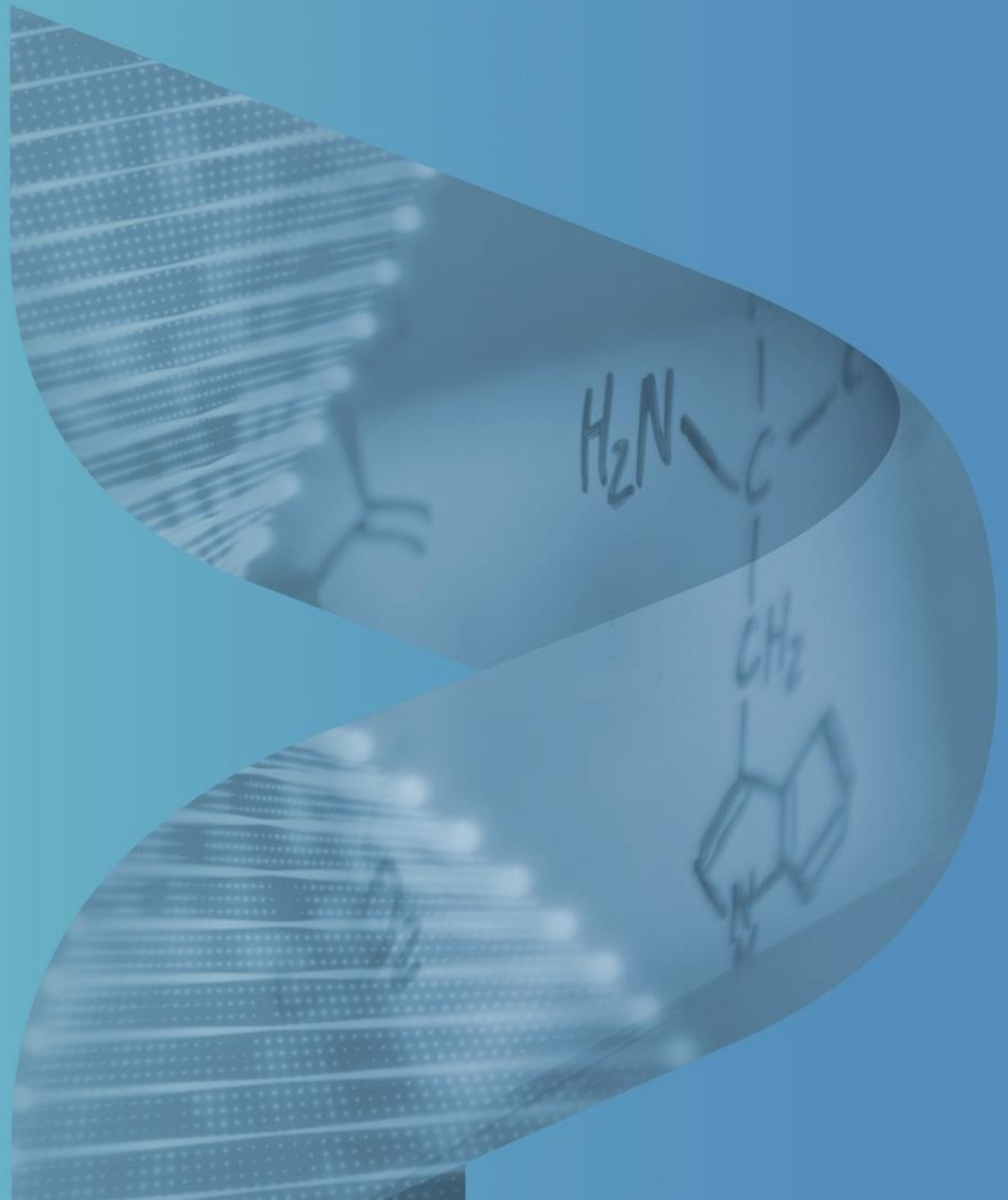
PepGen™

Company Presentation

May 2024



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PepGen: Who We Are

Our mission

- Transforming the lives of patients with severe neuromuscular and neurological diseases

Proprietary delivery platform

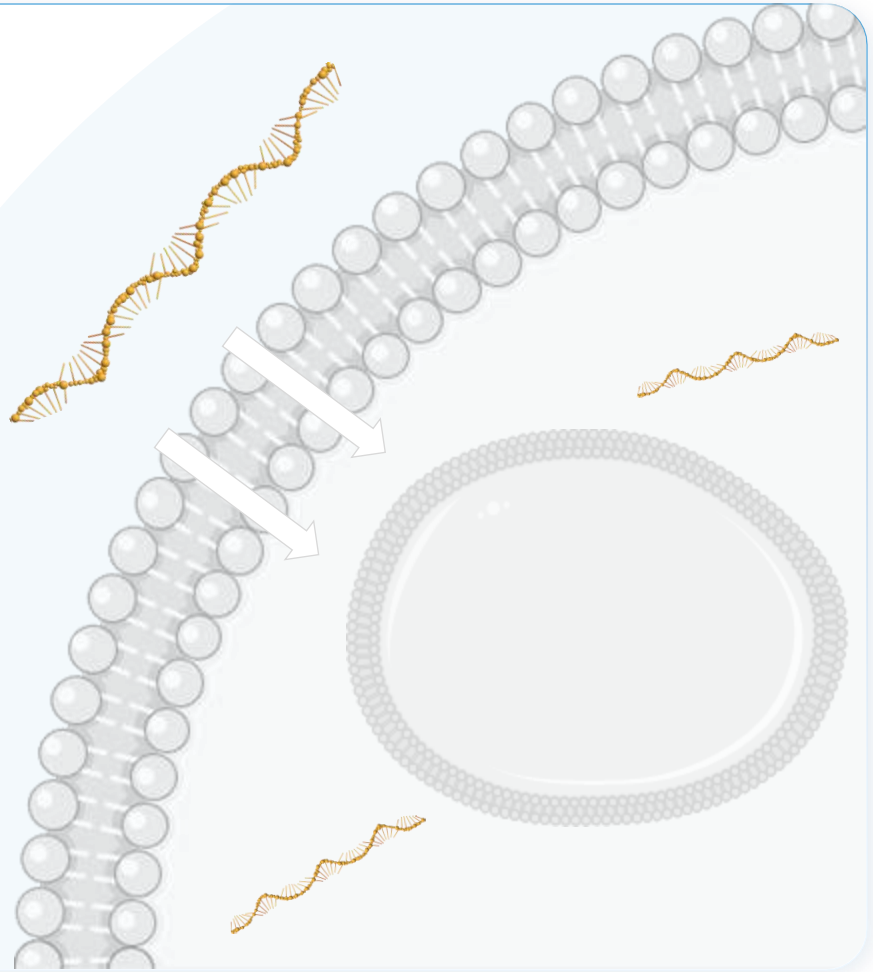
- Enhanced Delivery oligonucleotide (EDO) platform
  - Increased cellular uptake
  - Increased nuclear uptake
  - Enhanced potency at tolerable doses

Clinical stage pipeline: patient read outs in 2024

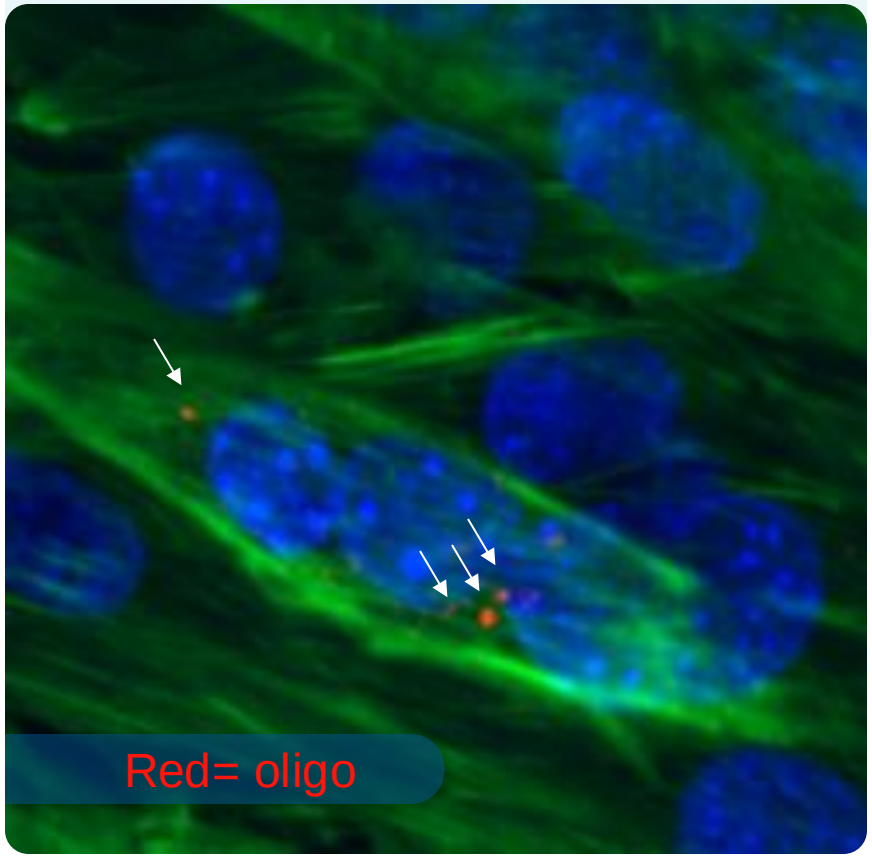
- Duchenne Muscular Dystrophy (DMD): Initial patient read out from multiple ascending dose study (Phase 2) expected mid-2024
- Myotonic dystrophy type 1 (DM1): Initial patient read out from single ascending dose study (Phase 1) expected 2H:2024

The Challenge of Oligonucleotides

Naked oligonucleotides are not efficiently taken up into the muscle cells and the nucleus



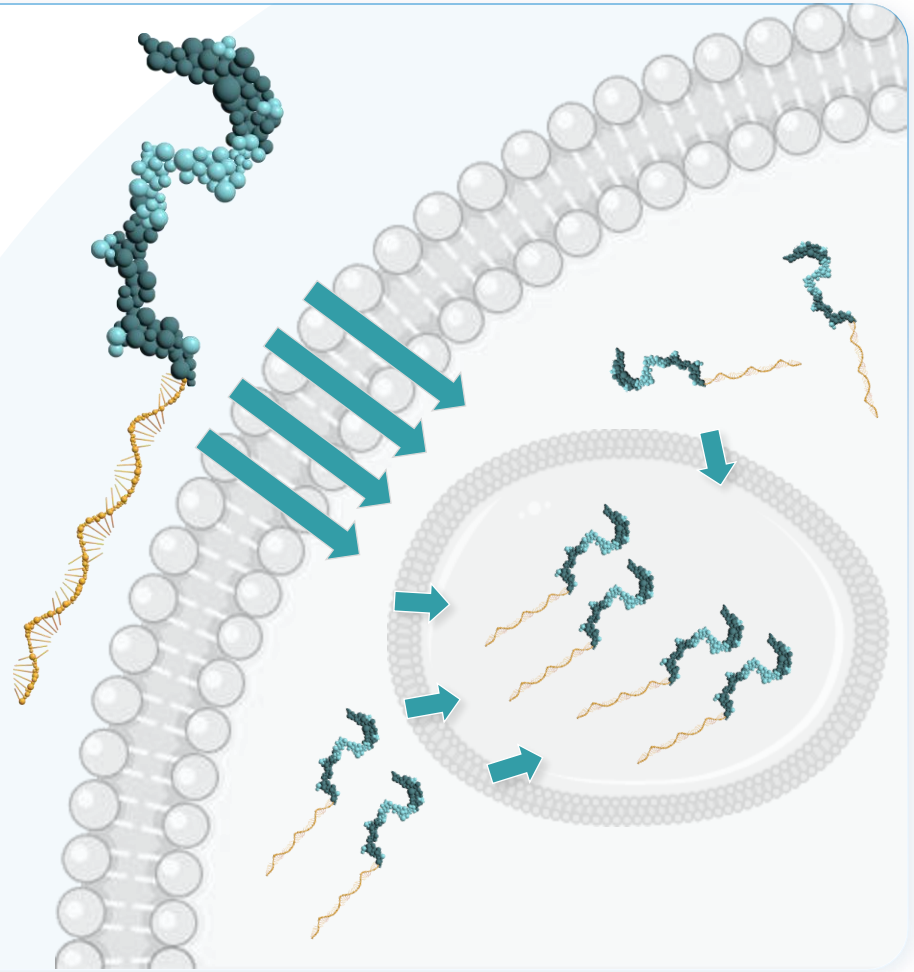
Naked Oligo (PMO)



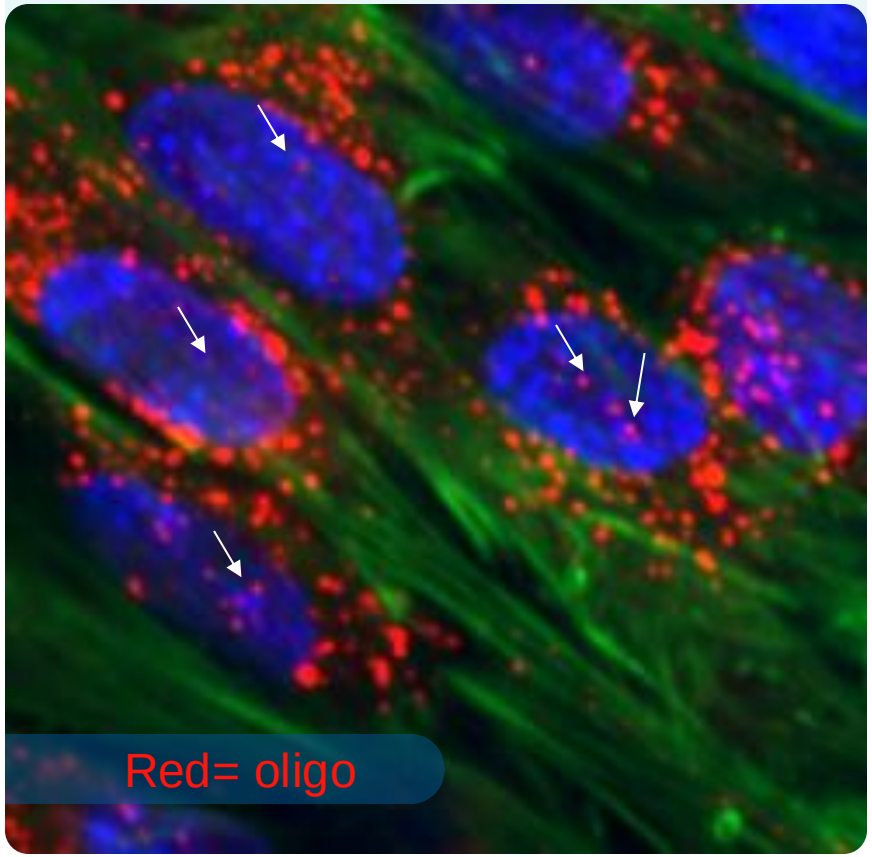
Note: 1. In vitro staining image is shown with 10µM conc. of PMO23 (naked oligonucleotide); 2. C2C12 mouse cells were differentiated for 4 days into myotubes and treated with fluorescently tagged compounds for 24h. PMO: phosphorodiamidate morpholino oligonucleotide

PepGen's EDO platform has been designed and developed to solve this decades long problem

EDO platform results in nuclear delivery of oligonucleotide therapeutics



PepGen's EDO: Up to 25-fold higher nuclear uptake of oligo



Note: 1. In vitro staining image is shown with 10µM conc. of EDO23; 2. C2C12 mouse cells were differentiated for 4 days into myotubes and treated with fluorescently tagged compounds for 24h.

PepGen's advanced pipeline enabled by EDO technology

PROGRAM	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PIVOTAL
PGN-EDO51	**Duchenne muscular dystrophy** *Exon 51*				
PGN-EDODM1	**Myotonic dystrophy type 1** *DMPK*				
PGN-EDO53	**Duchenne muscular dystrophy** *Exon 53*				

Research

- DMD *Exon 45, Exon 44*
- Additional neuromuscular diseases
- Neurological Diseases

Note: Clinical plans are subject to alignment with regulatory authorities

Latest milestones achieved and upcoming for 2024

	Achieved	Upcoming
DMD	• CONNECT1 Phase 2 initiated and 5 mg/kg dose cohort fully enrolled • CONNECT2 Phase 2 open in UK	• Preliminary data from CONNECT1 5 mg/kg dose cohort expected in mid-2024 • Dosing of first patient in CONNECT2 expected in 2H:2024
DM1	• FREEDOM Phase 1 open in US, Canada and UK	• Preliminary data from at least the 5 mg/kg dose cohort of FREEDOM expected in 2H:2024 • FREEDOM2 initiation expected in 2H:2024

Q1 2024: Completed $80 million follow-on common stock offering; cash runway into 2026[1]

1. Based on current operating plan

PGN-EDO51 for Duchenne muscular dystrophy (DMD)

DMD presents with a significant unmet medical need

Disease overview

- Caused by mutation in dystrophin gene resulting in progressive muscle damage
- Onset of symptoms in early childhood
  - Loss of ambulation by early adolescence
  - Loss of respiratory and cardiac function resulting in early adulthood mortality

Market opportunity

- US and EU ~40,000 patients
- ~21% patients amenable to:
  - PGN-EDO51: Phase 2 (exon 51)
  - PGN-EDO53: CTA/IND enabling studies advancing in 2024 (exon 53)
- Novel therapies needed to restore functional dystrophin and prevent loss of muscle function and early mortality

Source: https://www.cureduchenne.org/cure/exon-skipping/.

EDO technology resulted in significant increase in exon skipping and dystrophin in mdx mice that was uniformly distributed across muscle

PGN-EDO23
(murine analogue of PGN-EDO51)

mdx

Week:

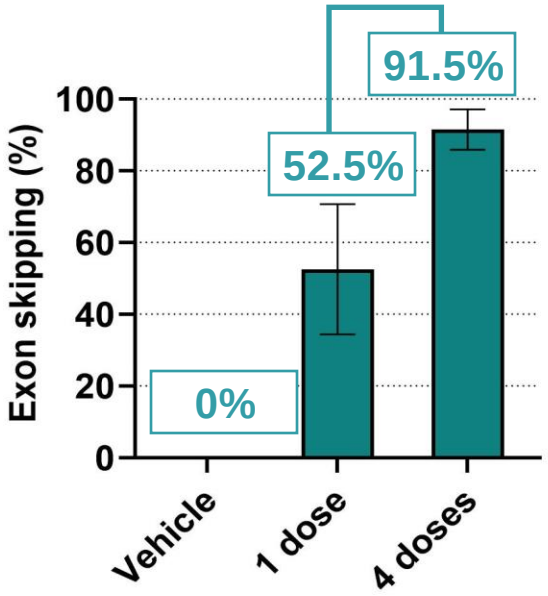
PGN-EDO23

Tissue analysis

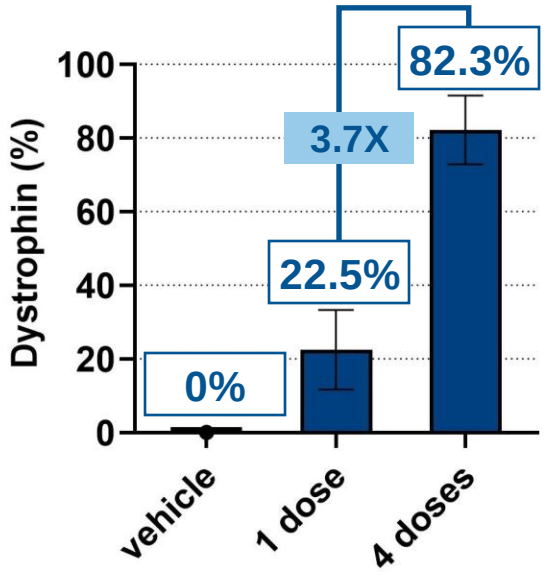
EXON SKIPPING

DYSTROPHIN (WESTERN BLOT)

Biceps, 30 mg/kg, Q4W

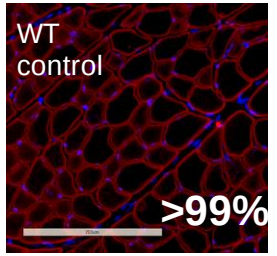


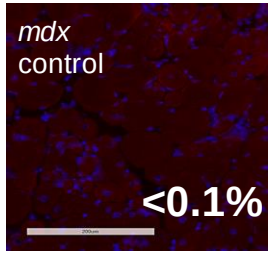
PGN-EDO23

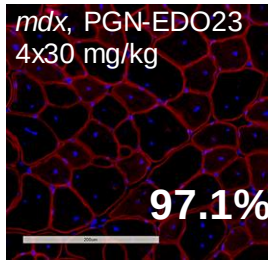


PGN-EDO23

DYSTROPHIN (IF) and % POSITIVE FIBERS







Dystrophin / Nucleus

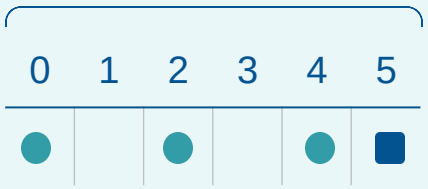
Protocol: mdx mice received up to 4 doses of PGN-EDO23, with 4-week intervals between doses. Tissue samples were collected 4 weeks post-each dose. Exon skipping was evaluated by RT-PCR and dystrophin protein was evaluated by western blot and immunofluorescence (IF). IF scale bar = 200 µM. Graph is presented as mean ± SD; n = 4-5 per cohort; grey band is dystrophin LLOQ (2.5%).

Repeat dose exon skipping levels of >70% observed in skeletal muscles and diaphragm at 30 mg/kg in non-human primates (NHPs)

PGN-EDO51

WT

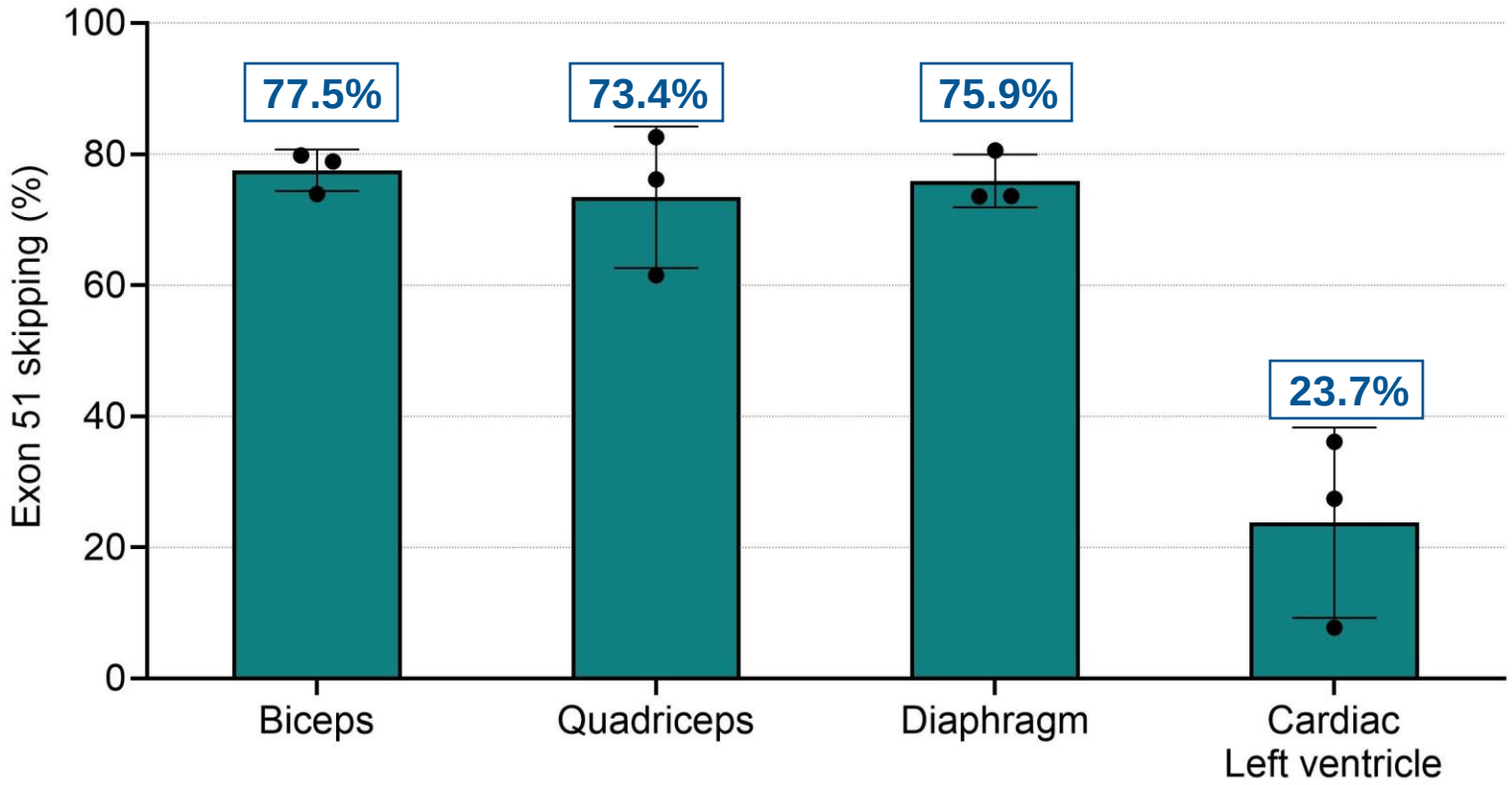
Week:



PPMO dose

Tissue analysis

EXON SKIPPING

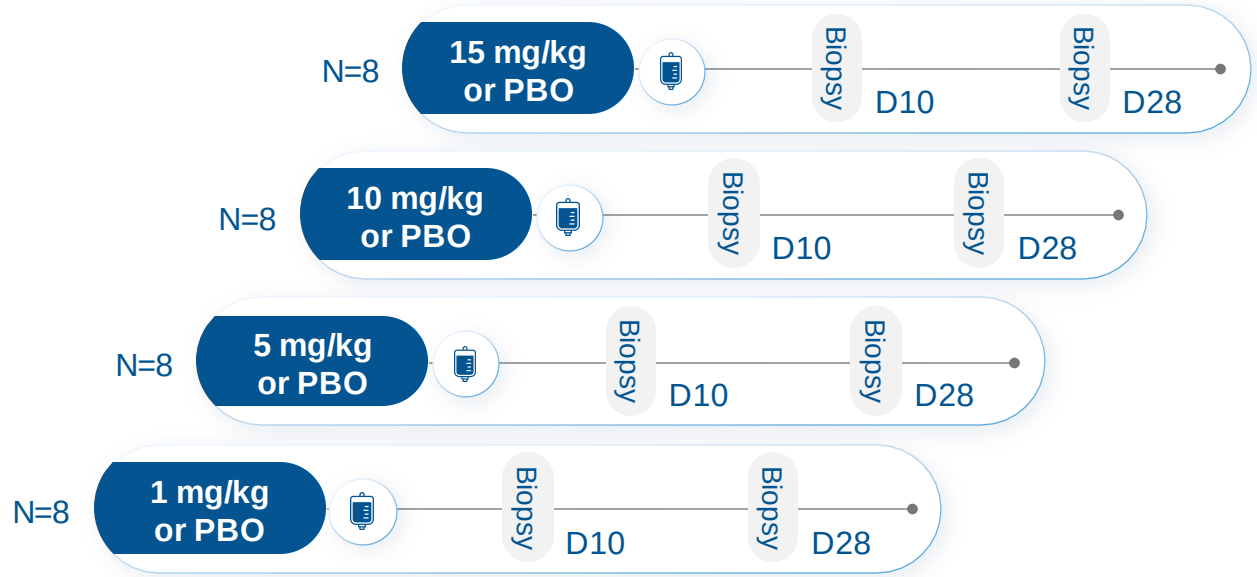


Protocol: Three doses of 30 mg/kg PGN-EDO51 were administered by IV over 30 min every two weeks (n=3). Tissues were harvested 7 days after final administration. Shown as mean ± SD; n = 3 per group. Study was not powered for statistical significance.

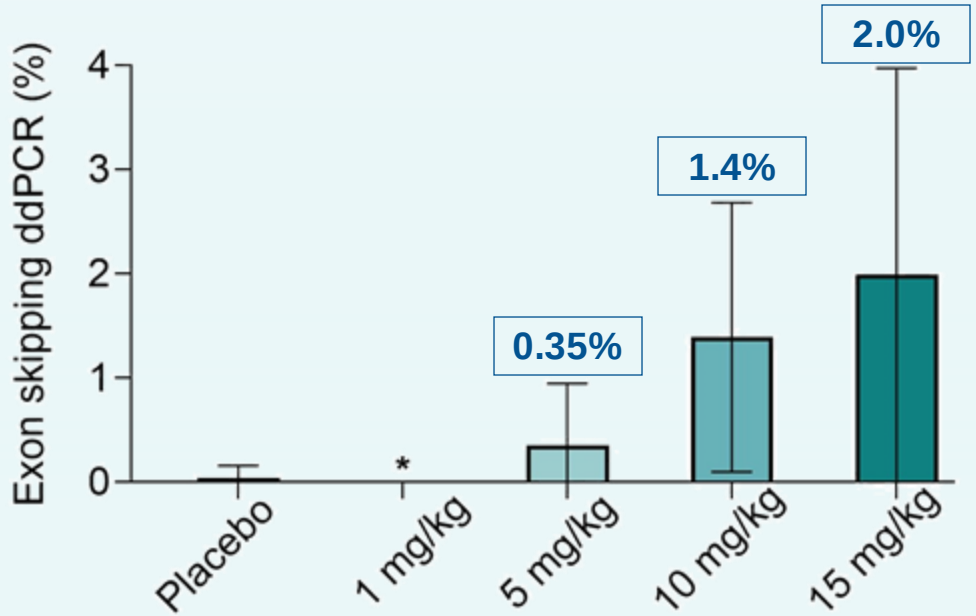
Clinical activity: Highest levels of exon 51 skipping in humans following a single dose of PGN-EDO51[1]

PH1 HEALTHY NORMAL VOLUNTEER (HNV) TRIAL DESIGN

- Study population: Healthy adult males (n = 32; 8 per cohort, 3:1 PGN-EDO51:placebo)
- Dosing: Single dose, IV administration
- Biceps biopsies conducted on Day 10 and Day 28



TRIAL RESULTS: D28 EXON SKIPPING (BICEPS)



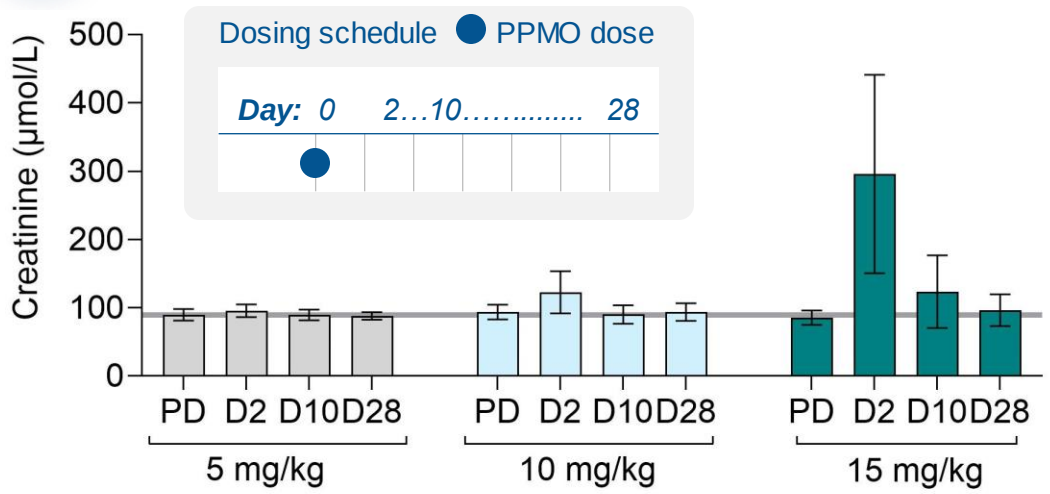
Protocol PGN-EDO51-101: Phase 1, first in human, randomized double blind, placebo (PBO) controlled single ascending dose study in healthy adult volunteers. Single dose of either PGN-EDO51 or Placebo were administered by IV infusion at doses indicated. Participants were followed for 28-day period following dose administration to evaluate safety, tolerability, PK, and PD. Needle biopsies of biceps muscle were taken on Day 28. Exon skipping measured by ddPCR. Shown as mean ± SD; n = 6 PGN-EDO51: 2 Placebo per cohort (n = 5 for D10 at 15 mg/kg). Asterisk indicates value that were under the lower level of quantification

1.Comparative statement based on cross-trial comparison of Phase 1 HV data of single dose administration of EDO51 with publicly-available Phase 1 HV data following a single dose of other exon skipping approaches (vesleteplirsen and eteplirsen).

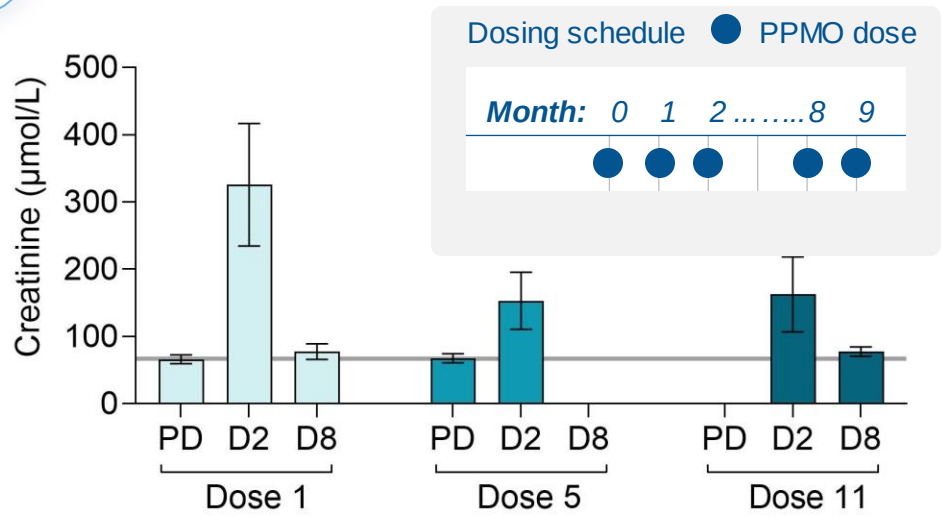
Safety: Observed changes in creatinine are transient and not associated with adverse kidney findings

We believe these results support the potential tolerability of PGN-EDO51 with repeat dosing

PGN-EDO51 SINGLE-DOSE SERUM CREATININE



PGN-EDO51 REPEAT-DOSE SERUM CREATININE



- No clinical symptoms of acute kidney injury in humans
- No hematologic, cardiovascular or hepatic clinical signs or symptoms in humans
- No persistent, abnormal kidney parameters in humans or NHPs

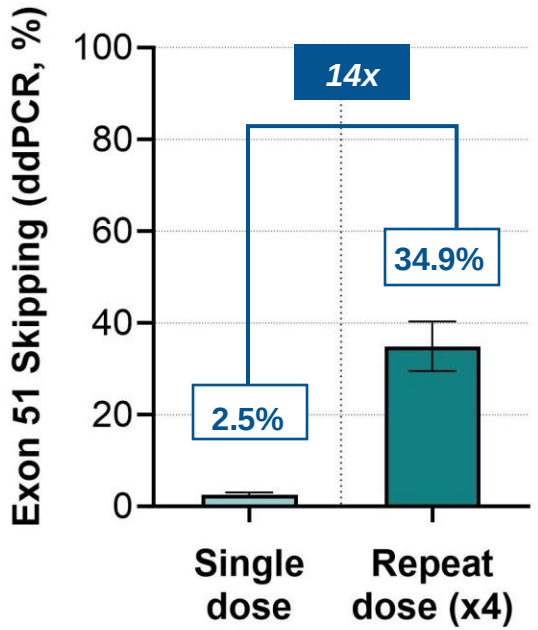
- No adverse findings in the kidney following 11 doses in NHPs through 45 mg/kg (highest dose tested)

PD = Pre-dose. NHP Protocol: PGN-EDO51 was administered to NHP by IV infusion at 45 mg/kg over 60 min (n=12) for 11 doses. Dosing schedule was once every 28 days.
Data shown as mean ± SD. PGN-EDO51 HV study: Data shown as mean ± SD; n = 6 per dose cohort

Increased exon skipping in NHPs with repeat dosing supports transformative potential for PGN-EDO51 in patients

NHP SINGLE VS. REPEAT DOSE

Biceps, 20 mg/kg, ddPCR



14X increase in exon skipping with repeat dosing in NHPs supports transformative potential for PGN-EDO51 in DMD patients

PATIENT REPEAT DOSE

Connect 1
EDO51

12-week study with once every 4-week (Q4W) dosing

NHP protocol: Single (30 min) or repeat (60 min) IV doses with PGN-EDO51 were administered in male NHP. For repeat dose evaluation, NHP received 4 doses with 4-week intervals between doses. Tissue samples were collected 1-week post-final dose as indicated on graphs. Exon skipping was assessed by ddPCR. Graph is presented as mean ± SD; n = 3-8 per group.

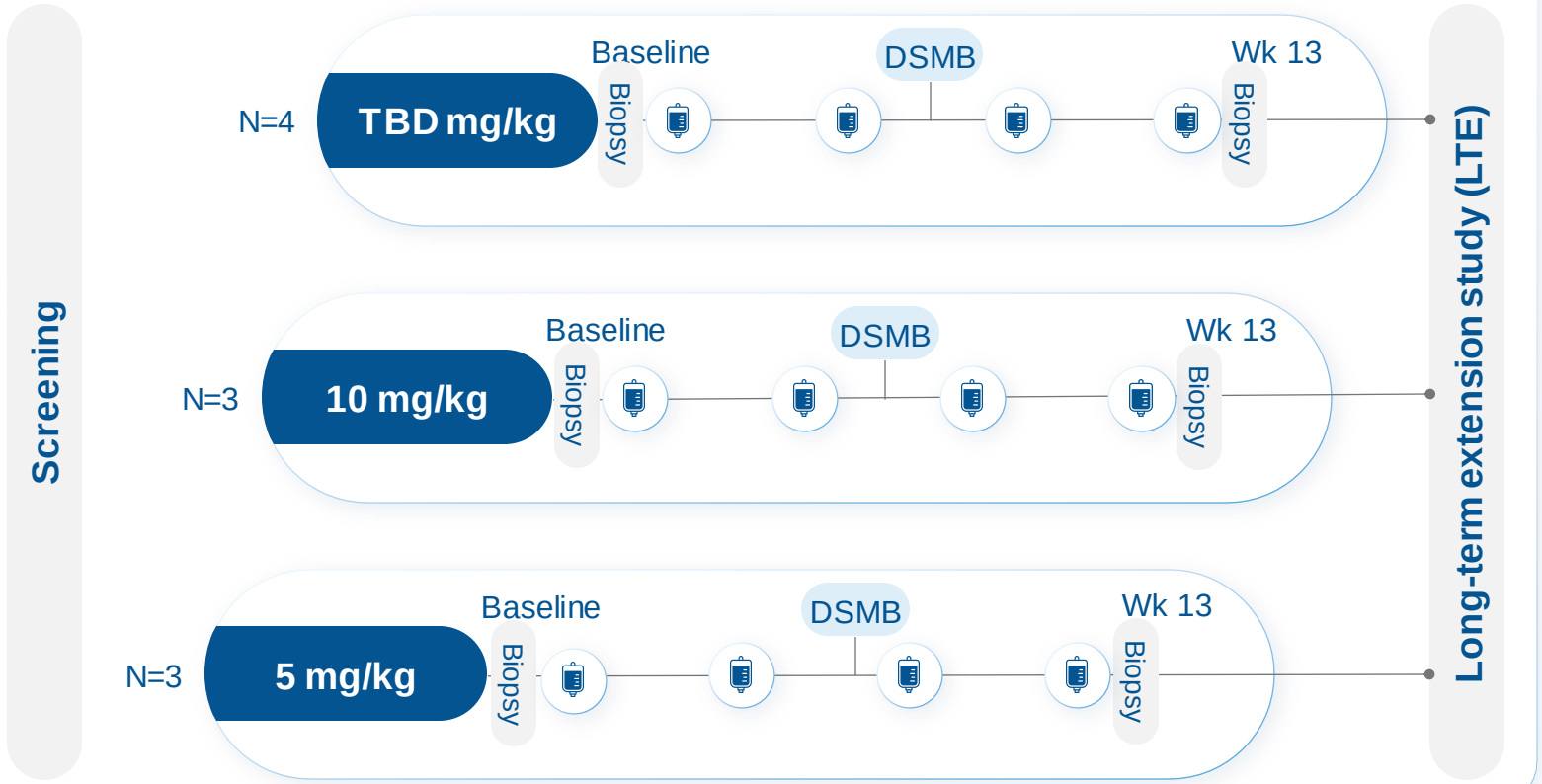
CONNECT1 Phase 2 PGN-EDO51 Multiple-Ascending Dose (MAD) study

Connect 1
EDO51

CONNECT1 study overview

- Open label study in DMD patients
- Study is open in Canada
- IV administration of PGN-EDO51 every 4 weeks
- Muscle biopsies in biceps at baseline and week 13
- Key endpoints: Safety biomarkers, dystrophin, exon skipping

PGN-EDO51 dosing Q4W for a treatment period of 12 weeks



PGN-EDO51 development path to support registration

Ongoing

Phase 2: Open-label MAD study in patients

Open in Canada

Fast path to clinical proof-of-concept: Dystrophin expression at 13 weeks

Preliminary data from 5 mg/kg dose cohort in mid-2024

Open

Phase 2: Randomized, double-blind, placebo-controlled MAD study in patients

Multinational study

Potential to support accelerated approval[1]: Dystrophin expression at 25 weeks

1. Subject to alignment with regulatory authority feedback

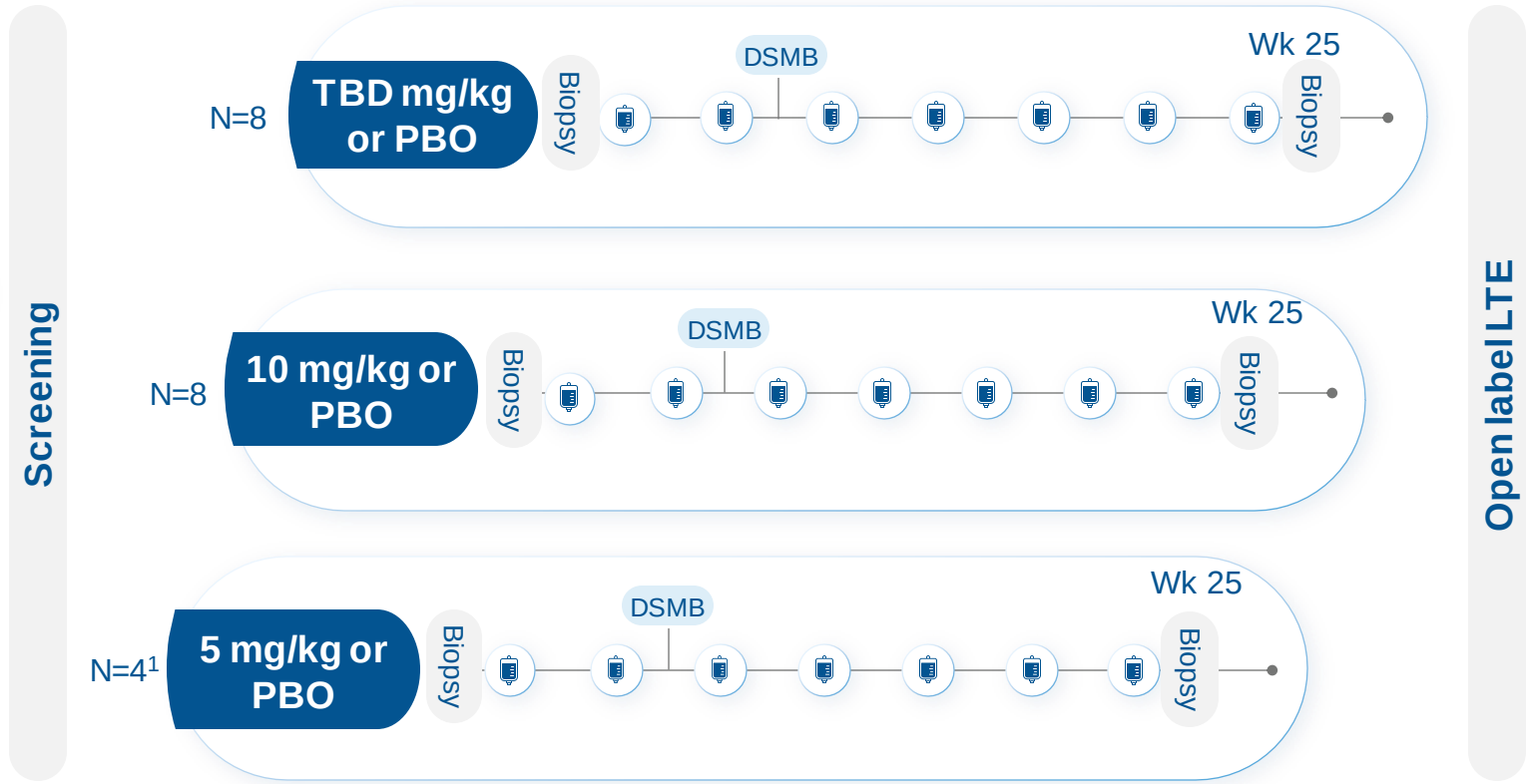
CONNECT2 Phase 2 PGN-EDO51 MAD study

Connect 2
EDO51

CONNECT2 study overview

- Multinational, randomized, double-blind, placebo-controlled study
- IV administration of PGN-EDO51 every 4 weeks
- Muscle biopsies in biceps at baseline and week 25
- Key endpoints: Safety biomarkers, dystrophin, exon skipping, North Star Ambulatory Assessment (NSAA), Time to stand from supine, Performance of Upper Limb

PGN-EDO51 dosing Q4W for a treatment period of 24 weeks prior to rolling over into LTE study (randomized 2:1)



1. Approved for n=8 in UK; amendment being submitted for the truncated cohort (n=4); truncated cohort submitted for EU CTR

We believe that our EDO delivery platform has the power to unlock the therapeutic potential of oligonucleotides

		EXON SKIPPING	DYSTROPHIN
		1 dose (HV)	*>3 doses (DMD patients)*
PGN-EDO51 (Phase 2 ongoing) • Potential for greater dystrophin production • Generally, well tolerated in single dose study through 15 mg/kg	**10 mg/kg**	**1.1%**	**CONNECT1 study**
		>6x[1]	
SRP-5051 (vesleteplirsen) Phase 2b – *Sarepta Therapeutics*	**20 mg/kg**	~0.18%[2]	3.06%[2]
EXONDYS 51® (eteplirsen) – *Sarepta Therapeutics*	**30 mg/kg**	<0.05%[2]	0.44%[3]

1. Comparative statement based on cross-trial comparison of Phase 1 HV data of single dose administration of PGN-EDO51 with publicly-available Phase 1 HV data following a single dose of other exon skipping approaches (vesleteplirsen and eteplirsen). 2..Source: Sarepta MOMENTUM study updates, 07Dec20 and 03May21. 3. Data included in drug label (FDA).

PGN-EDODM1 for myotonic dystrophy type 1 (DM1)

Myotonic Dystrophy Type 1 (DM1) Overview and Unmet Medical Need

Overview

- Mutation in DMPK gene
- Onset of symptoms variable-childhood to adulthood
  - Myotonia
  - Muscle weakness
  - Cardiac arrythmias
  - Loss of lung function
- Average life expectancy is 50-60 years for adults with DM1

Market opportunity

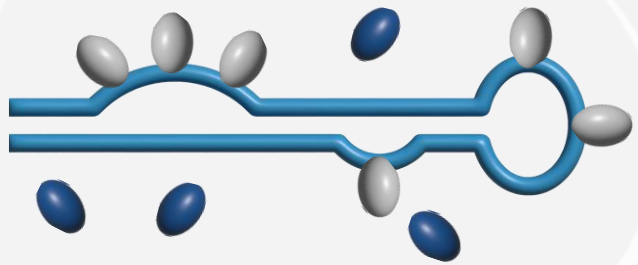
- US and EU over 110,000 patients
- No approved therapies that address underlying cause of the disease

Sources: Neuroepidemiology (2022) 56 (3): 163–173., Neurology 2021 Feb 16;96(7):e1045-e1053

Mutant *DMPK* transcript is the driver of pathology in DM1

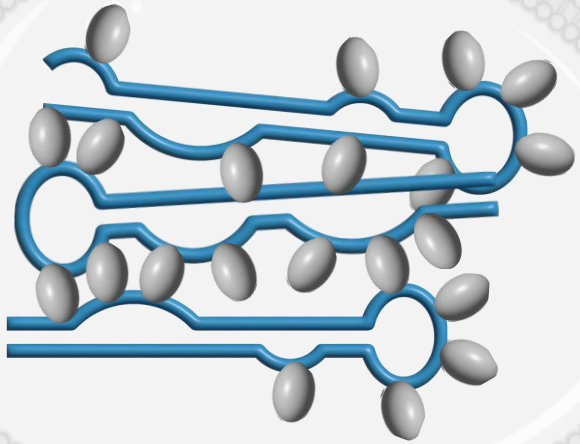
DM1 CUG REPEAT

Pathogenic *DMPK* transcripts with CUG repeat expansion form hairpin loops that bind MBNL1



DMPK PATHOLOGY

Pathogenic *DMPK* CUG repeat RNA accumulate and form foci that further traps MBNL1 protein leading to extensive RNA mis-splicing

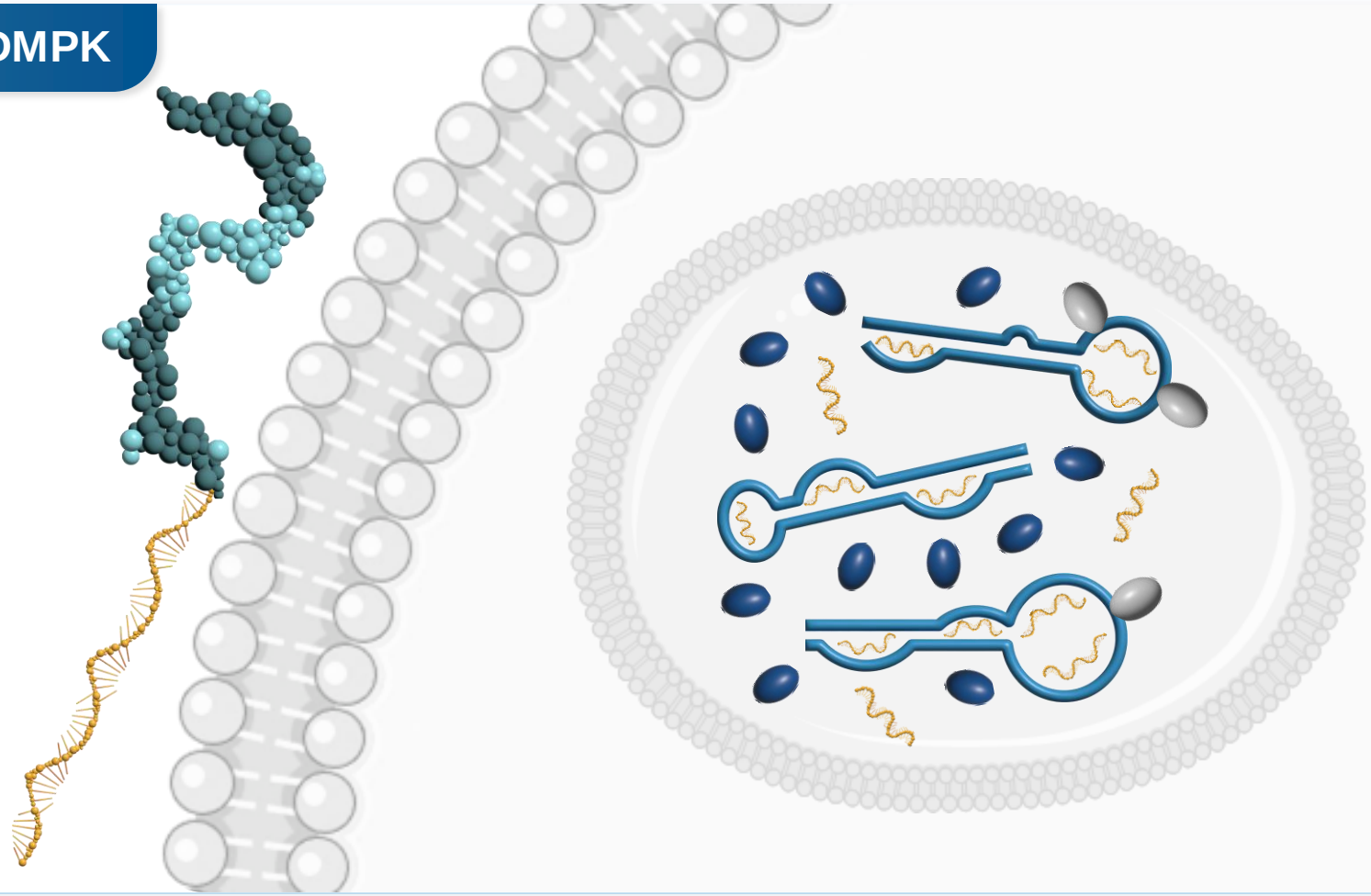


PepGen™ Free (active) MBNL1 Bound (inactive) MBNL1

PepGen's novel therapeutic approach to treating DM1

PGN-EDODM1 TARGETS TOXIC DMPK

PGN-EDODM1 binds pathogenic CUG *DMPK* transcript loops, reducing toxic foci, and liberating MBNL1 to restore normal splicing

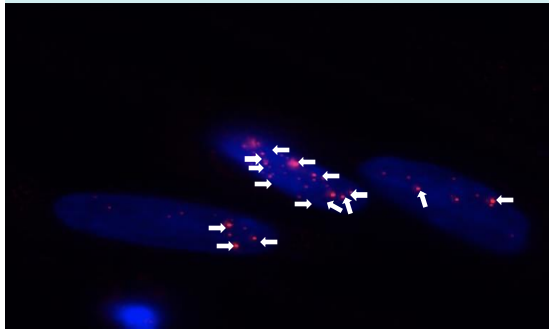


PepGen™ Free (active) MBNL1 Bound (inactive) MBNL1 PGN-EDODM1

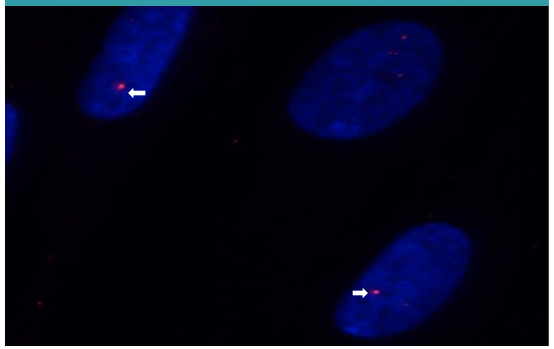
PGN-EDODM1 reduced pathogenic nuclear foci, liberated MBNL1 and corrected mis-splicing in patient cells with long CUG repeats

FOCI REDUCTION

Not treated (NT)



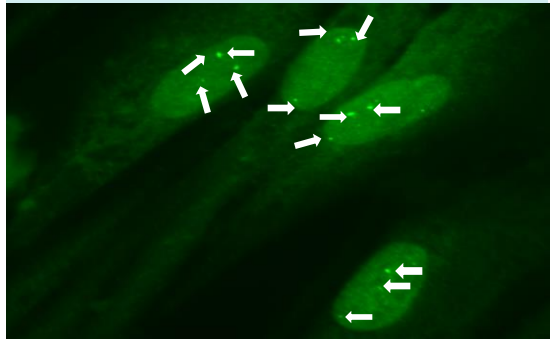
PGN-EDODM1 treated



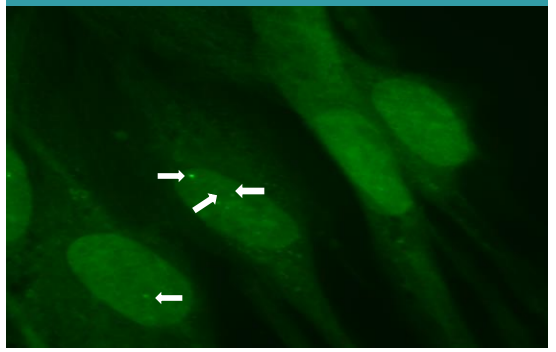
54%
reduction in toxic foci

MBNL1 LIBERATION

Not treated (NT)



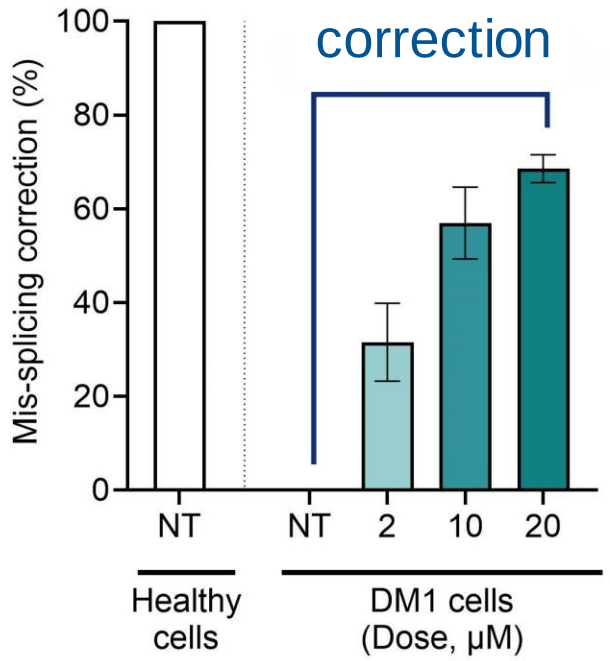
PGN-EDODM1 treated



MIS-SPLICING CORRECTION

Across multiple transcripts

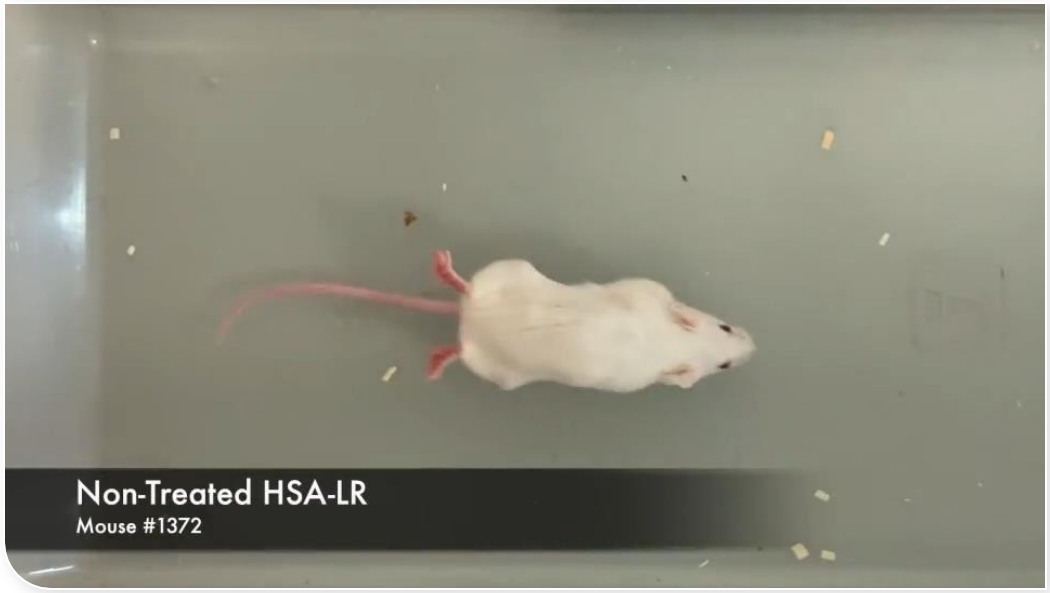
69%
correction



Immortalized myoblasts from healthy individual or DM1 patient with 2600 CTG repeats were cultured then differentiated for 4 days into myotubes. Treatment with peptide-PMO conjugates at concentrations given. Cells were harvested for analysis 24h after treatment. RNA isolation, RT-PCR and capillary electrophoresis (QIAxcel) analysis was performed. Visualization with FISH and immunofluorescence microscopy. Mean ± SD; n = 5 per group.

PGN-EDODM1 corrected movement disorder of DM1 mouse model

UNTREATED HSA^{LR}



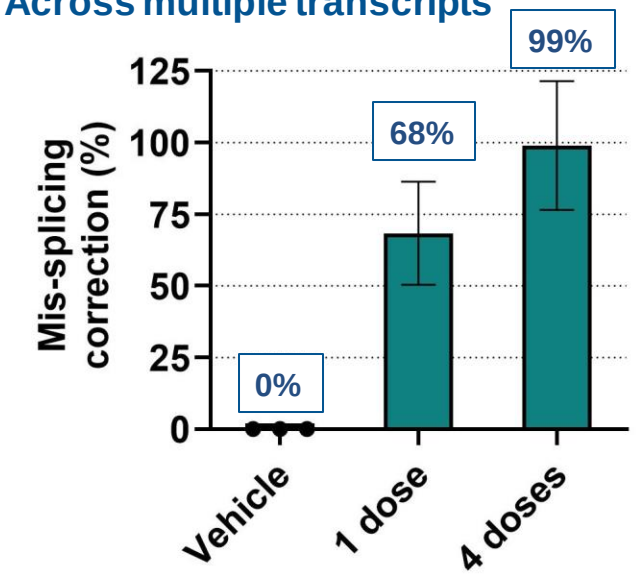
TREATED HSA^{LR}

Protocol: PGN-EDODM1 was administered intravenously (IV) to WT and HSA^{LR} mice at 50 mg/kg (n=4-16); myotonia assessed two weeks post-administration.

Resolution of myotonia correlated with robust correction of splicing at tissue concentration achieved in single dose Phase 1 study of PGN-EDO51

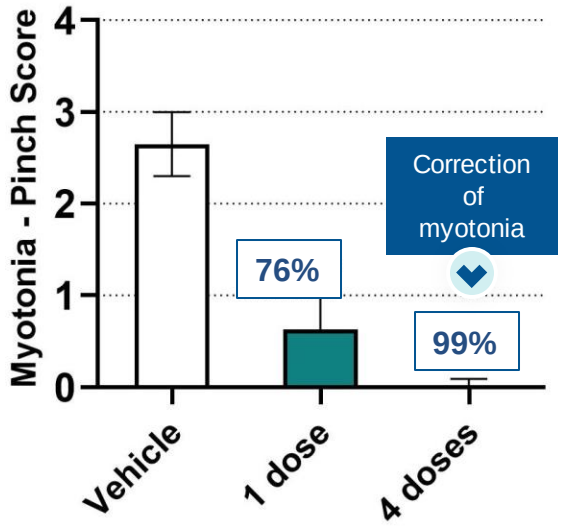
Mis-splicing correction

Across multiple transcripts



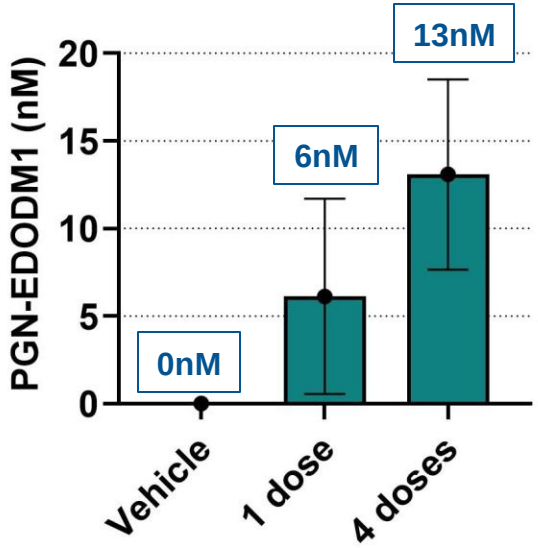
Reversal of myotonia

Pinch test



Tissue concentration

Skeletal muscle



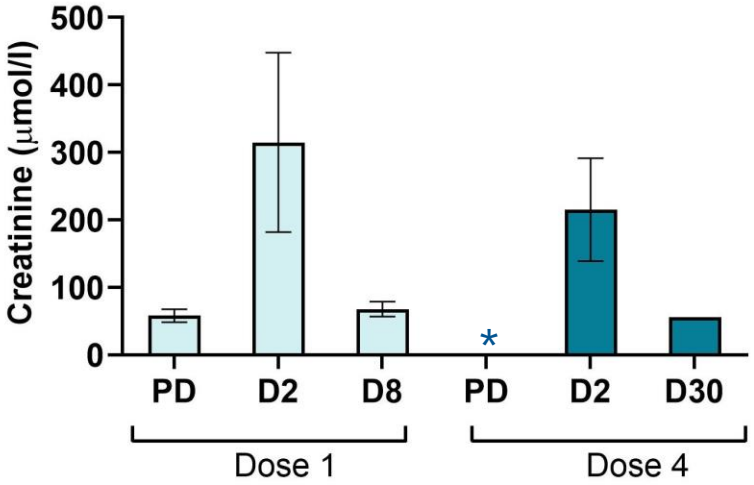
EDO technology (PGN-EDO51) resulted in activity in HVs while achieving PMO conc. >11nM with a single dose; therefore, we expect meaningful improvement in key biomarkers with a single dose of PGN-EDODM1 in FREEDOM

Protocol: HSA^{LR} mice received 1 or 4 doses of PGN-EDODM1, with 4-week intervals between doses. Skeletal muscle tissues were collected 4 weeks post-final dose. Mis-splicing analysis considers multiple transcripts. Graph is presented as mean ± SD; n = 8-12 per cohort per transcript. Myotonia pinch test was performed 4 weeks post-final dose. Grade 3 = Clear sign of myotonia strong AND reproducible, Grade 2 = Clear sign of myotonia, strong OR reproducible, Grade 1 = Clear sign of myotonia but non reproducible, Grade 0 = No sign of myotonia. Graph is presented as mean ± SD; n = 12-43 per cohort. Skeletal muscle tissue concentration was measured by fluorescent based HPLC method. Graph is presented as mean ± SD; n = 8-12 per cohort.

Safety: Observed changes in creatinine are transient and not associated with adverse kidney findings

We believe these results support the potential tolerability of PGN-EDODM1 with repeat dosing

PGN-EDODM1 REPEAT-DOSE SERUM CREATININE



Dosing schedule

Month:	0	1	2	3
	●	●	●	●

● PPMO dose- 60 mg/kg

- Transient increase in serum creatinine resolved within a week postdose
- No adverse findings in the kidney even after 4 doses through 60 mg/kg
- No notable hematologic, cardiovascular or hepatic effects in 13-week study

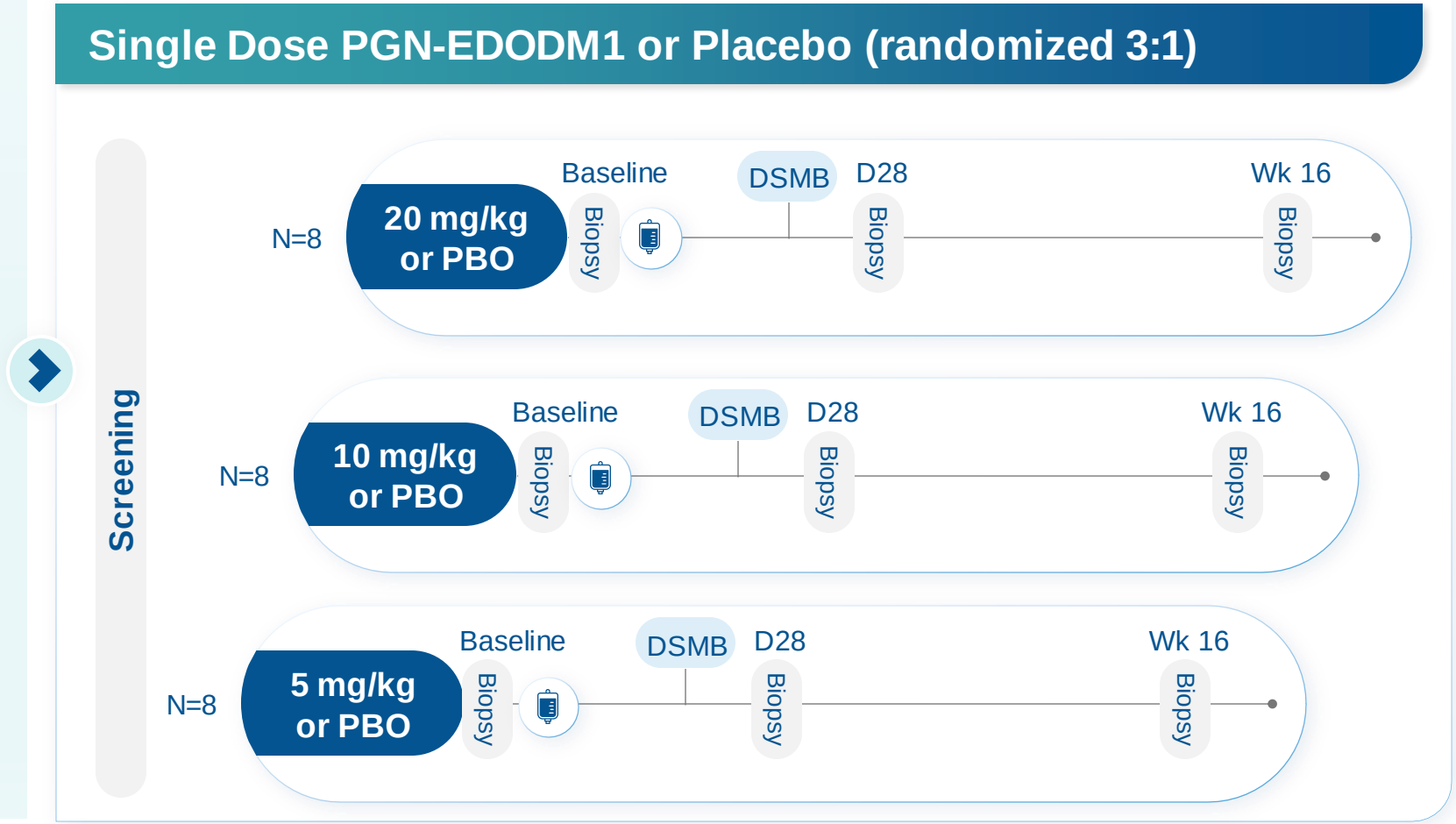
PD = pre-dose. * Data not collected. NHP Protocol: PGN-EDODM1 was administered to NHP (males and females) by IV infusion at 60 mg/kg over 60 min (n=5/sex) for 4 doses. Dosing schedule was once every 28 days. Male and female results were comparable with only male data presented. Shown as mean ± SD.

FREEDOM: Phase 1 PGN-EDODM1 Single-Ascending Dose (SAD) study

Freedom
DM1

FREEDOM 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
- Initial functional assessments, correction of mis-splicing and safety data anticipated in 2H:2024



PGN-EDODM1 clinical development path

Freedom DM1

FREEDOM2

Ongoing

Phase 1: Randomized, double-blind, placebo-controlled SAD study in patients
Open in USA, Canada & UK

Preliminary data read out expected in 2H:2024

Planned

Phase 2: Randomized, double-blind, placebo-controlled MAD study in patients
Multinational study

Initiation expected in 2H:2024

*Subject to alignment with regulatory authorities

FREEDOM will inform design of Phase 2 FREEDOM2 study

Freedom DM1

Open in USA, CANADA & UK

FREEDOM: Phase 1 SAD study

Preliminary data read out expected in 2H:2024

FREEDOM2

Multinational study planned

FREEDOM2: Phase 2 MAD study

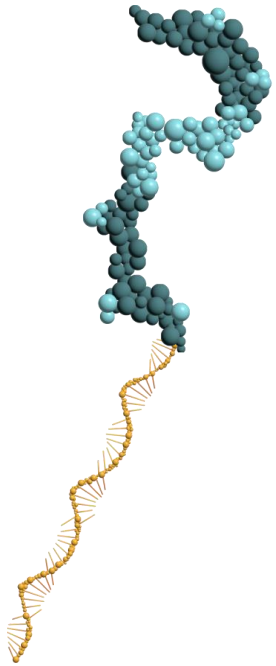
Initiation expected in 2H:2024; to be informed by Phase 1 safety data

- Randomized, double-blind, placebo-controlled trial
- IV administration of EDODM1 every 4 weeks up to 12 weeks
- Key anticipated readouts: Functional assessments, correction of mis-splicing, safety data

Conclusion

The future of PepGen: Building therapeutic area leadership in neuromuscular and neurological diseases

Cellular and nuclear delivery of EDOs



Deliver best-in-class transformative therapies for DMD and DM1 patients

- PGN-EDO51: Highest level of single-dose exon 51 skipping[1]
- PGN-EDODM1: Specific modulation of mutant DMPK transcript in the nucleus
- PGN-EDO53: 7X higher exon skipping than R6G-PMO53 comparator in NHPs

Near-term multi-billion dollar opportunity

Expand EDO platform to neuromuscular and neurological diseases

Long-term multi-billion dollar value

PepGen: Key clinical readouts for DMD and DM1 programs in 2024 with existing cash funding operations into 2026[1]

Key expected data read outs/milestones

PGN-EDO51
DMD Exon 51

- CONNECT1 preliminary dystrophin, exon skipping and safety data in DMD patients in mid-2024

PGN-EDODM1
DM1

- Preliminary data from FREEDOM in 2H:2024
  - Safety, splicing correction and functional assessments
- FREEDOM2 DM1 initiation in 2H:2024

PGN-EDO53
DMD Exon 53

- Advancing into IND/CTA enabling studies in 2024

Note: Clinical plans are subject to alignment with regulatory authorities. 1. Based on current operating plan