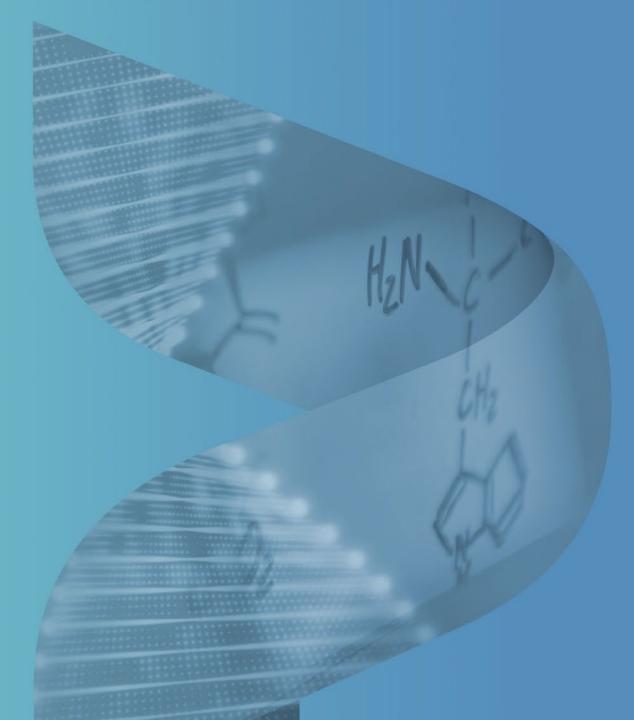


Empowering Oligonucleotide Therapeutics

Company Presentation January 2024



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Our vision

Transforming the lives of patients with severe neuromuscular and neurological diseases





PepGen: Empowering oligonucleotide therapeutics

DMD Program: EDO51

- 20-fold higher exon 51 skipping than naked oligo following a single dose in humans²
- Phase 2 CONNECT1-ED051 DMD patient MAD: Dystrophin readout mid-2024
- U.S. revenues of approved therapy (naked oligo): \$512M¹

DM1 Program: EDODM1

- Rx targets toxic DMPK RNA
- Multi-dose study demonstrates
 99% correction of splicing & myotonia in mice
- Human PK data supports EDO ability to achieve target PK
- US & Canada Phase 1 FREEDOM-DM1 study in DM1 patient SAD:
 Splicing & Functional readout in 2024

Company

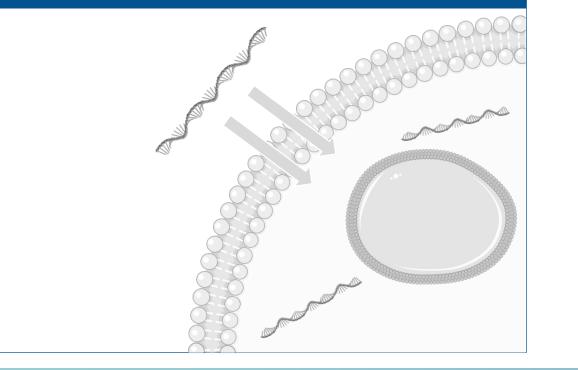
- Cash supports operations into 2025
- Boston based
- Robust IP portfolio on platform technology
- Compelling pipeline



DMD = Duchenne muscular dystrophy; DM1 = myotonic dystrophy type 1 1. EXONDYS 51® 2022 revenue from Sarepta 2022 10K filing, 2. Comparative statements are based on cross-trial comparisons with publicly-available data for other exon skipping approaches that have been assessed following a single dose in humans and following single and multiple doses in NHPs. PepGen's EDO platform is designed to address the delivery challenges that limit oligonucleotide therapeutics

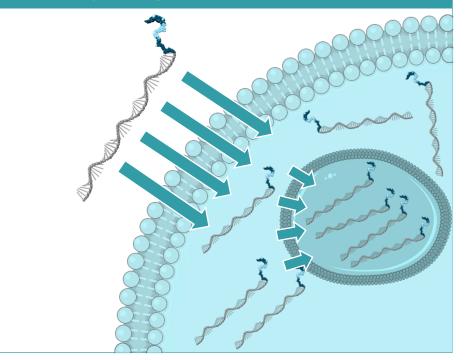
The Challenge of Oligonucleotides

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



PepGen's Enhanced Delivery Oligonucleotides (EDO) Solution

Our EDO platform results in up to 25-fold higher levels of nuclear delivery of oligonucleotide therapeutics





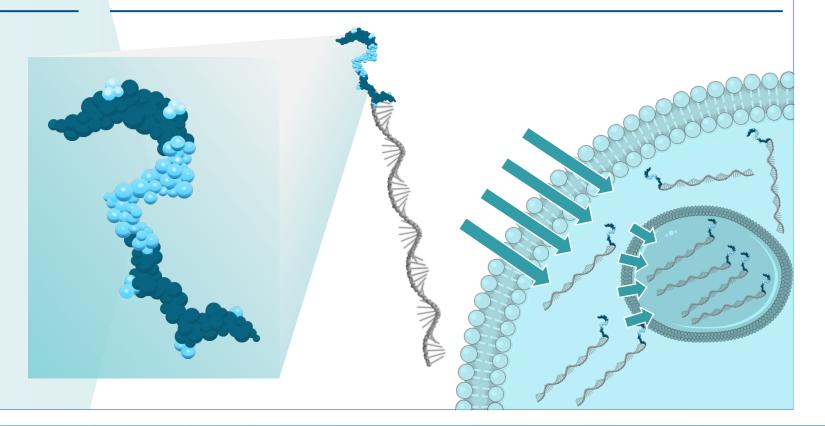
EDOs were designed to optimize delivery of therapeutic oligonucleotides

PepGen's EDO Peptides

Designed for enhanced uptake and improved tolerability

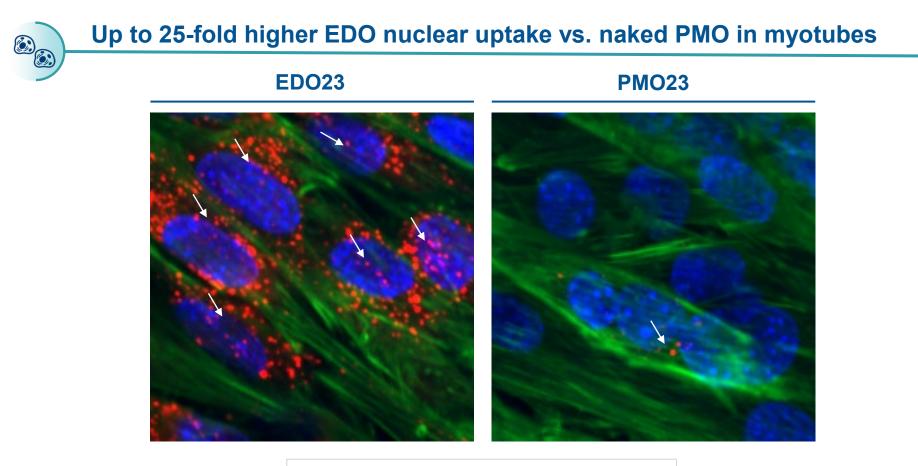
- Two poly-Arg domains where the number of arginines have been minimized are interspersed with non-natural amino acids to confer greater peptide stability
- Hydrophobic core coupled with poly-Arg domains contributes to endosomal escape
- Peptide sequence is linear with a length of less than 20 amino acids and is designed to be non-immunogenic

PepGen's EDOs Designed to increase nuclear uptake of oligos in muscle and other target tissues





EDO technology resulted in higher nuclear uptake of oligonucleotides vs. naked PMO in muscle cells



Green = actin Red = PMO/EDO Blue = nucleus



Note: 1. In vitro staining image is shown with 10µM conc. of EDO or PMO (naked oligonucleotide); 2. C2C12 mouse cells were differentiated for 4 days into myotubes and treated with fluorescently tagged compounds for 24h. Microscopy: Total spot intensity normalized to cellular or nuclear area (± s.d.). PMO: phosphorodiamidate morpholino oligonucleotide

PepGen's advanced pipeline enabled by EDO technology

PROGRAM	INDICATION TARGET	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	REGISTRA- TIONAL ¹
PGN-EDO51	Duchenne muscular dystrophy <i>Exon 51</i>					
PGN-EDODM1	Myotonic dystrophy type 1 ² DMPK					
PGN-EDO53	Duchenne muscular dystrophy <i>Exon 53</i>					
PGN-EDO45	Duchenne muscular dystrophy <i>Exon 45</i>					
PGN-EDO44	Duchenne muscular dystrophy Exon 44					
FUTURE PIPELINE OPPORTUNITIES						
Additional neuromuscular indications Neurologic indications						



1. A registrational study is designed to generate data to support a regulatory application, subject to alignment with regulatory authorities. 2. FREEDOM-DM1 study for PGN-EDODM1 has been approved in USA & Canada.

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

	EX	ON SKIPPING	DYSTROPHIN
		1 dose (HV)	>3 doses (patients)
PGN-EDO51 (Phase 2)	15 mg/kg	1.4%	
 Potential for greater dystrophin production Generally, well tolerated 	10 mg/kg	>6x1 >20x1 1.1%	CONNECT1 study
SRP-5051 (vesleteplirsen) Phase 2b – Sarepta Therapeutics	20 mg/kg	~0.18% ³	3.06% ³
EXONDYS 51® (eteplirsen) – Sarepta Therapeutics	30 mg/kg	<0.05%3	0.44%4

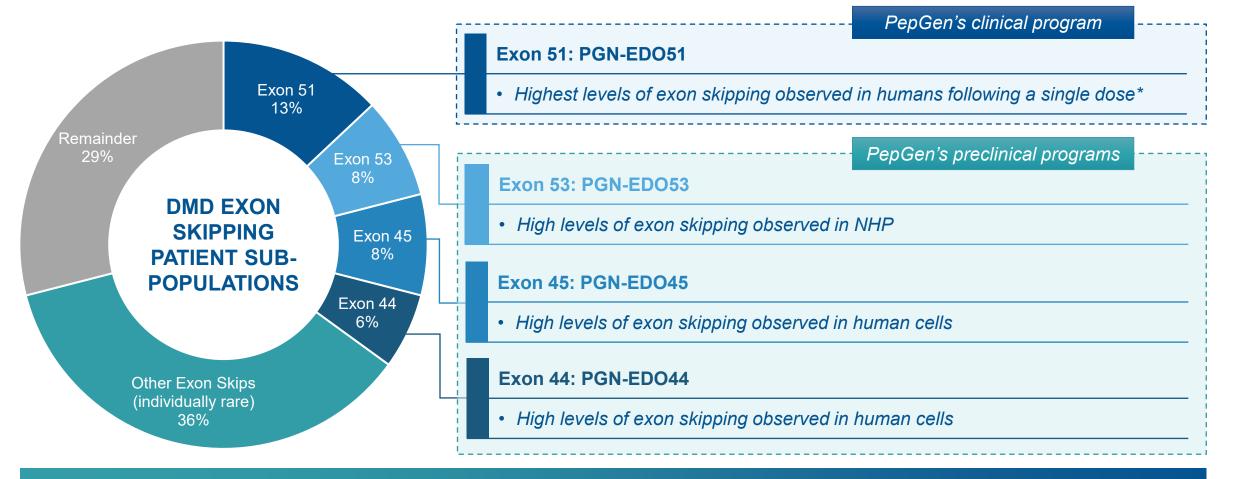


1. Comparative statements are based on cross-trial comparisons with publicly-available data for other exon skipping approaches that have been assessed following a single dose. 2. Source: Sarepta 2022 10K filing. 3.Source: Sarepta MOMENTUM study updates, 07Dec20 and 03May21. 4. Clinical data included in drug label (FDA).



PGN-EDO51 for Duchenne muscular dystrophy

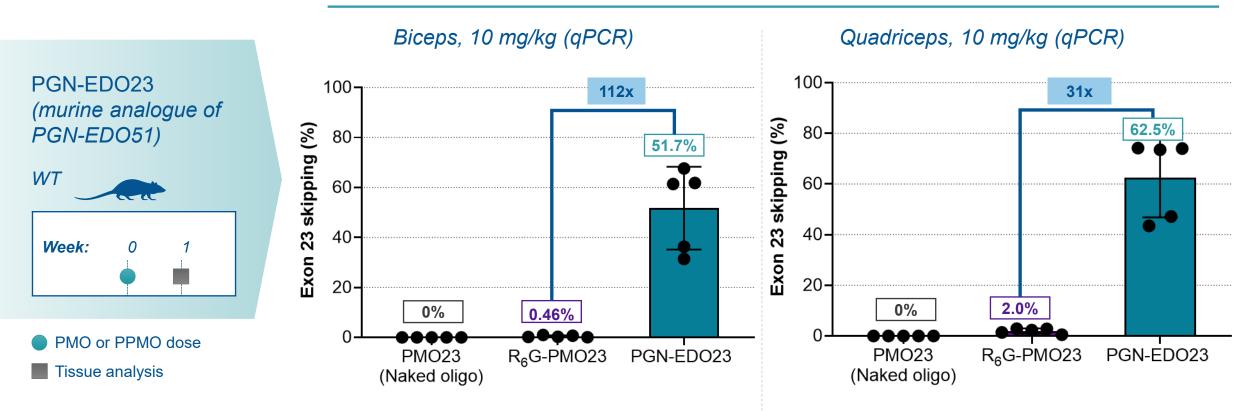
PepGen's lead program targets largest exon skipping patient population in DMD



We believe we have potential to address at least 35% of total DMD patient population amenable to exon skipping



EDO technology increases the potency of exon skipping oligonucleotides



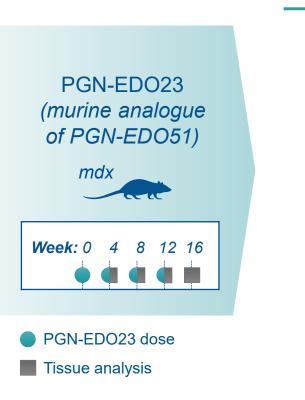
EXON SKIPPING



PPMO: Peptide phosphorodiamidate morpholino oligomers. Protocol: PMO23, PGN-EDO23 or R_6 G-PMO23 were administered a single intravenous (IV) 10 mg/kg dose to WT male mice; tissues collected 7 days after injection. Exon skipping was evaluated by qPCR. Graph plotted as mean ± SD, n = 5. R_6 G-PMO23 is believed to be structurally equivalent to the peptide component of SRP-5051 conjugated to a murine exon 23 skipping oligonucleotide.

Significant increase in dystrophin observed with repeat dosing

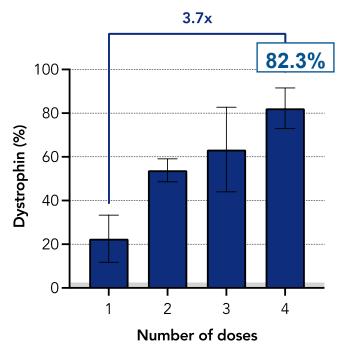
EXON SKIPPING



Biceps, 30 mg/kg, Q4W 1.7x 91.5% 100 80 Exon Skipping (%) 60 40 20 0 2 3 4 Number of doses

DYSTROPHIN



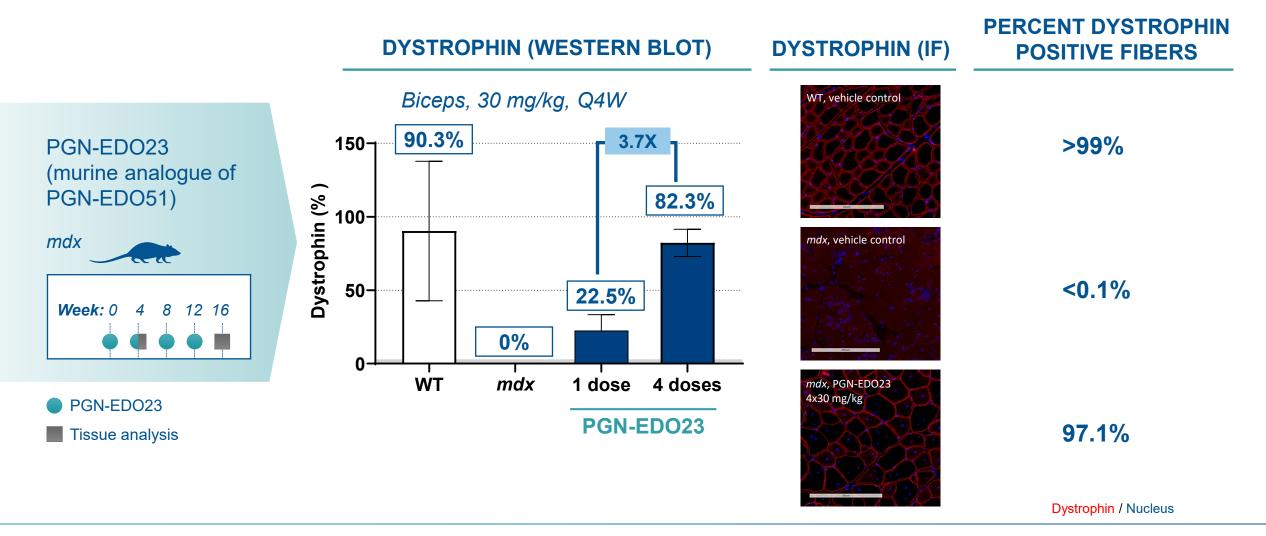


We believe these findings support Q4W dosing in the clinic



Protocol: mdx mice received 2, 3 or 4 doses, with 4-week intervals between doses. Tissue samples were collected 4 weeks post-each dose at time points indicated. Exon skipping was evaluated by RT-PCR and dystrophin was measured by western blot. Graph is presented as mean ± SD; n = 4-5 per cohort; grey band is dystrophin LLOQ (2.5%).

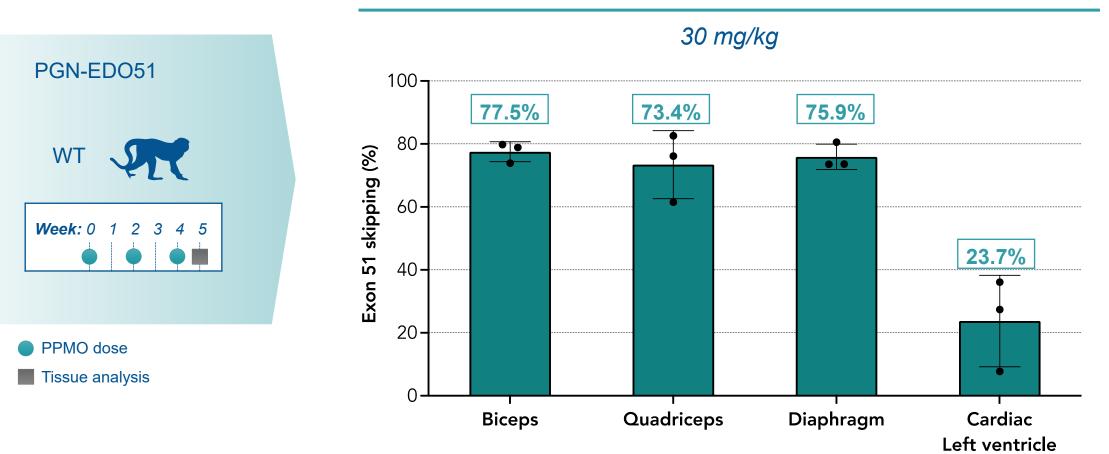
Significant increase in dystrophin that was uniformly distributed across muscle





Protocol: mdx mice received 1 or 4 doses of PGN-EDO23, with 4-week intervals between doses. Tissue samples were collected 4 weeks post-each dose. Dystrophin protein evaluation 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%).

NHP: Q2W repeat dose exon skipping levels of >70% observed in skeletal muscles and diaphragm at 30 mg/kg

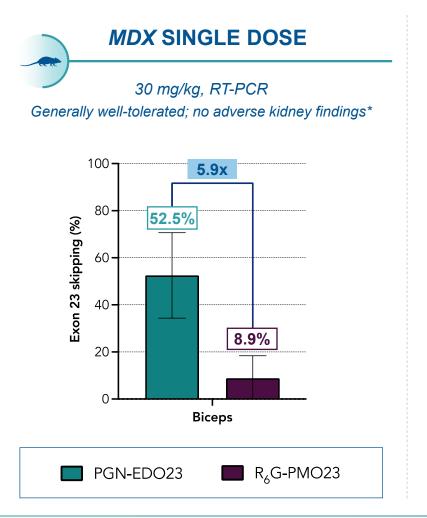


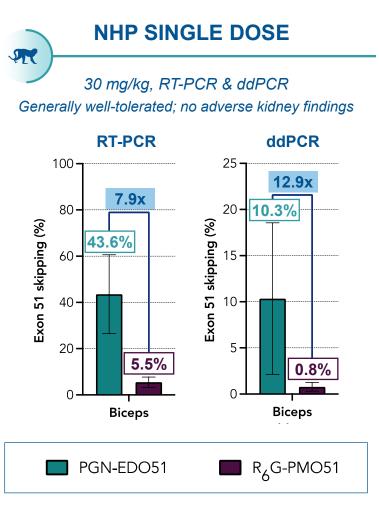
EXON SKIPPING

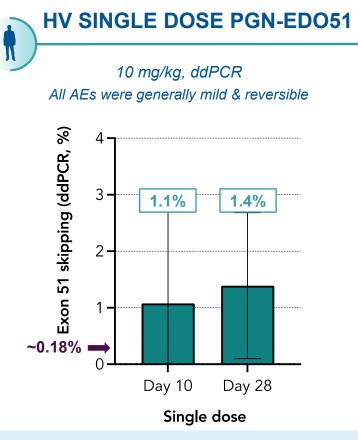


Protocol: Three doses of PGN-EDO51 were administered by IV over 30 min every two weeks (n=3). Tissues were harvested 7 days after final administration. Shown as mean ± SD; n = 3 per group. Study was not powered for statistical significance.

Consistent potency of EDO platform: mouse → NHP → human







~6x higher than previously reported exon 51 skipping approaches following a single dose



Mdx protocol: PGN-EDO23 and R6G-PMO23 were administered to mdx mice via a single bolus IV injection. Tissues were harvested after four weeks and exon skipping was analyzed via RT-PCR. Data presented as mean ± SD; n = 4 per group. *Tolerability statement supported by single dose GLP study conducted in WT mice. SRP-5051 20 mg/kg HV data from Momentum update, 07Dec20 (comparative statements for human data are based on cross-trial comparisons). R₆G-PMO51 is believed to be structurally equivalent to SRP-5051, R₆G-PMO23 utilizes the murine exon 23 skipping oligo

Highest levels of exon 51 skipping in humans following a single dose of PGN-EDO51

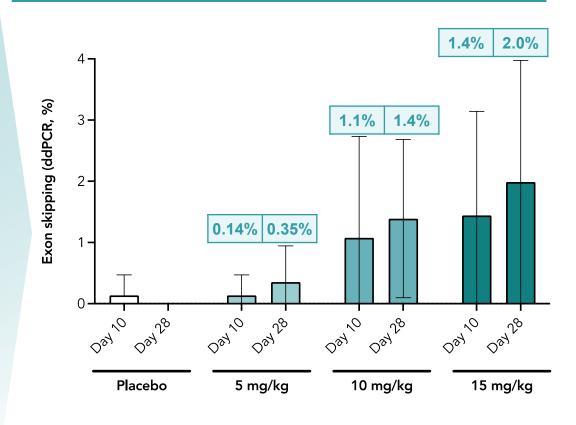
Biopsy

D28

PH1 HEALTHY NORMAL VOLUNTEER (HNV) TRIAL DESIGN

 Study population: Healthy adult Biopsy 15 mg/kg males (n = 32; 8 per cohort, 3:1 or PBO PGN-EDO51:placebo) D10 N=8 Dosing: Single dose, IV administration Biopsy Biopsy Dose escalation occurred after 10 mg/kg or PBO safety committee review Biceps biopsies conducted on N=8 D10 D28 Day 10 and Day 28 Biopsy Biopsy 5 mg/kg or **PBO** N=8 D10 D28 Biopsy Biopsy 1 mg/kg or **PBO** D10 D28 N=8

TRIAL RESULTS: EXON SKIPPING (BICEPS)

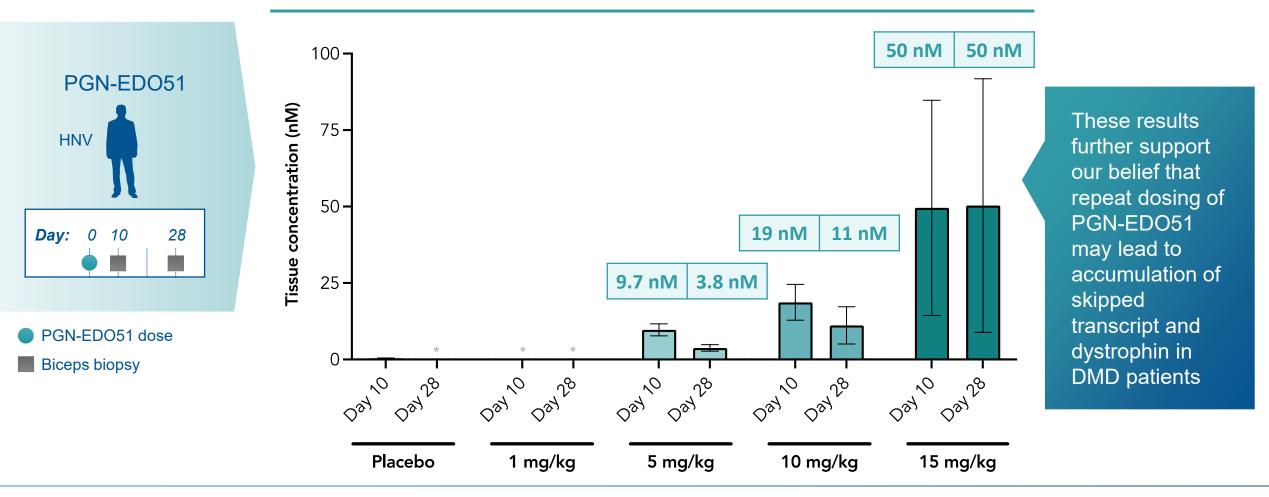




Protocol PGN-EDO51-101: Phase 1, first in human, randomized double blind, placebo controlled single ascending dose study in healthy adult volunteers. Single dose of either PGN-EDO51 or Placebo were administered by IV infusion at doses indicated. Participants were followed for 28-day period following dose administration to evaluate safety, tolerability, PK, and PD. Needle biopsies of biceps muscle were taken on Day 10 and 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).

HNV: High, persistent tissue concentrations of oligonucleotide were observed

TISSUE CONCENTRATION (BICEPS)

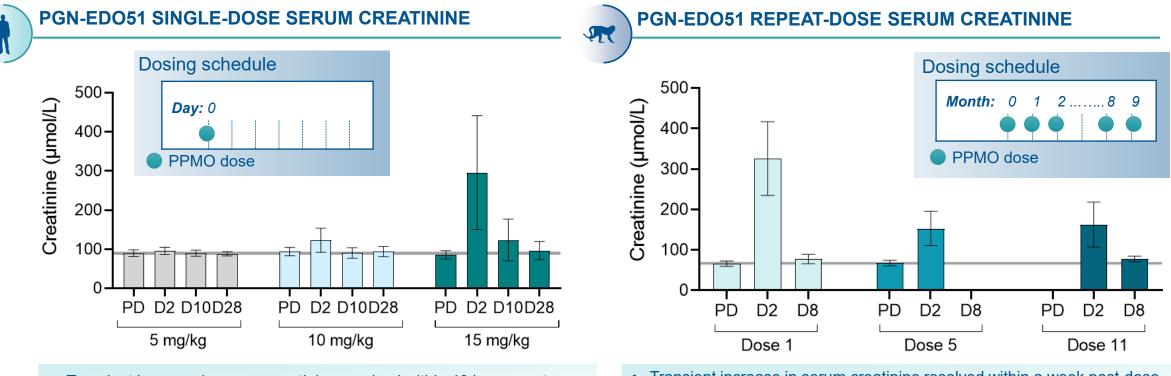




Protocol PGN-EDO51-101: Phase 1, first in human, randomized double blind, placebo controlled single ascending dose study in healthy adult volunteers. Single dose of either PGN-EDO51 or Placebo were administered by IV infusion at doses indicated. Participants were followed for 28 day period following dose administration to evaluate safety, tolerability, PK, and PD. Needle biopsies of biceps muscle were taken on Day 10 and Day 28. Tissue concentration measured by ELISA. Shown as mean ± SD; n = 6 PGN-EDO51: 2 Placebo per cohort (n = 5 for D10 at 15 mg/kg. Asterix indicates that values were under the lower limit of quantitation.

Changes in creatinine are transient and are minimal with repeat dosing

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

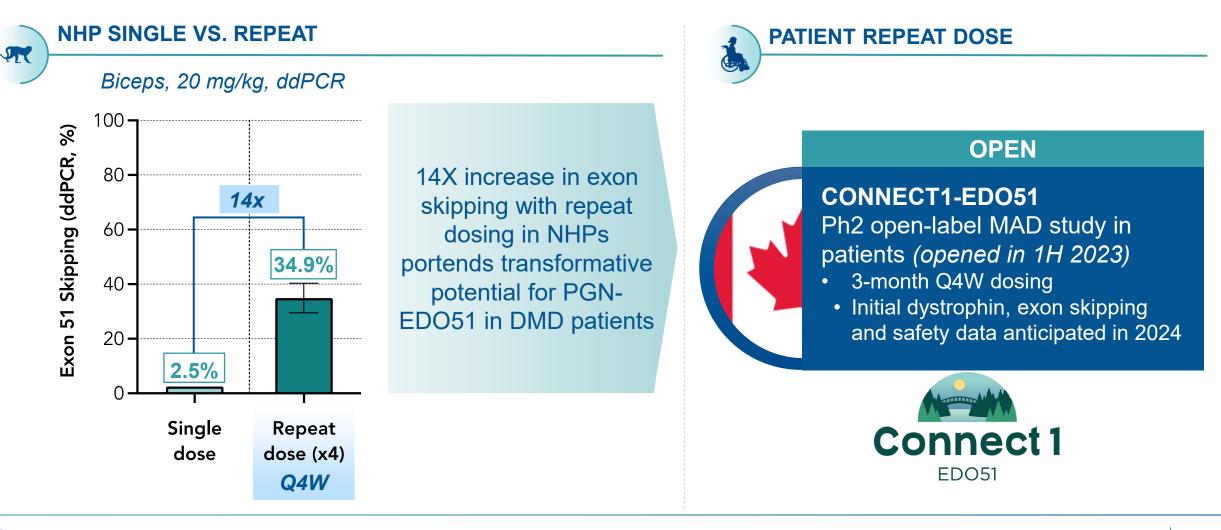


- Transient increase in serum creatinine resolved within 48 hours postdose in the majority of HVs
- No clinical symptoms of acute kidney injury
- No hematologic, cardiovascular or hepatic clinical signs or symptoms

- Transient increase in serum creatinine resolved within a week post-dose
- No adverse findings in the kidney even after 11 doses at all dose levels tested
- No notable hematologic, cardiovascular or hepatic effects



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



PepGen[®]

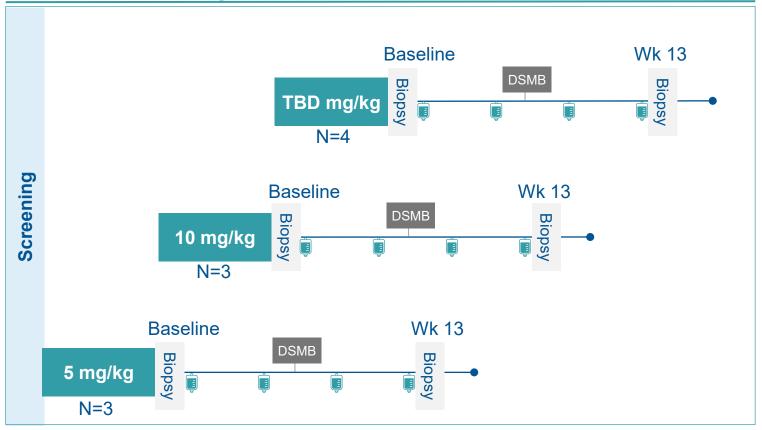
NHP protocol: Single (30 min) or repeat (60 min) IV doses with PGN-EDO51 were administered in male NHP. For repeat dose evaluation, NHP received 4 doses with 4-week intervals between doses. Tissue samples were collected 1-week post-final dose as indicated on graphs. Exon skipping was assessed by ddPCR.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

CONNECT1 Phase 2 PGN-EDO51 MAD study



CONNECT1 study overview

- Open label study in DMD patients
- Study is open in Canada
- IV administration of PGN-EDO51 every 4 weeks
- Muscle biopsies at baseline and week 13
- Key endpoints: Safety biomarkers, dystrophin, exon skipping
- Data expected in 2024



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

PGN-EDO51 dose



Two PGN-EDO51 Phase 2 MAD studies in 2024



PLANNED



CONNECT2-EDO51

Ph2 randomized, double-blind, placebo-controlled MAD study in patients



- 6-month Q4W repeat dosing
- Exon skipping, dystrophin and safety data
- Functional measures
- Designed to provide potential path to accelerated approval





PGN-EDODM1 for myotonic dystrophy type 1 (DM1)

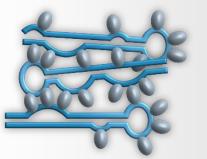
PepGen's novel therapeutic approach to DM1

DM1 PATHOLOGY

DMPK transcript CUG repeat hairpin loops bind MBNL1 and form cross-linked foci

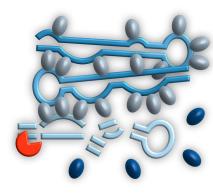


Expanding toxic foci trap more MBNL1



DMPK DEGRADATION

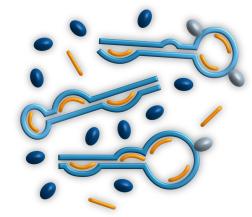
ASO / siRNA degrade *DMPK* transcript to reduce toxic foci



- Treatment results in non-specific degradation of *DMPK* transcript; potential risk of haploinsufficiency
- Correlation between level of knockdown and level of splicing correction is uncertain

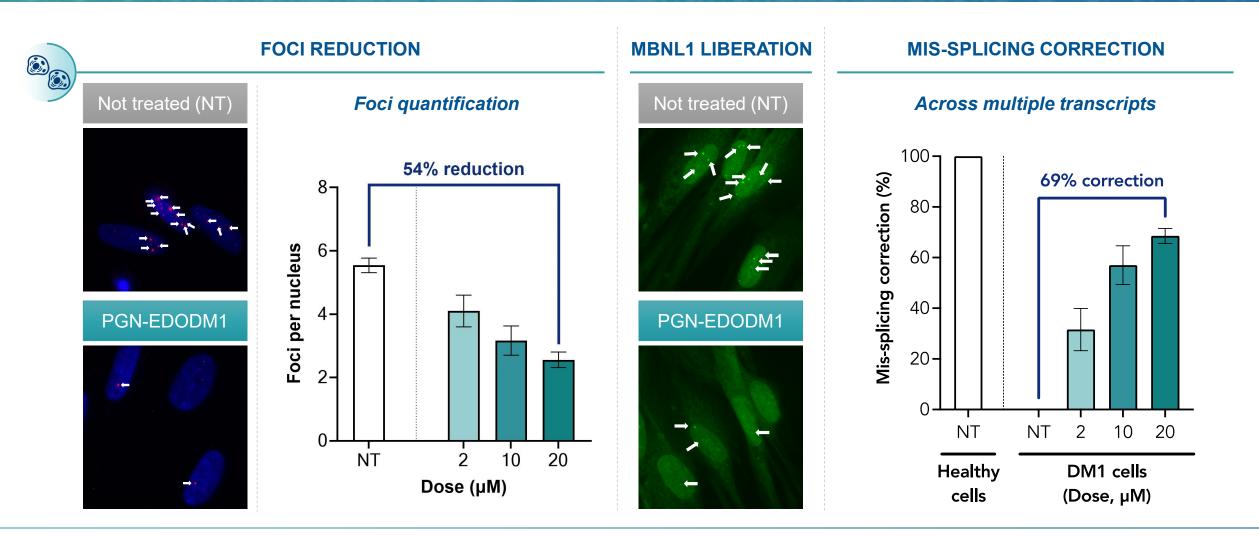
DMPK COMPETITION

PGN-EDODM1 binds *DMPK* transcript, reducing toxic foci



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

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

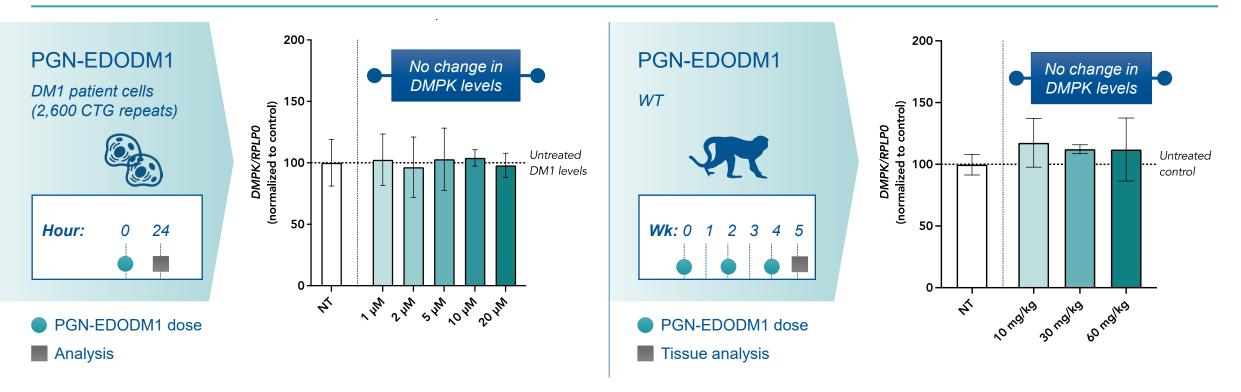




Immortalized myoblasts from healthy individual or DM1 patient with 2600 CTG repeats were cultured then differentiated for 4 days into myotubes. Treatment with peptide-PMO conjugates at concentrations given. Cells were harvested for analysis 24h after treatment. RNA isolation, RT-PCR and capillary electrophoresis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

Our DMPK competition mechanism of action does not degrade DMPK

DMPK TRANSCRIPT LEVELS

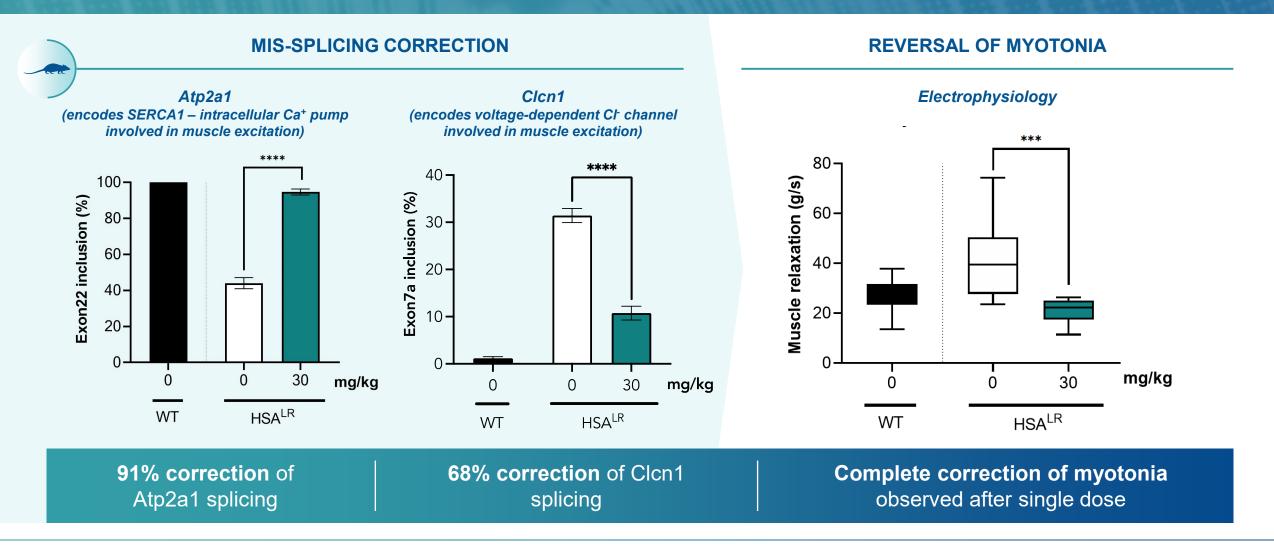


DMPK transcript levels remained unchanged across multiple preclinical models



In vitro: Immortalized myoblasts from DM1 patient with 2600 CTG repeats were differentiated for 4 days to myotubes and treated for 24h hours with PGN-EDODM1 from 1-20 µM. NT = not treated. DMPK transcript levels were evaluated by qPCR and normalized to RPLP0. Graphs plotted as mean ± SD, n=3-4. NHP: PGN-EDODM1 was administered to NHPs at the doses and regimen indicated. DMPK transcript levels were evaluated by RT-PCR and normalized to RPLP0. Graphs plotted as mean ± SD, n=4. NT = not treated. RPLP0 Ribosomal Protein Large, P0.

PGN-EDODM1 achieved >68% correction of mis-splicing and complete reversal of myotonia with a single dose in HSA^{LR} mice





Protocol: PGN-EDODM1 was administered IV to HSA^{LR} mice at 30 mg/kg (n=8) against a saline control (n=16) and wild-type (WT) saline control (n=8). Myotonia assessed, tissues harvested 2 weeks post-administration. Mis-splicing data is quadriceps. Mean \pm SEM or min to max. **** = p≤0.0001; *** = p≤0.001. Mis-splicing correction of Mbnl1 was also assessed

PGN-EDODM1 corrected movement disorder of DM1 mouse model

UNTREATED HSALR



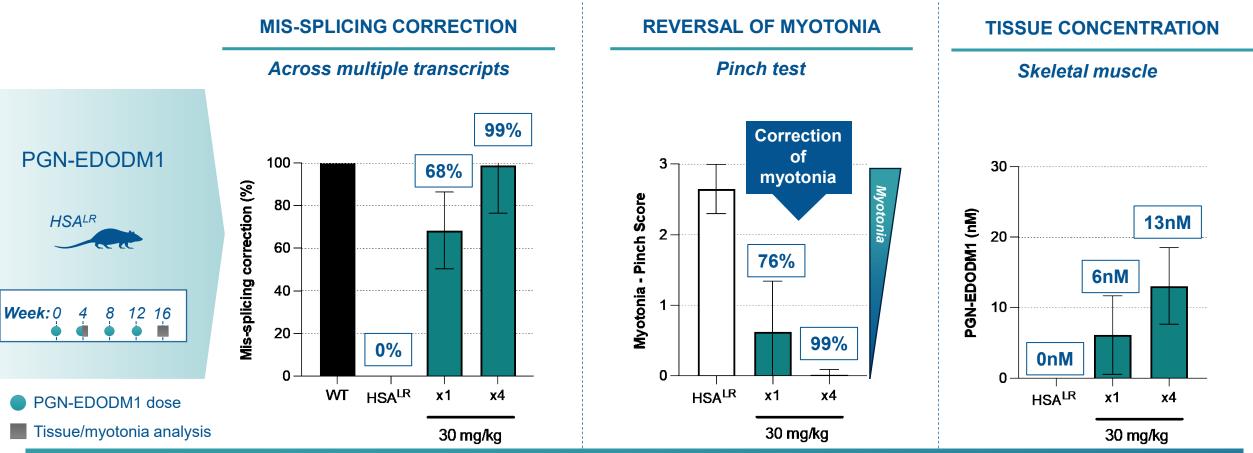
TREATED HSALR





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

Significant improvement of DM1 pathology with a single dose further increased with repeat dosing



EDO technology 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 in FREEDOM DM1



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.

FREEDOM-DM1 clinical development strategy



OPEN in USA, CANADA & UK

FREEDOM-DM1: PHASE 1 Single ascending dose (SAD): Interim data readout expected in 2024

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



FREEDOM-DM1: Phase 1 PGN-EDODM1 SAD study

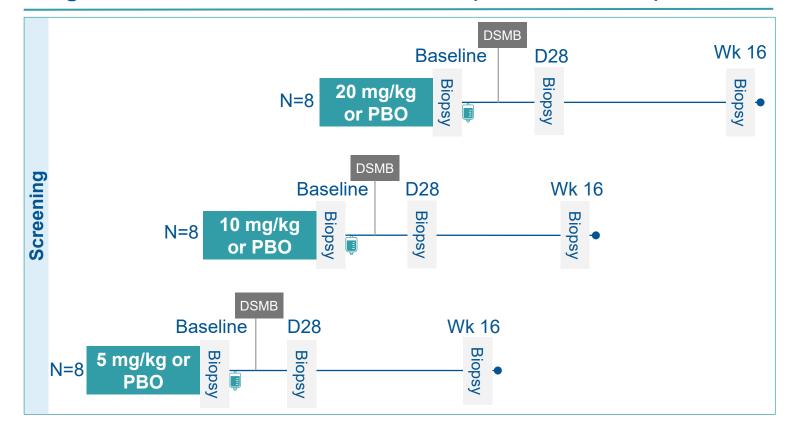


FREEDOM-DM1 study overview

- Ph1 global, randomized, doubleblind, placebo-controlled SAD study in patients
- Single IV administration of PGN-EDODM1
- Muscle biopsies at baseline, day 28, week 16
- Initial functional assessments, correction of mis-splicing and safety data anticipated in 2024

PBO[,] Placebo

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



PGN-EDODM1 dose

31

FREEDOM-DM1 will inform Phase 2 MAD study

OPEN in USA & CANADA & UK

FREEDOM-DM1: PHASE 1 Single ascending dose (SAD): Interim data read out expected in 2024

- To be conducted in DM1 patients
- Randomized, double-blind, placebo-controlled trial
- Key anticipated readouts: Functional assessments, correction of mis-splicing, safety data



GLOBAL STUDY PLAN

PHASE 2 MAD study (designed to support discussions for potential regulatory approvals)

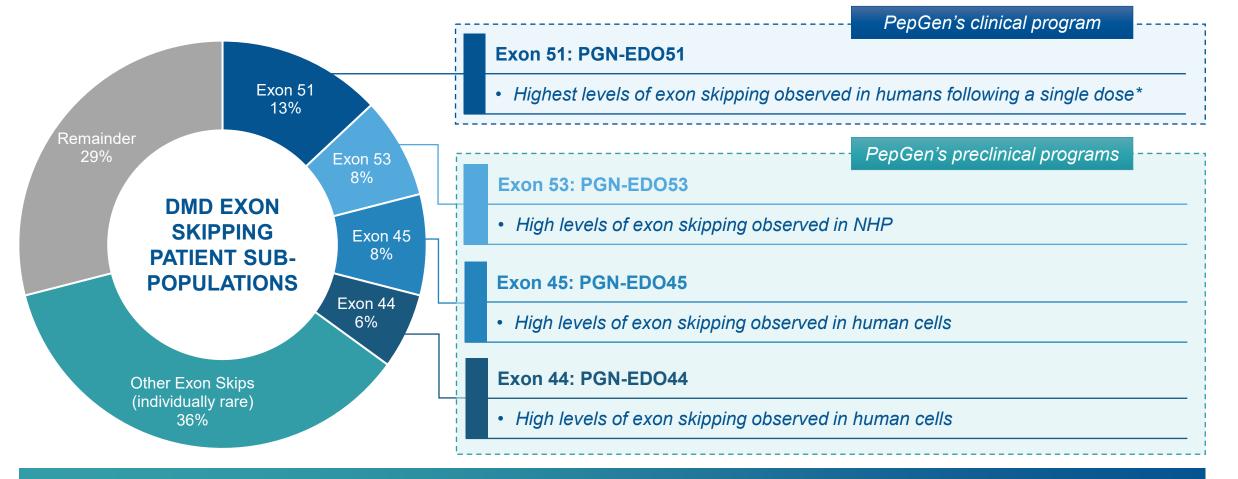
- To be informed by Phase 1 safety data
- 3-month study followed by LTE in DM1 patients
- Randomized, double-blind, placebo-controlled trial
- Key anticipated readouts: Functional assessments, correction of mis-splicing, safety data





EDO preclinical stage pipeline

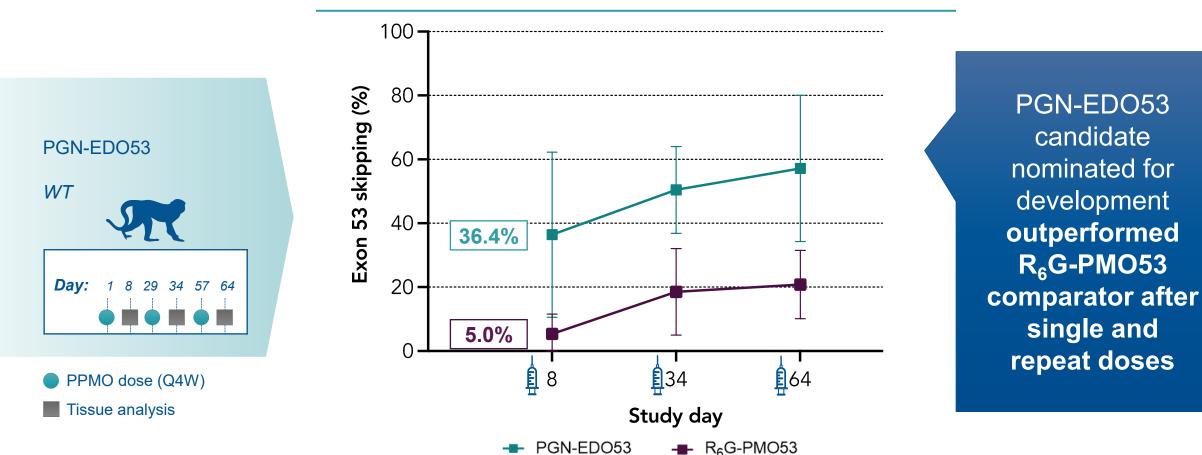
PepGen's lead program targets largest exon skipping patient population in DMD



We believe we have potential to address at least 35% of total DMD patient population amenable to exon skipping



Single-dose exon skipping levels for PGN-EDO53 almost 7X higher than for R6G-PMO53 comparator in NHPs



BICEPS (30 mg/kg)



Protocol: PGN-EDO53 and R_6 G-PMO53 were administered to NHP by IV infusion over 60 min (n=3). Q4W, three doses administered, PBS control. Biopsies taken 5 - 7 days after first and second administration; terminal samples collected 7 days after final dose. Study not powered for statistical significance. Data shown as mean ± SD; n = 3 per group. R_6 G-PMO53 was selected as a relevant comparator PPMO approach.



Conclusion

Pepgen: Transformational technology & key clinical readouts in DMD and DM1 programs in 2024 with cash funding operations into 2025

Key data read outs in 2024

PGN-EDO51 DMD Exon 51	Highest level of single-dose exon skipping & oligo delivery in humans ¹	 Dystrophin, exon skipping and safety data in DMD patients in mid-2024 			
PGN-EDODM1 DM1	Differentiated approach with robust preclinical dataset	 Functional assessments, correction of mis-splicing, safety data in DM1 patients 			
 Preclinical Pipeline • Five neuromuscular disease candidates in pipeline • Work underway to leverage EDO platform to expand to new tissues and new indications 					

PepGen