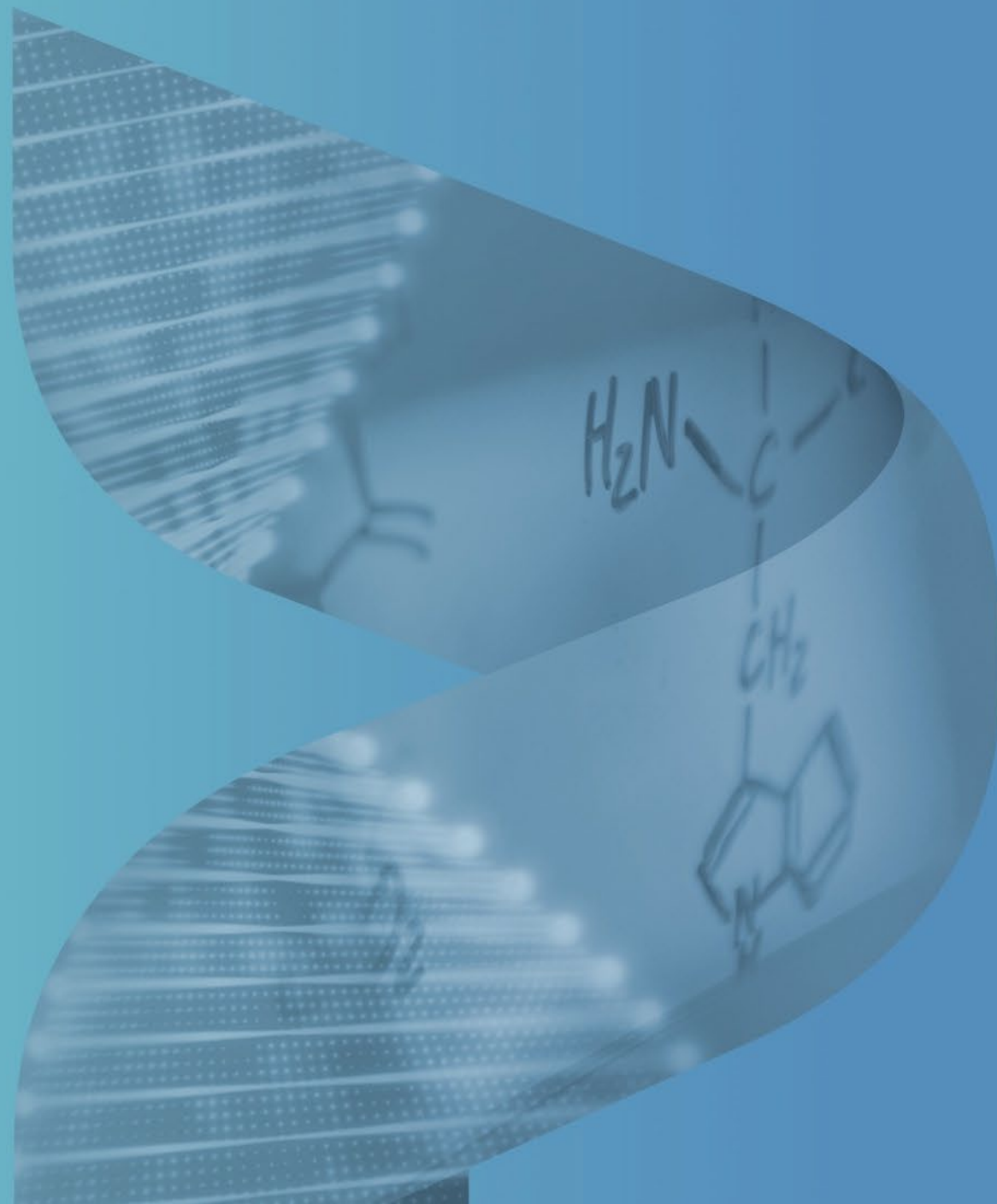




Empowering Oligonucleotide Therapeutics

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-EDO51 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**

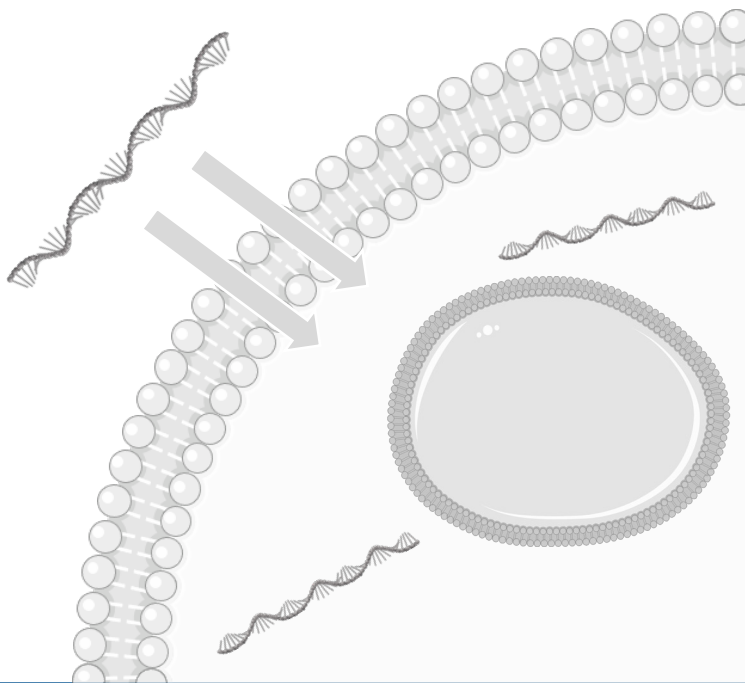
Company

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

PepGen's EDO platform is designed to address the delivery challenges that limit oligonucleotide therapeutics

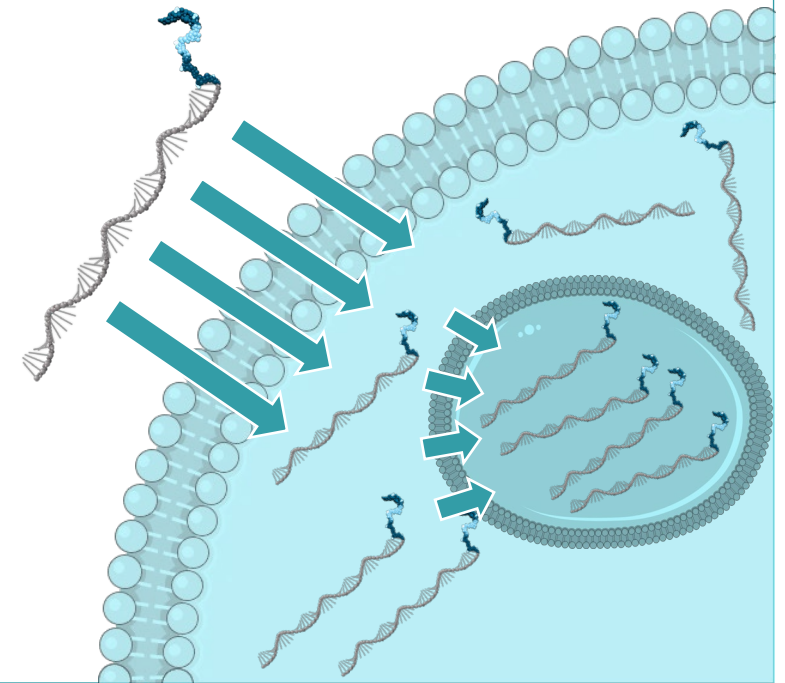
The Challenge of Oligonucleotides

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

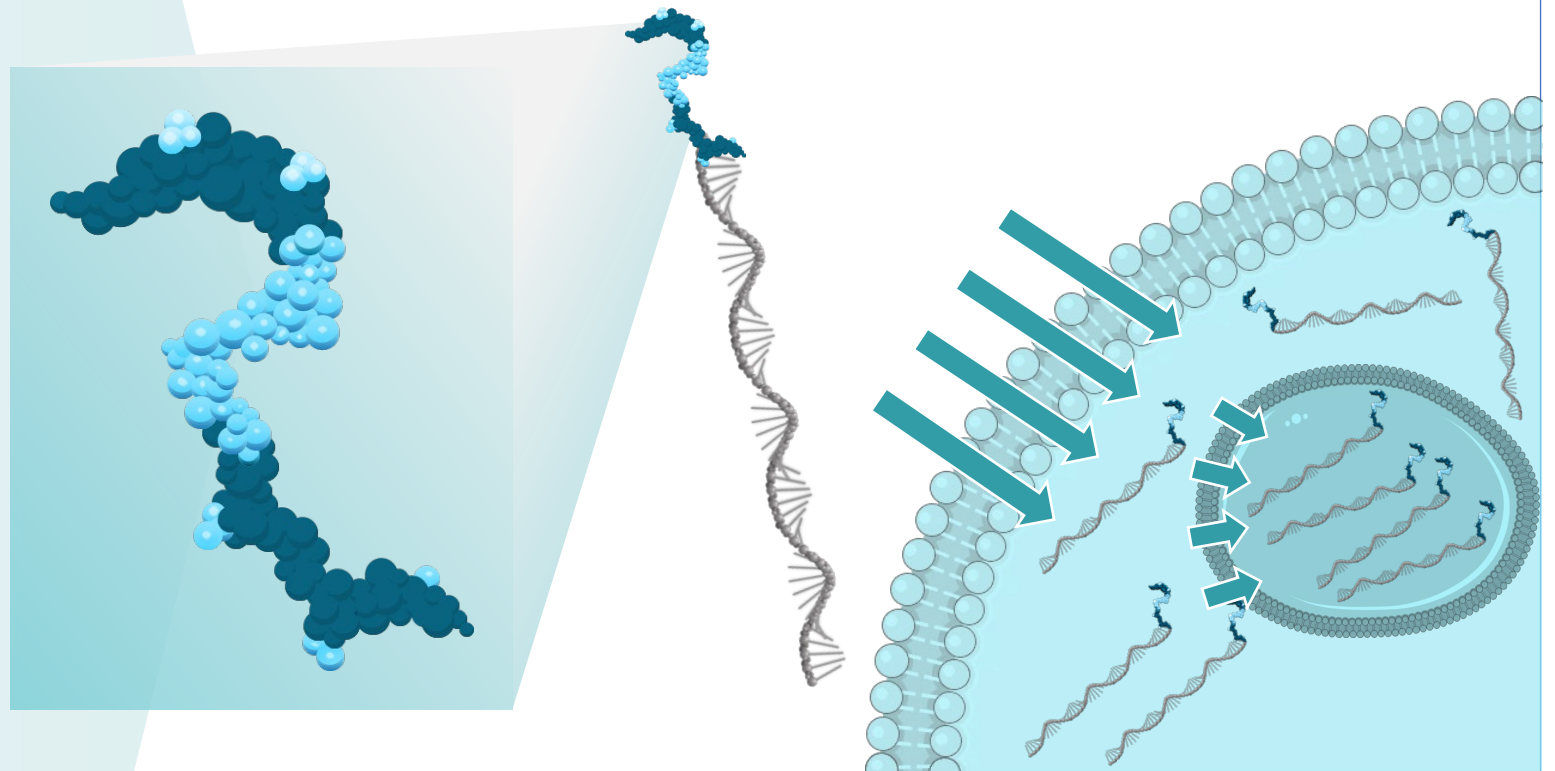
PepGen's EDO Peptides

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

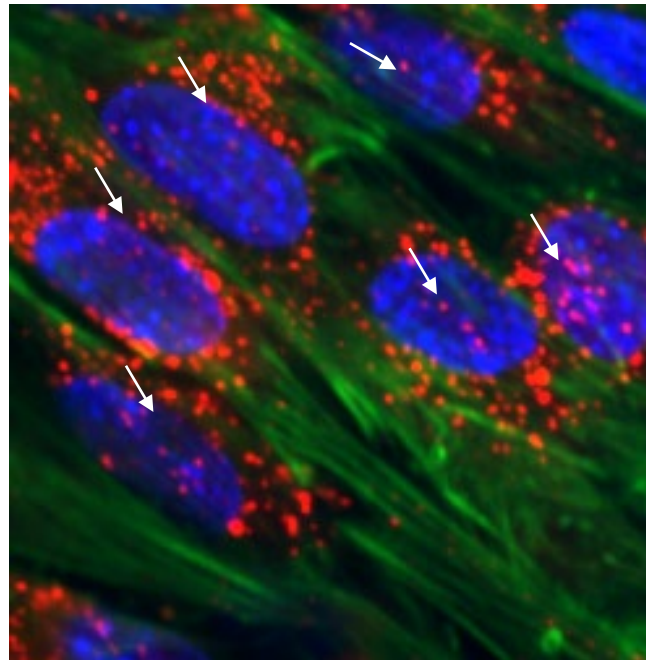


EDO technology resulted in higher nuclear uptake of oligonucleotides vs. naked PMO in muscle cells

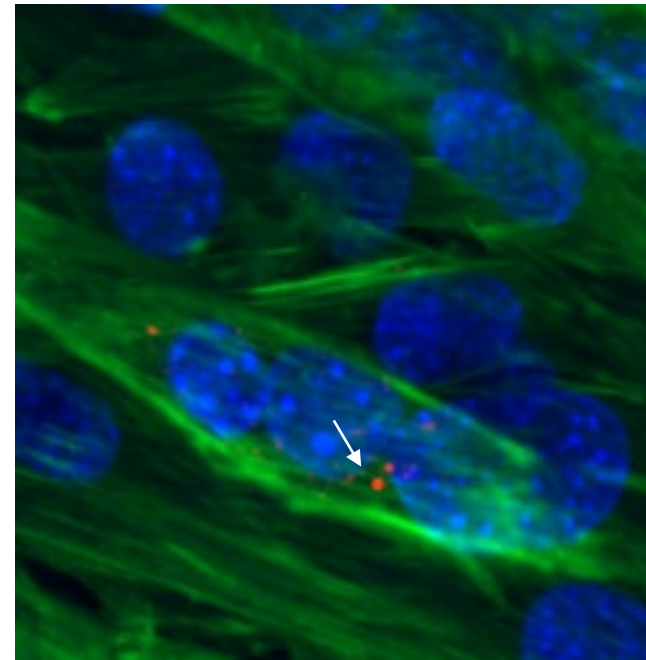


Up to 25-fold higher EDO nuclear uptake vs. naked PMO in myotubes

EDO23



PMO23



Green = actin Red = PMO/EDO Blue = nucleus

PepGen's advanced pipeline enabled by EDO technology

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

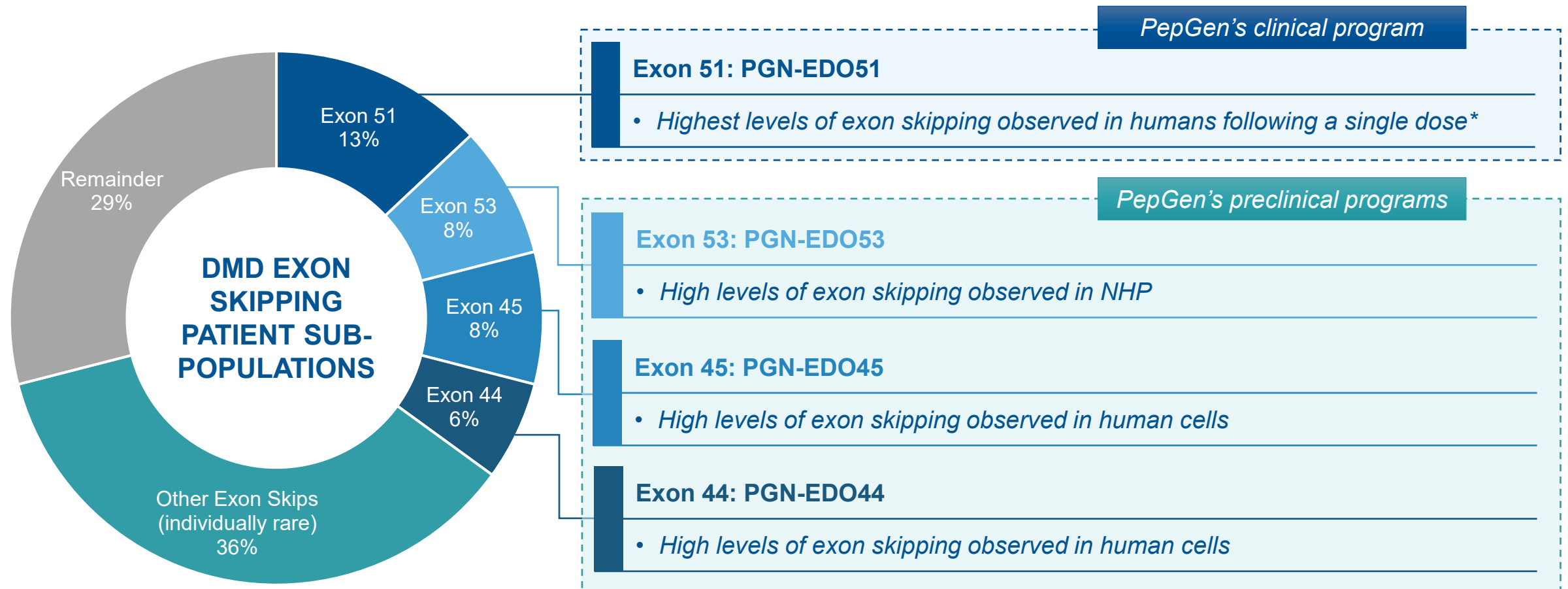
We believe that our delivery platform has the power to unlock the therapeutic potential of oligonucleotides

	<u>EXON SKIPPING</u>		<u>DYSTROPHIN</u>
	<i>1 dose (HV)</i>		<i>>3 doses (patients)</i>
PGN-EDO51 (Phase 2) <ul style="list-style-type: none"> Potential for greater dystrophin production Generally, well tolerated 	15 mg/kg	1.4%	CONNECT1 study
	10 mg/kg	$>6\times^1$ 1.1%	
SRP-5051 (vesleteplirsen) Phase 2b – Sarepta Therapeutics	20 mg/kg	$\sim 0.18\%^3$	$3.06\%^3$
EXONDYS 51® (eteplirsen) – Sarepta Therapeutics	30 mg/kg	$<0.05\%^3$	$0.44\%^4$



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

PGN-EDO23
(murine analogue of
PGN-EDO51)

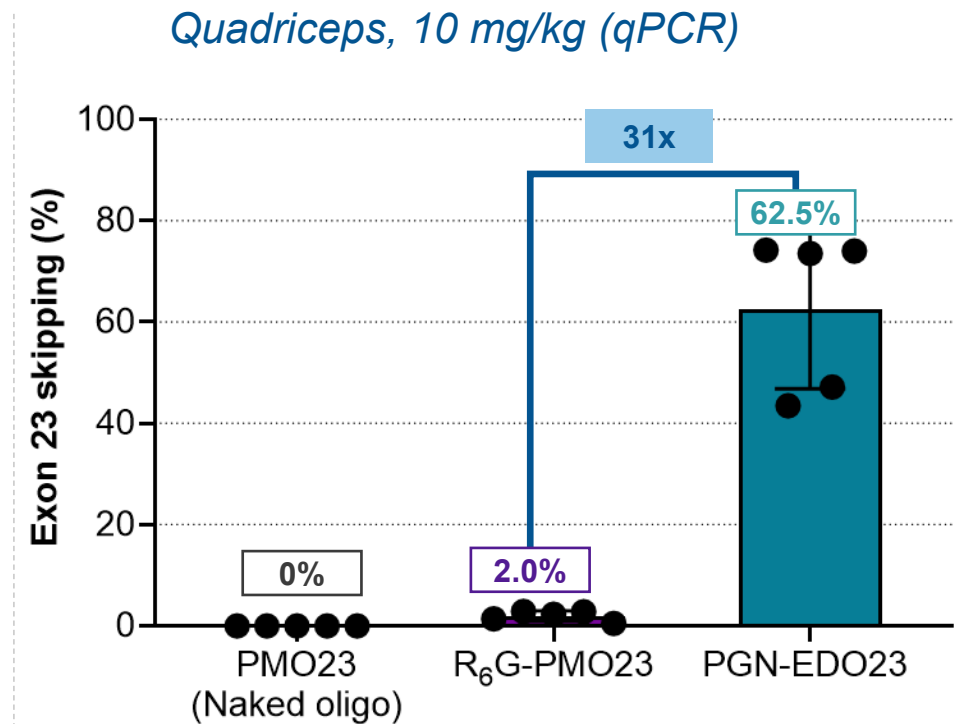
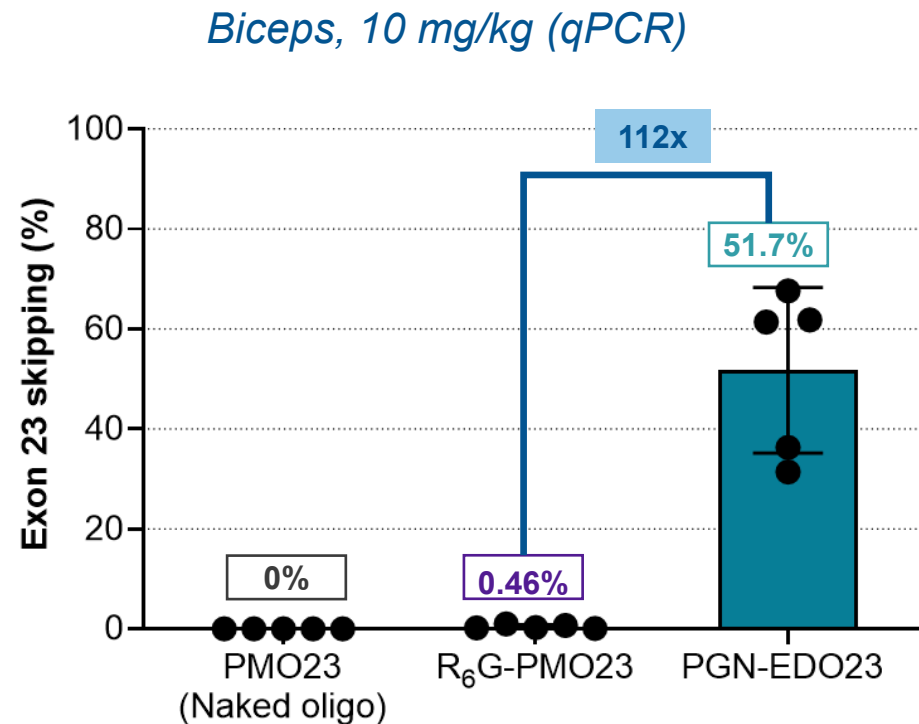
WT



Week: 0 1

● PMO or PPMO dose

■ Tissue analysis



Significant increase in dystrophin observed with repeat dosing

PGN-EDO23
(murine analogue
of PGN-EDO51)



Week: 0 4 8 12 16

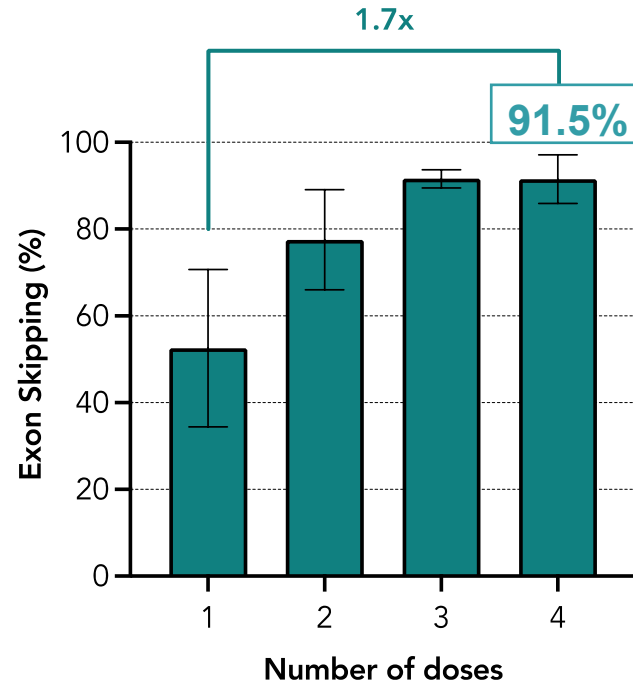


● PGN-EDO23 dose

■ Tissue analysis

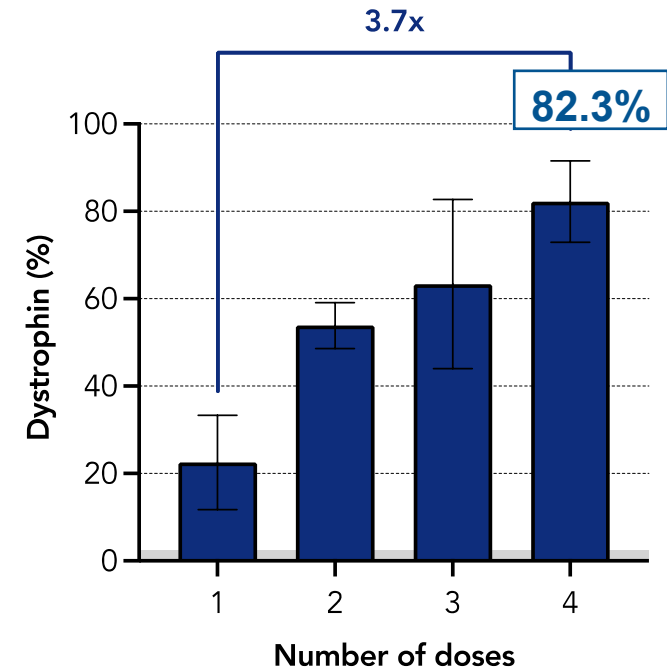
EXON SKIPPING

Biceps, 30 mg/kg, Q4W



DYSTROPHIN

Biceps, 30 mg/kg, Q4W



We believe these findings support Q4W dosing in the clinic

Significant increase in dystrophin that was uniformly distributed across muscle

PGN-EDO23
(murine analogue of
PGN-EDO51)

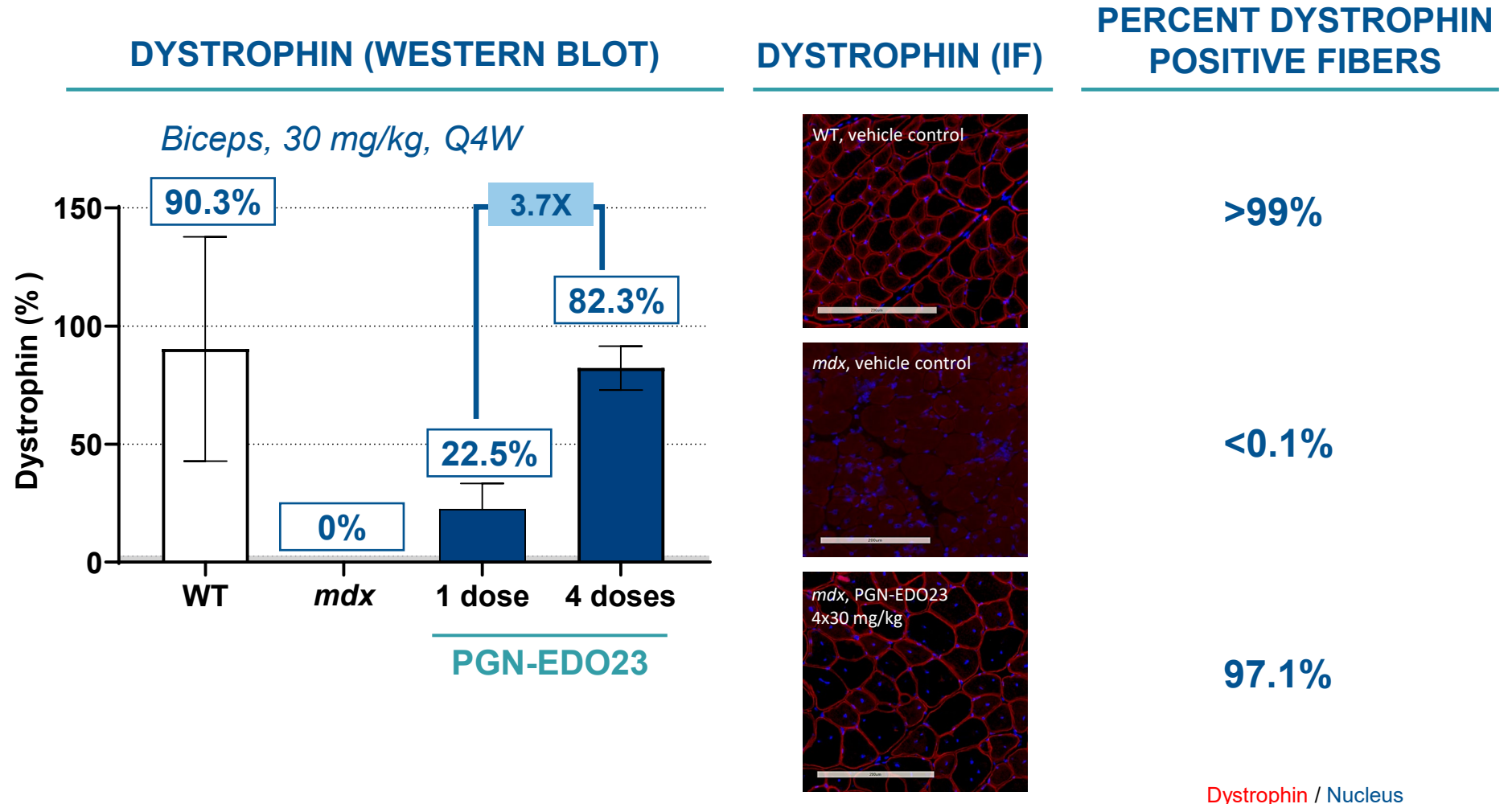
mdx



Week: 0 4 8 12 16



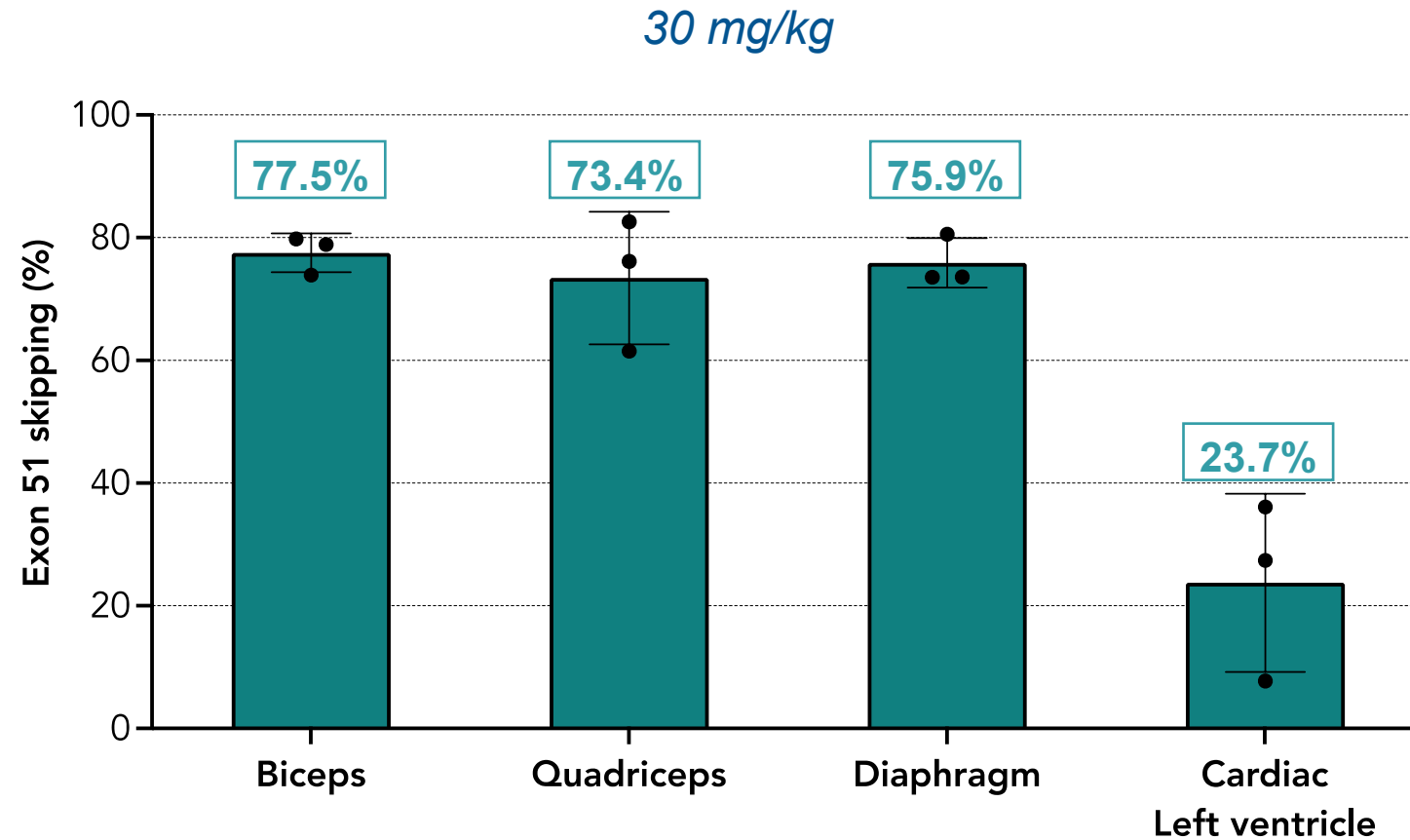
- PGN-EDO23
- Tissue analysis



Dystrophin / Nucleus

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

EXON SKIPPING



PGN-EDO51

WT



Week: 0 1 2 3 4 5



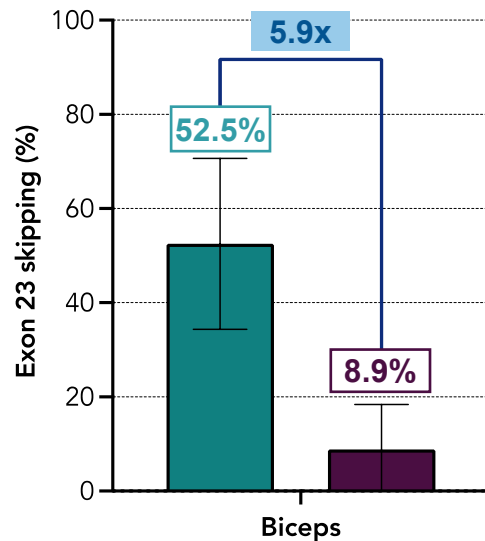
- PPMO dose
- Tissue analysis

Consistent potency of EDO platform: mouse → NHP → human

MDX SINGLE DOSE

30 mg/kg, RT-PCR

Generally well-tolerated; no adverse kidney findings*

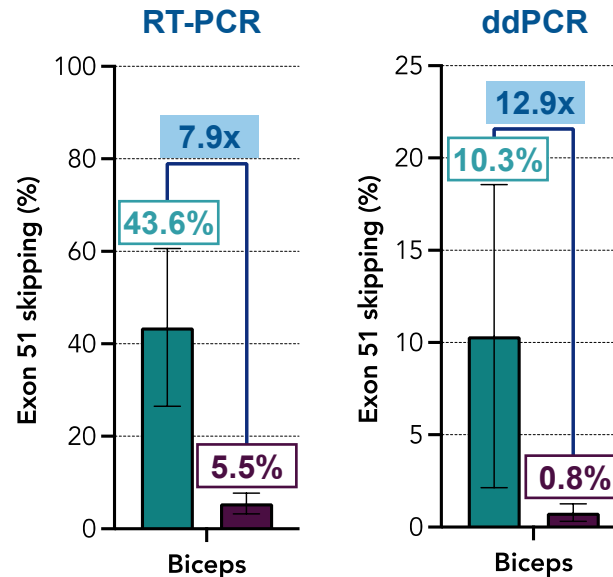


PGN-EDO23 R₆G-PMO23

NHP SINGLE DOSE

30 mg/kg, RT-PCR & ddPCR

Generally well-tolerated; no adverse kidney findings

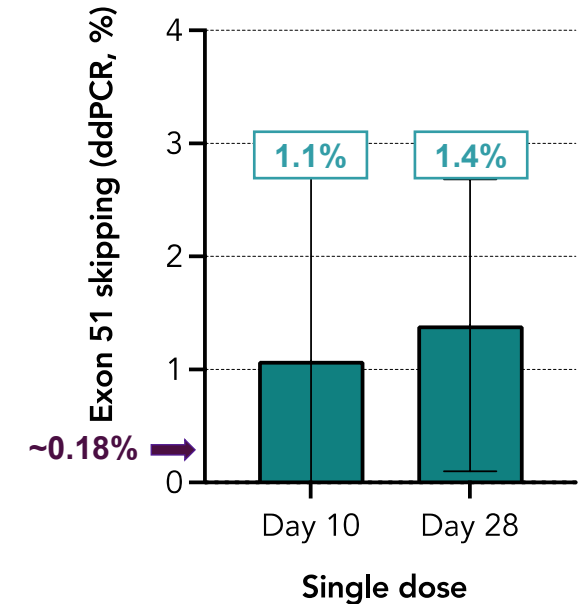


PGN-EDO51 R₆G-PMO51

HV SINGLE DOSE PGN-EDO51

10 mg/kg, ddPCR

All AEs were generally mild & reversible

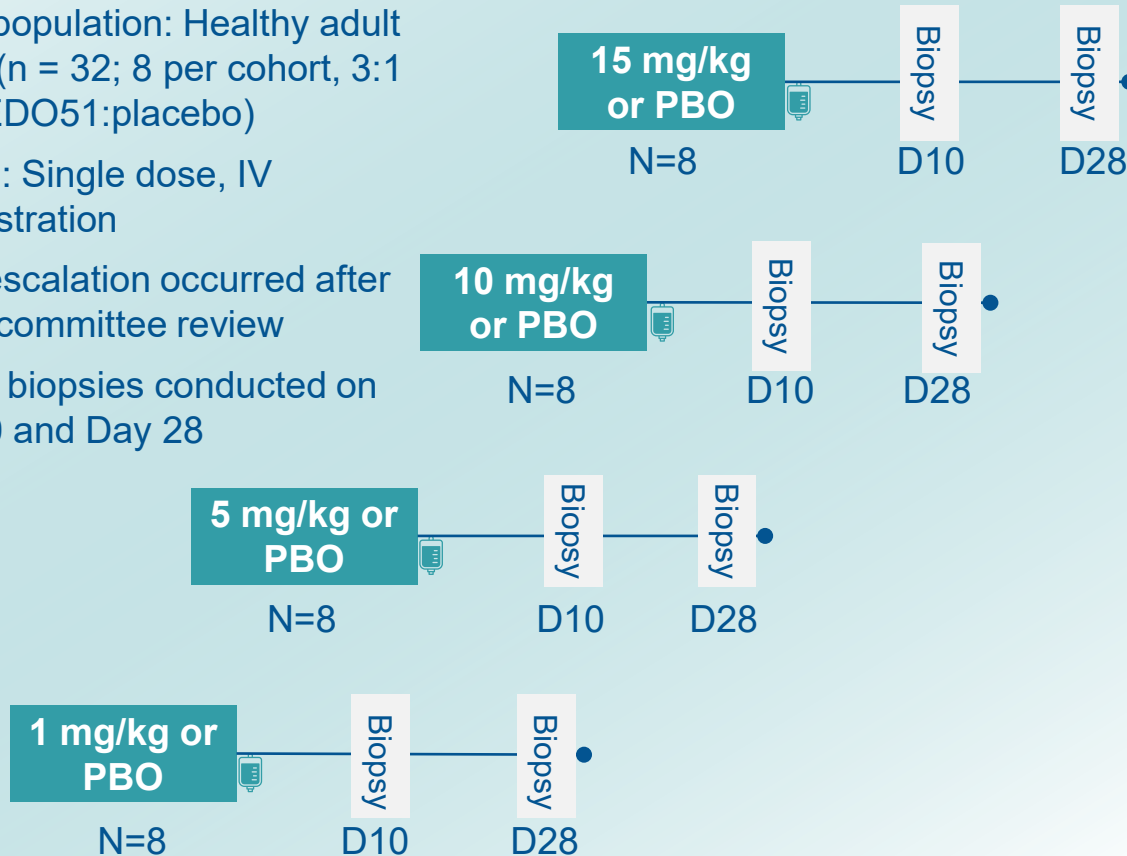


~6x higher than previously reported exon 51 skipping approaches following a single dose

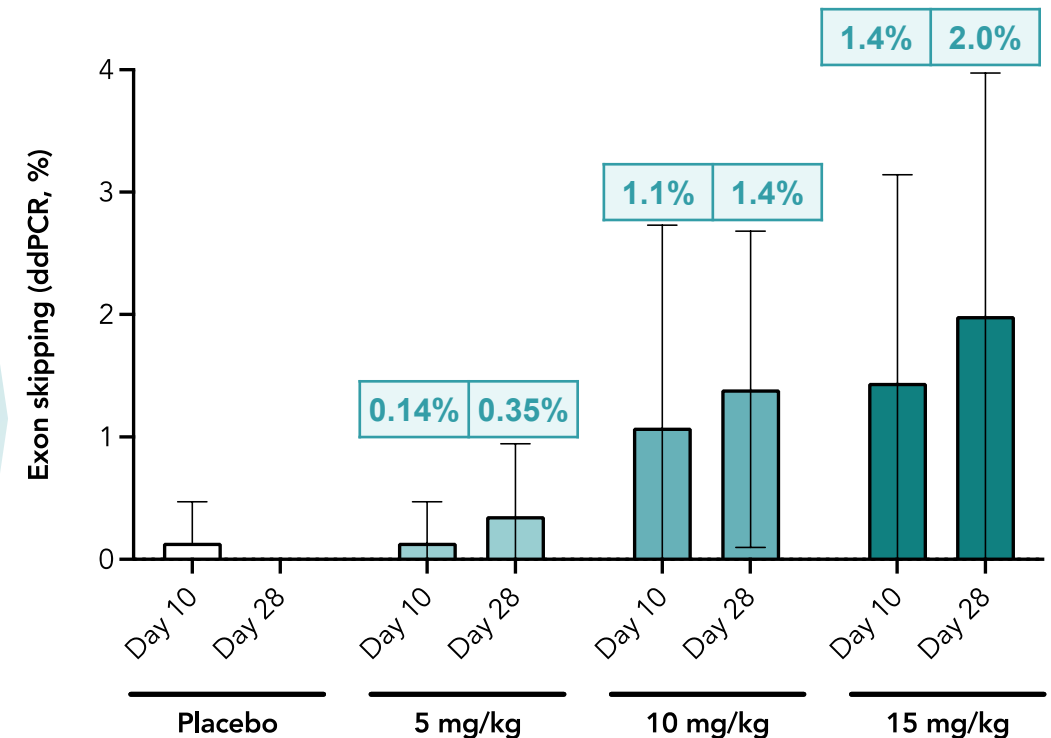
Highest levels of exon 51 skipping in humans following a single dose of PGN-EDO51

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
- Dose escalation occurred after safety committee review
- Biceps biopsies conducted on Day 10 and Day 28

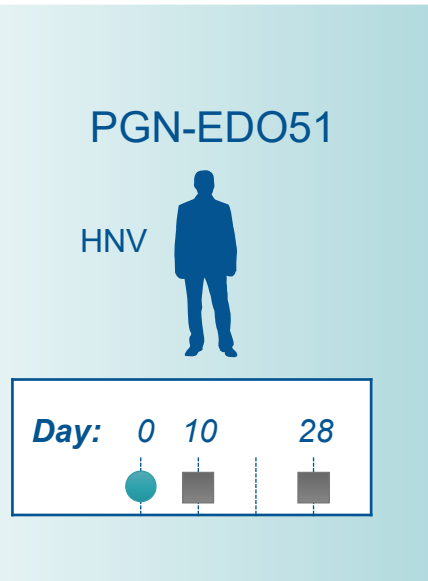


TRIAL RESULTS: EXON SKIPPING (BICEPS)

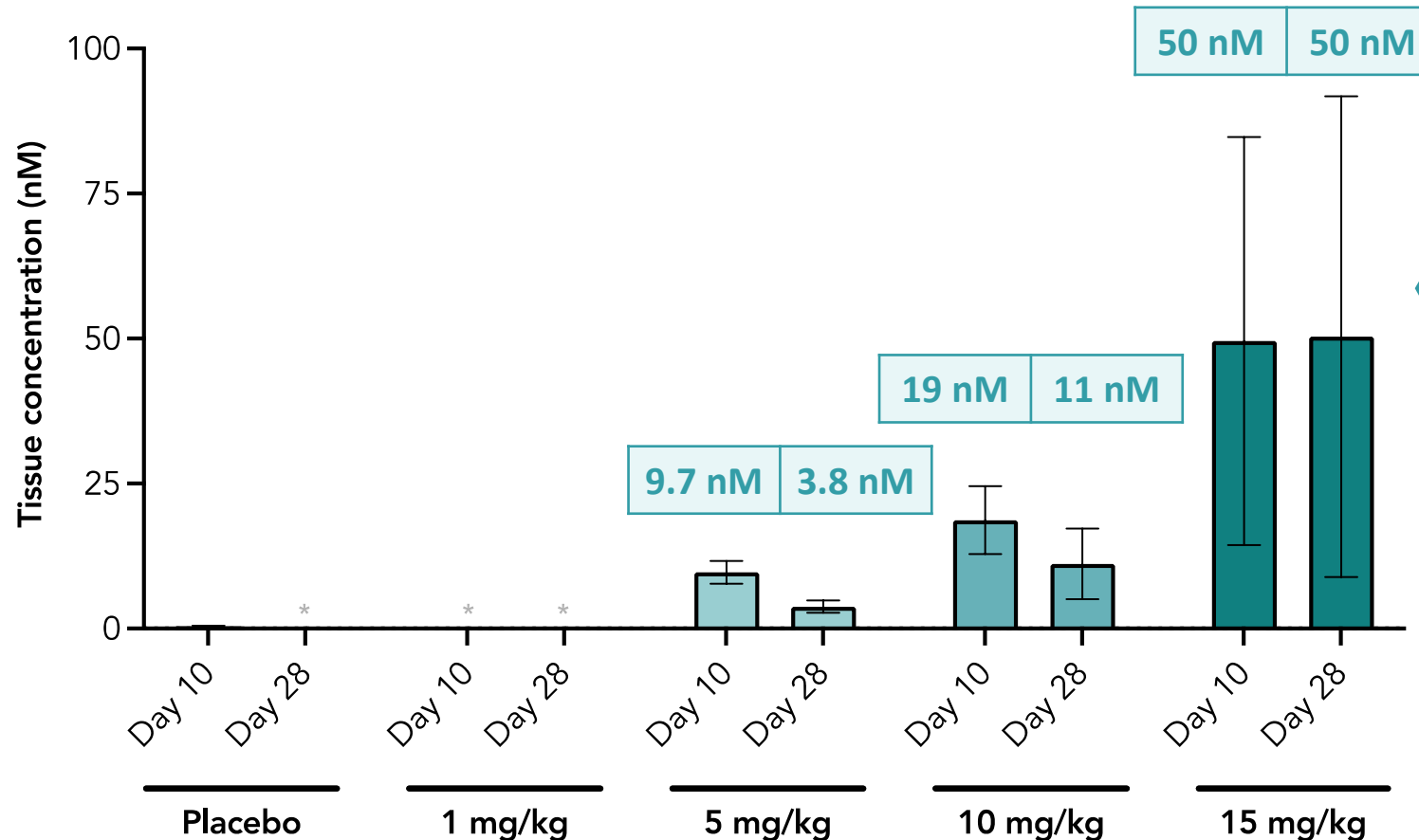


HNV: High, persistent tissue concentrations of oligonucleotide were observed

TISSUE CONCENTRATION (BICEPS)



● PGN-EDO51 dose
■ Biceps biopsy



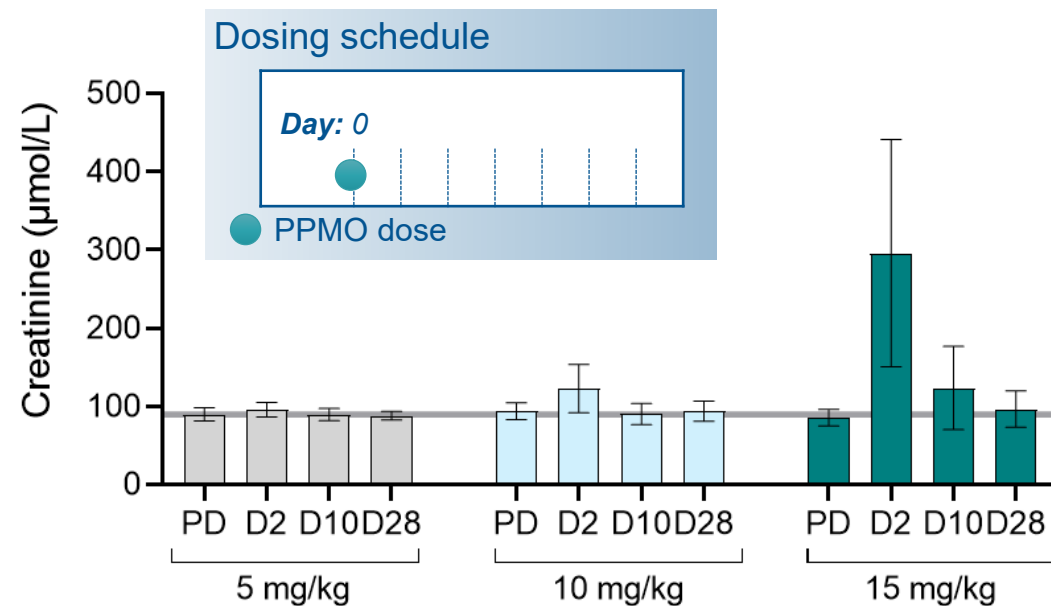
These results further support our belief that repeat dosing of PGN-EDO51 may lead to accumulation of skipped transcript and dystrophin in DMD patients

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



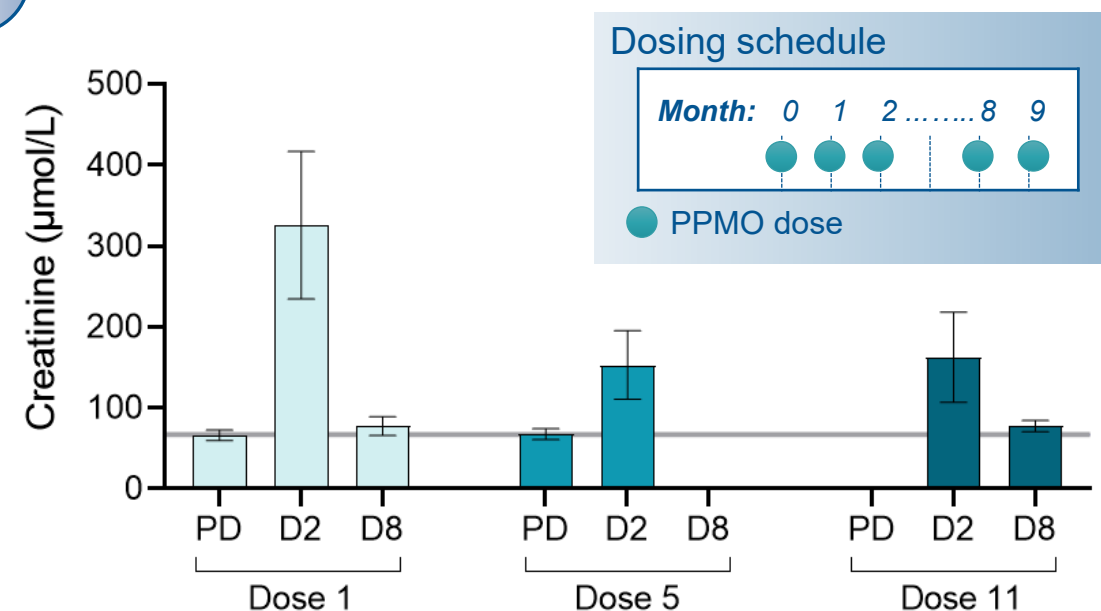
PGN-EDO51 SINGLE-DOSE SERUM CREATININE



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



PGN-EDO51 REPEAT-DOSE SERUM CREATININE



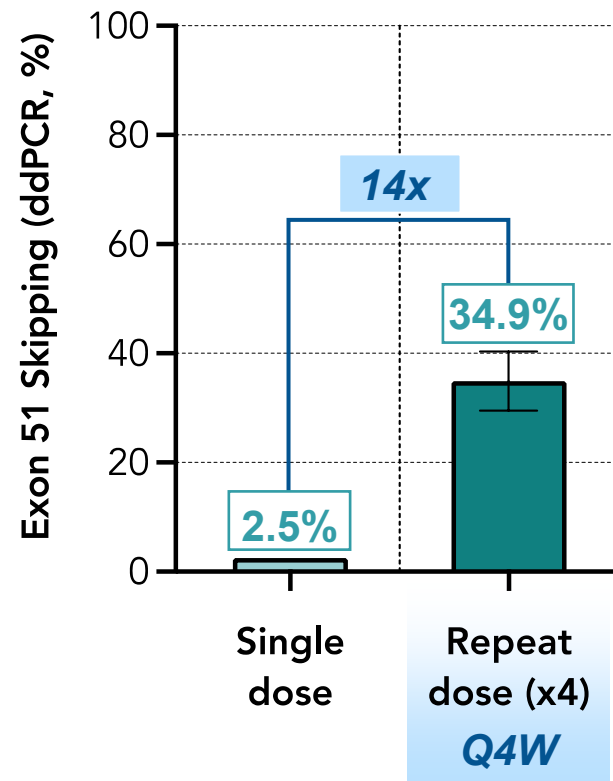
- Transient increase in serum creatinine resolved within a week post-dose
- No adverse findings in the kidney even after 11 doses at all dose levels tested
- No notable hematologic, cardiovascular or hepatic effects

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



NHP SINGLE VS. REPEAT

Biceps, 20 mg/kg, ddPCR



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



PATIENT REPEAT DOSE

OPEN

CONNECT1-EDO51

Ph2 open-label MAD study in patients (*opened in 1H 2023*)

- 3-month Q4W dosing
- Initial dystrophin, exon skipping and safety data anticipated in 2024



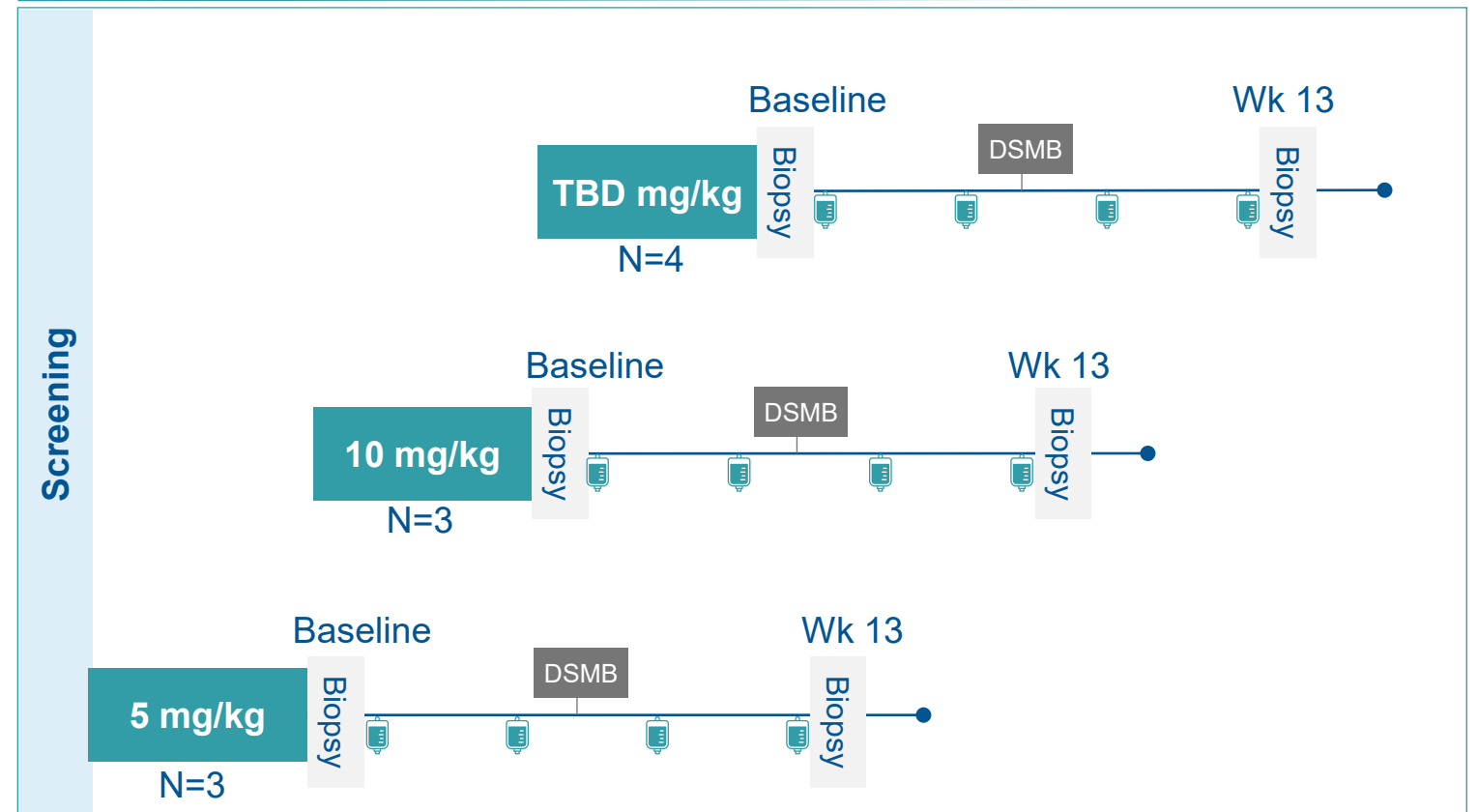
CONNECT1 Phase 2 PGN-EDO51 MAD study



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

OPEN



CONNECT1-EDO51

Ph2 open-label MAD study in patients (*opened in 1H 2023*)



- 3-month Q4W dosing
- Exon skipping, dystrophin and safety data anticipated 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

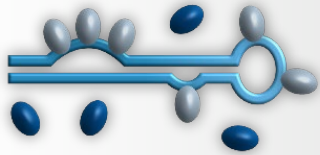


PGN-EDODM1 for myotonic dystrophy type 1 (DM1)

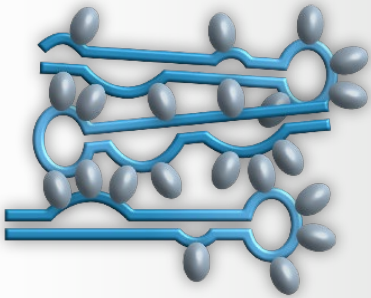
PepGen's novel therapeutic approach to DM1

DM1 PATHOLOGY

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

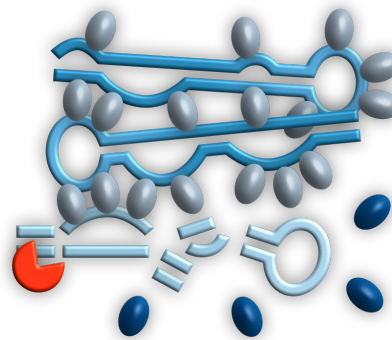


Expanding toxic foci trap more MBNL1



DMPK DEGRADATION

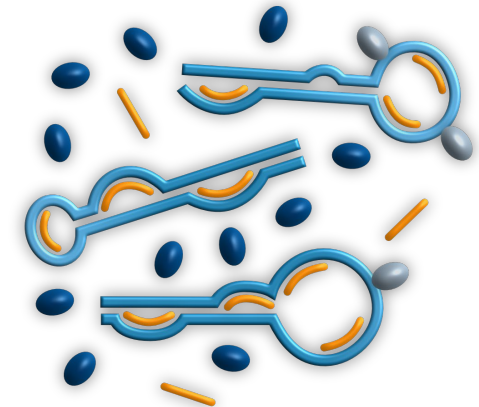
ASO / siRNA degrade *DMPK* transcript to reduce toxic foci



- 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

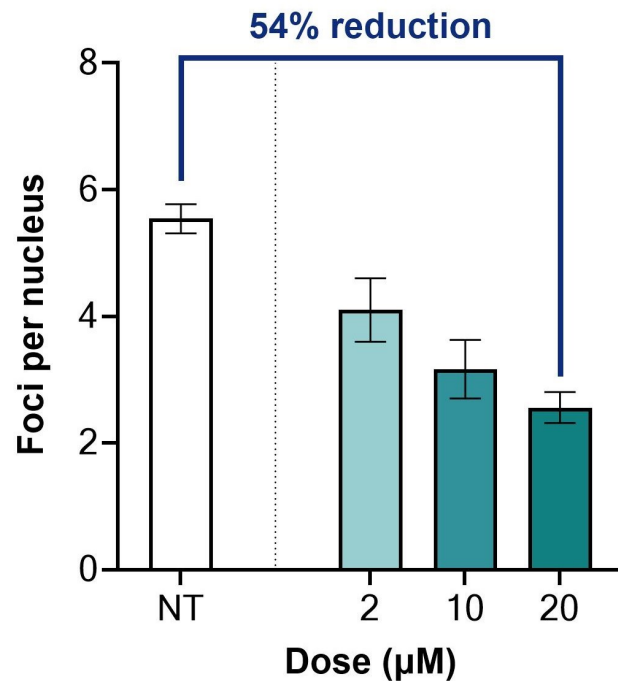
PGN-EDODM1 reduced pathogenic nuclear foci, liberated MBNL1 and corrected mis-splicing in patient cells



FOCI REDUCTION



Foci quantification

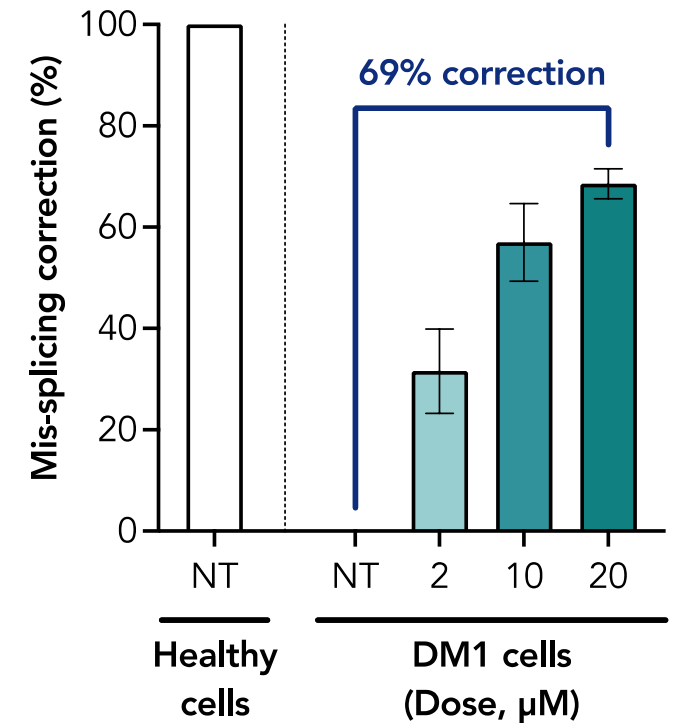


MBNL1 LIBERATION



MIS-SPLICING CORRECTION

Across multiple transcripts



Our *DMPK* competition mechanism of action does not degrade *DMPK*

DMPK TRANSCRIPT LEVELS

PGN-EDODM1

DM1 patient cells
(2,600 CTG repeats)

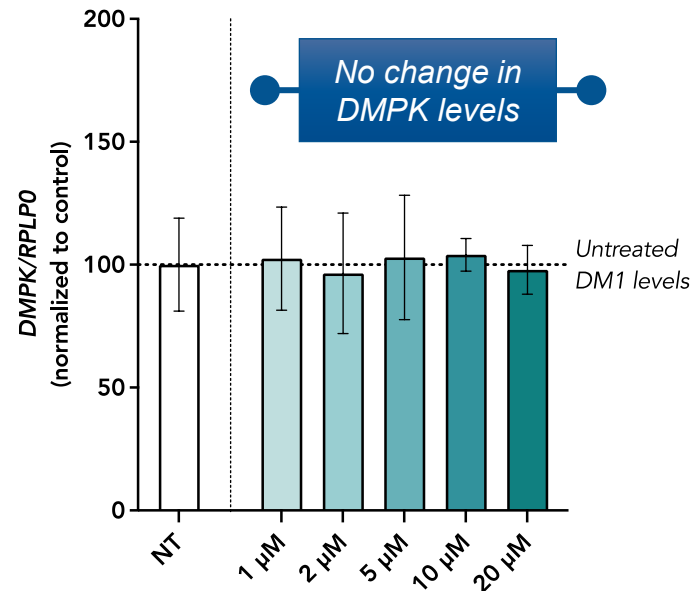


Hour: 0 24



PGN-EDODM1 dose

Analysis



PGN-EDODM1

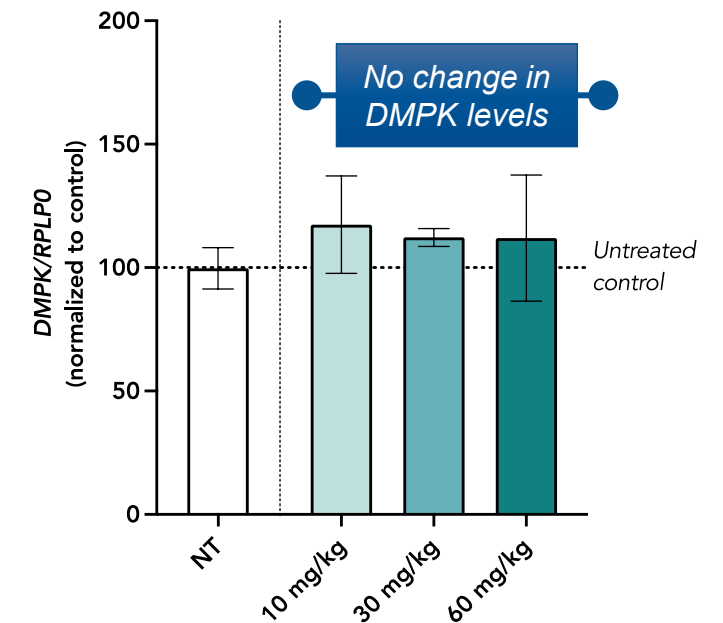
WT



Wk: 0 1 2 3 4 5

PGN-EDODM1 dose

Tissue analysis

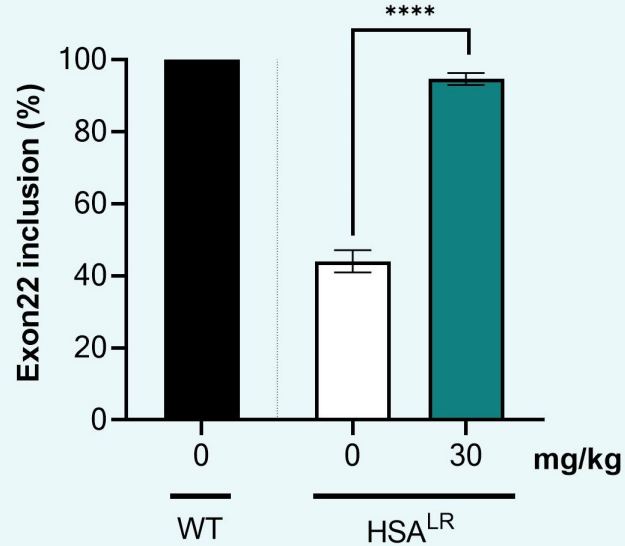


DMPK transcript levels remained unchanged across multiple preclinical models

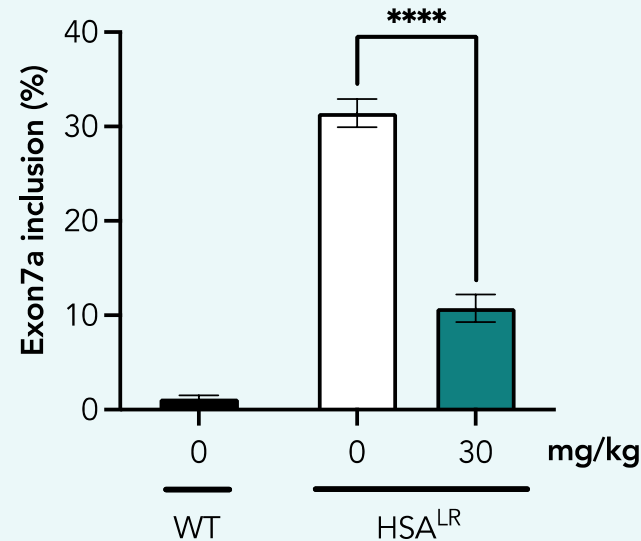
PGN-EDODM1 achieved >68% correction of mis-splicing and complete reversal of myotonia with a single dose in HSA^{LR} mice

MIS-SPLICING CORRECTION

Atp2a1
(encodes SERCA1 – intracellular Ca⁺ pump involved in muscle excitation)

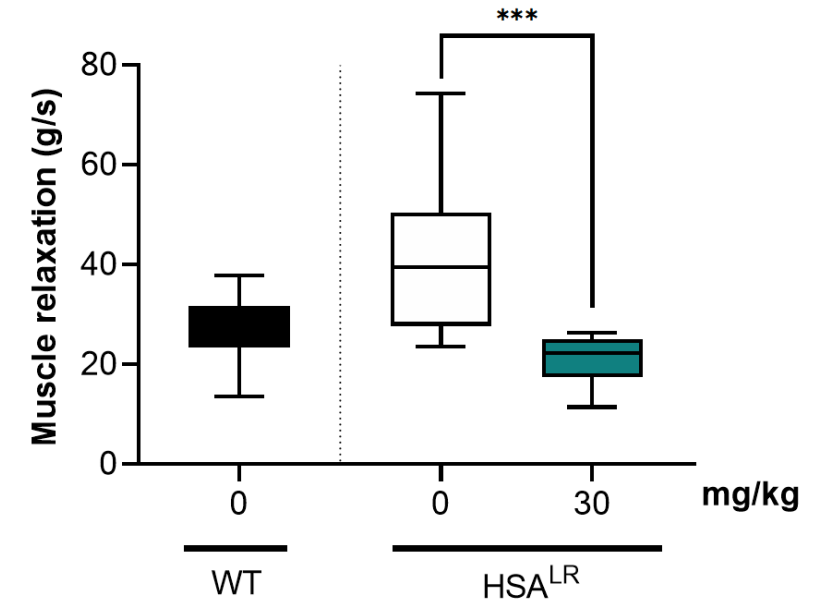


Clcn1
(encodes voltage-dependent Cl⁻ channel involved in muscle excitation)



REVERSAL OF MYOTONIA

Electrophysiology



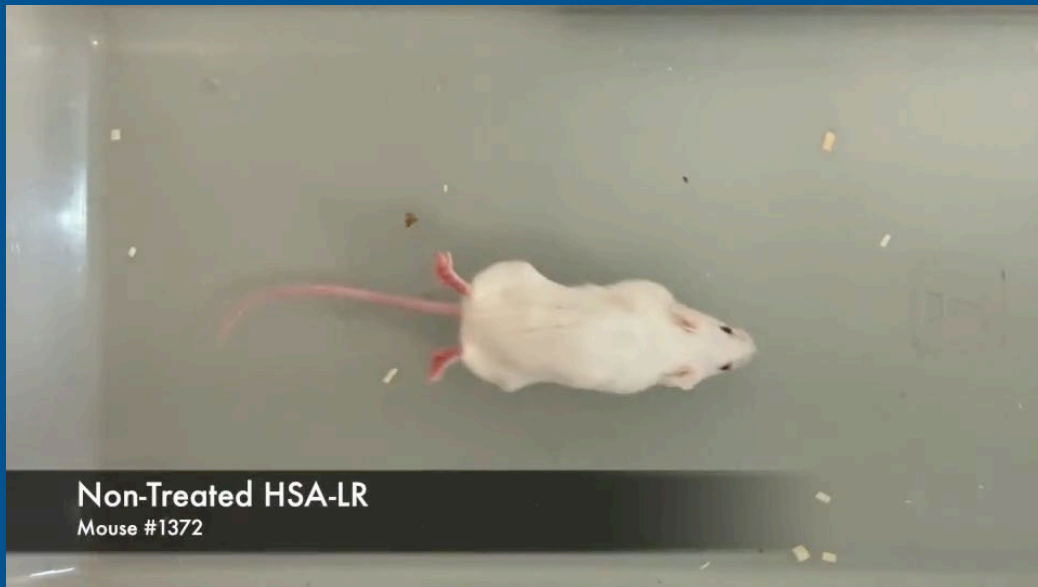
91% correction of
Atp2a1 splicing

68% correction of Clcn1
splicing

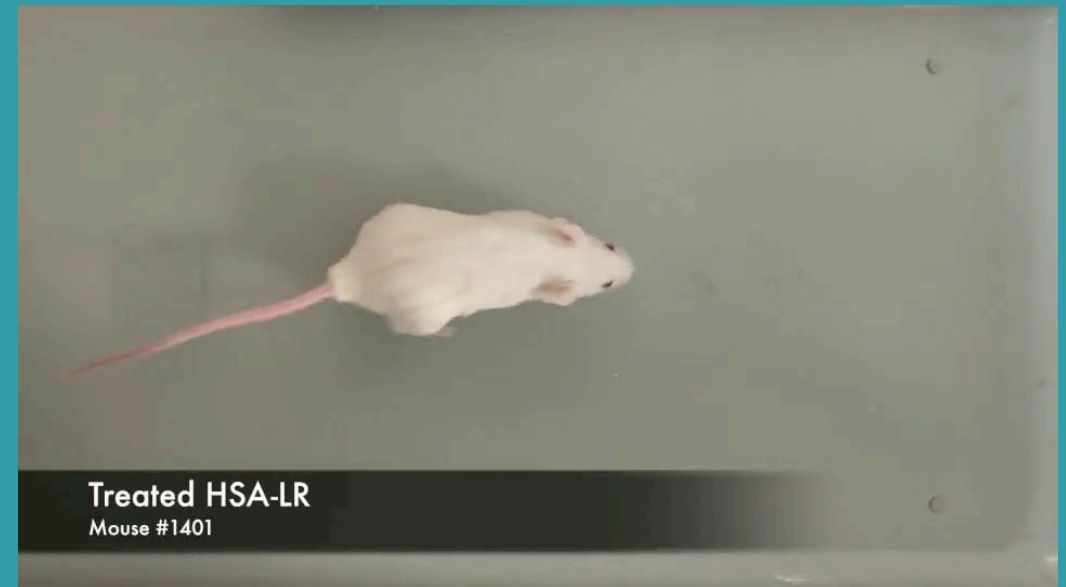
Complete correction of myotonia
observed after single dose

PGN-EDODM1 corrected movement disorder of DM1 mouse model

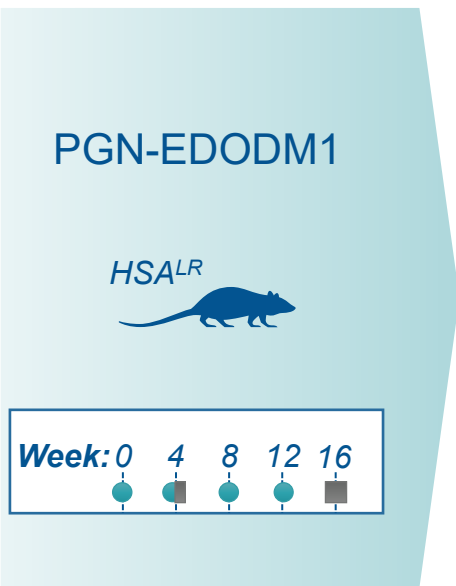
UNTREATED HSA^{LR}



TREATED HSA^{LR}

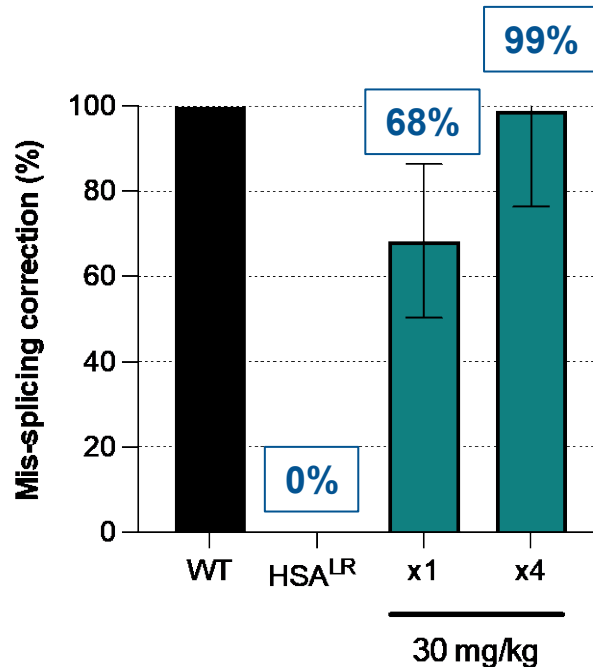


Significant improvement of DM1 pathology with a single dose further increased with repeat dosing



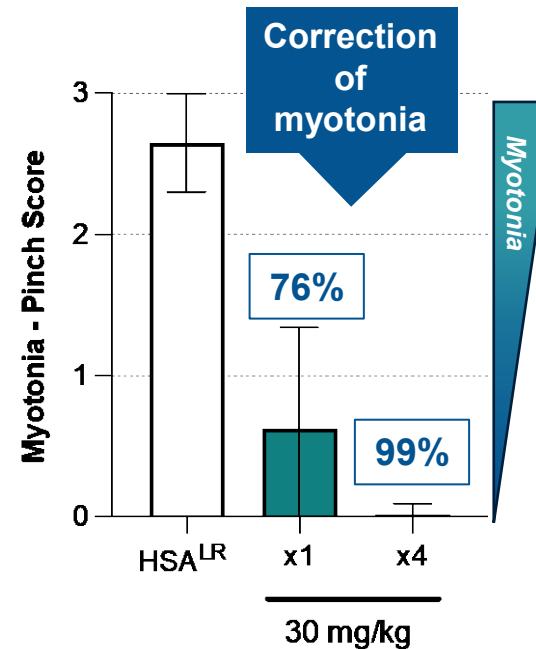
MIS-SPLICING CORRECTION

Across multiple transcripts



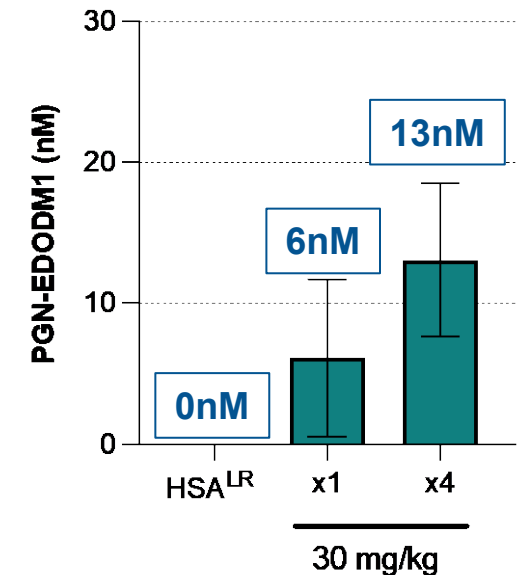
REVERSAL OF MYOTONIA

Pinch test



TISSUE CONCENTRATION

Skeletal muscle



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

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**

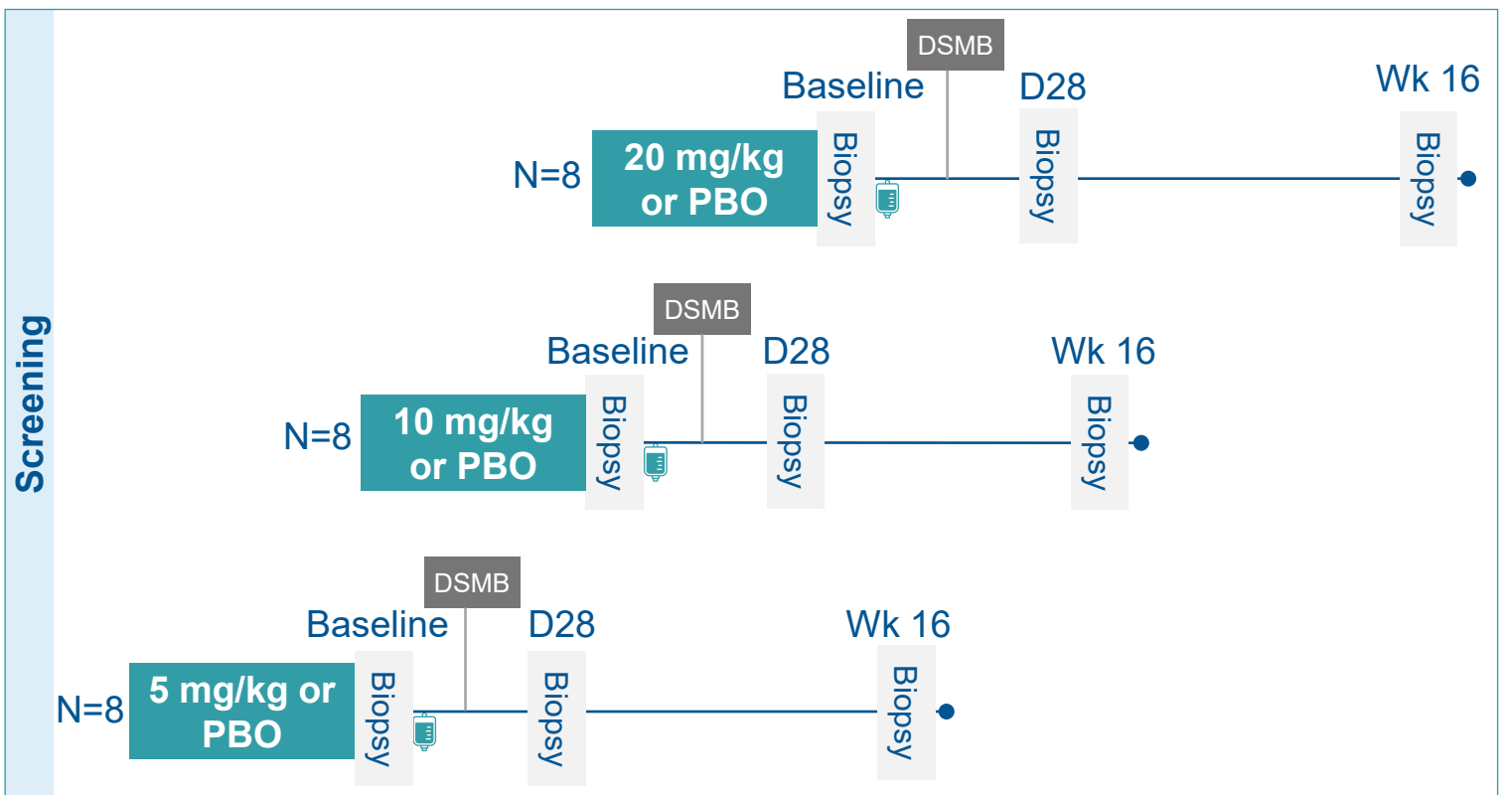
FREEDOM-DM1: Phase 1 PGN-EDODM1 SAD study



FREEDOM-DM1 study overview

- Ph1 global, randomized, double-blind, 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

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



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

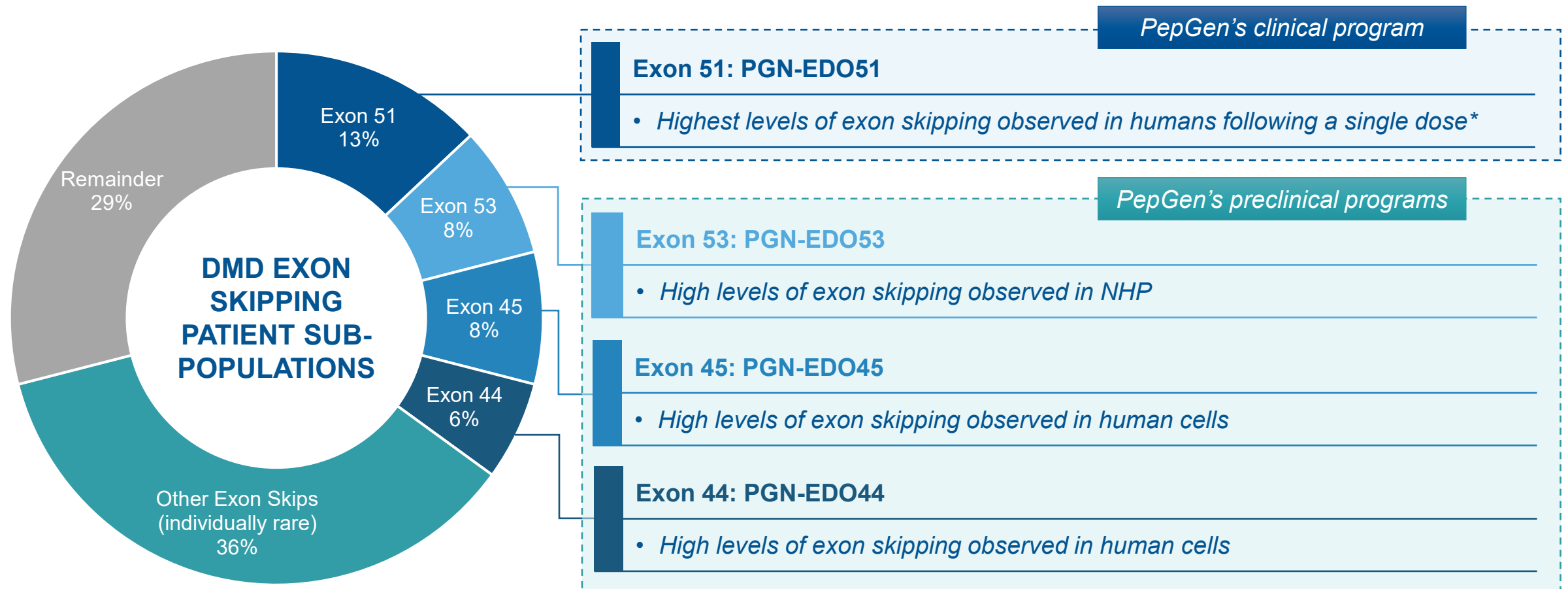
PHASE 2 MAD study (designed to support discussions for potential regulatory approvals)

- 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

PGN-EDO53

WT



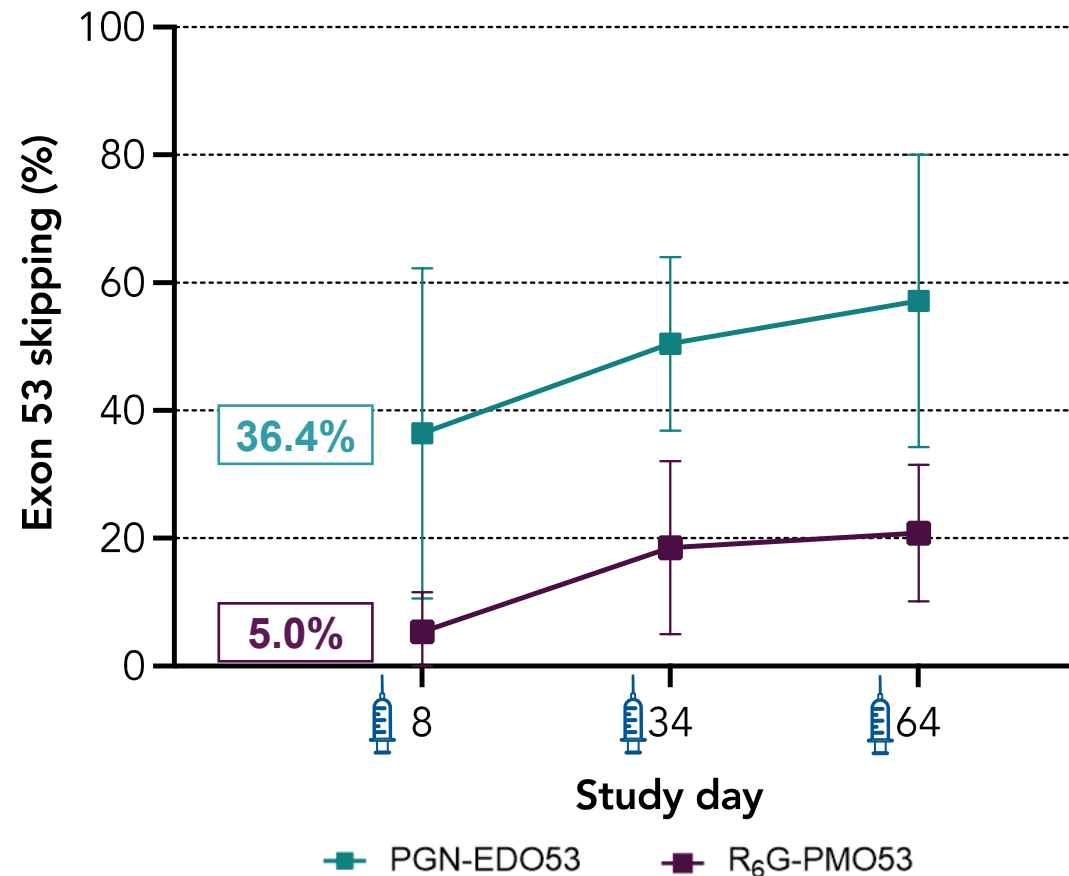
Day: 1 8 29 34 57 64



● PPMO dose (Q4W)

■ Tissue analysis

BICEPS (30 mg/kg)



PGN-EDO53 candidate nominated for development **outperformed** R₆G-PMO53 comparator after single and repeat doses



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 <i>DMD Exon 51</i>	Highest level of single-dose exon skipping & oligo delivery in humans¹	<ul style="list-style-type: none">• Dystrophin, exon skipping and safety data in DMD patients in mid-2024
PGN-EDODM1 <i>DM1</i>	Differentiated approach with robust preclinical dataset	<ul style="list-style-type: none">• Functional assessments, correction of mis-splicing, safety data in DM1 patients
Preclinical Pipeline	<ul style="list-style-type: none">• Five neuromuscular disease candidates in pipeline• Work underway to leverage EDO platform to expand to new tissues and new indications	