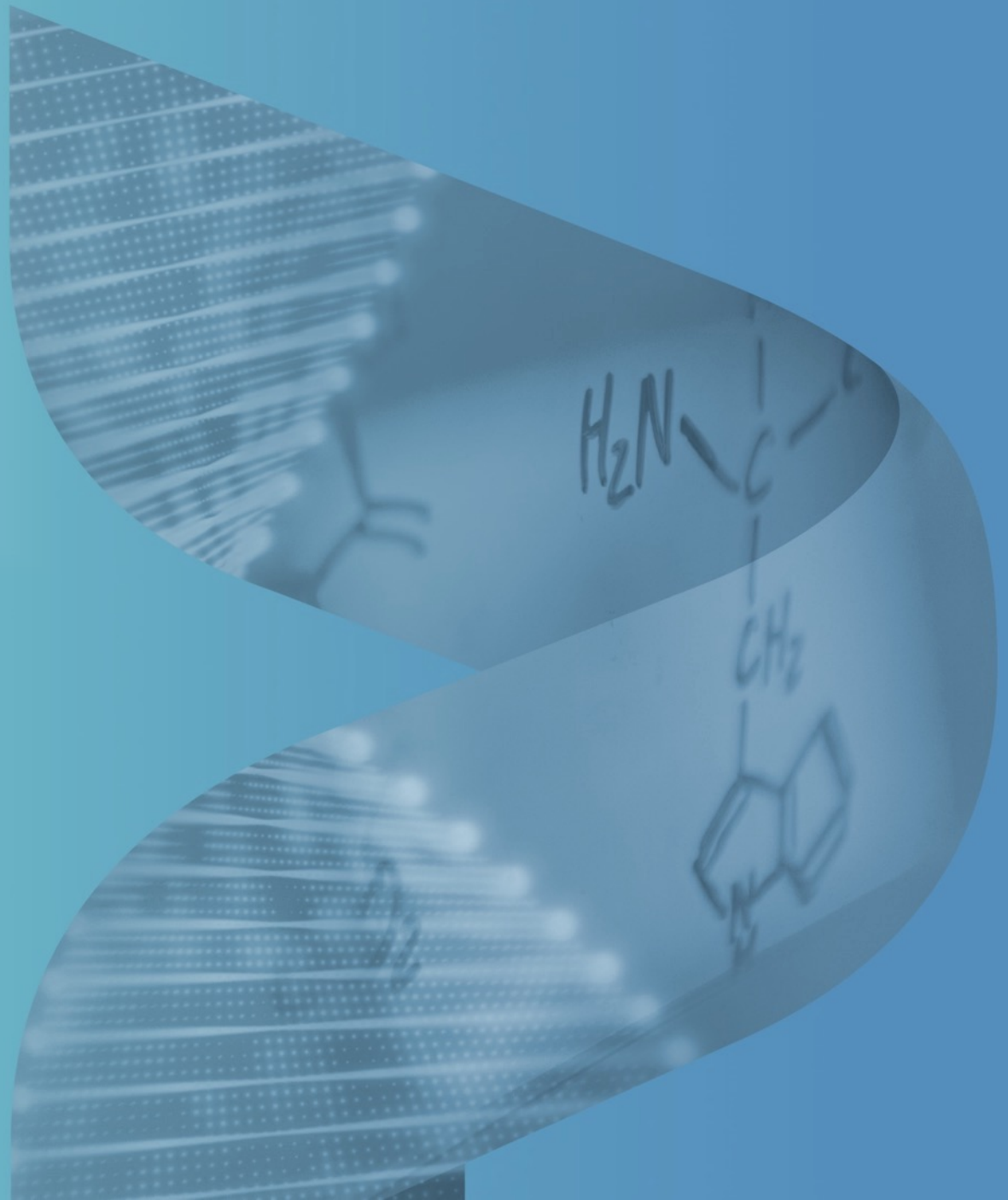
PepGen

EMPOWERING OLIGONUCLEOTIDE THERAPEUTICS

COMPANY PRESENTATION

SEPTEMBER 2022



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This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will," and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include, without limitation, statements about our clinical and preclinical programs, product candidates, including their planned development and therapeutic potential, plans for future development and clinical trials in our programs, including the planned initiation of a Phase 2a MAD trial of PGN-EDO51 in DMD patients, achievement of milestones, and corporate and clinical/preclinical strategies.

Any forward-looking statements in this presentation are based on current expectations, estimates and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to that we may fail to successfully complete preclinical studies and clinical trials of our product candidates or to obtain regulatory approval for marketing of such products; initial clinical trial results for one or more of our product candidates may not be predictive of future trial results for such candidates; our product candidates may not be safe and effective; there may be delays in regulatory clearance or changes in regulatory framework that are out of our control; we may not be able to nominate new drug candidates within the estimated timeframes; our estimation of addressable markets of our product candidates may be inaccurate; we may need additional funding before the end of our expected cash runway and may fail to timely raise such additional required funding; more efficient competitors or more effective competing treatments may emerge; we may be involved in disputes surrounding the use of our intellectual property crucial to our success; we may not be able to attract and retain key employees and qualified personnel; earlier-stage trial results may not be predictive of later stage trial outcomes; and we are dependent on third parties for some or all aspects of our product manufacturing, research and preclinical and clinical testing. Additional risks concerning PepGen's programs and operations are described in its most recent quarterly report on Form 10-Q on file with the SEC. PepGen explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

A NEXT-GENERATION OLIGONUCLEOTIDE DELIVERY PLATFORM WITH THE POTENTIAL TO TRANSFORM PATIENT OUTCOMES

Our **Enhanced Delivery Oligonucleotide (EDO)** platform is engineered to offer enhanced therapeutic activity and improved tolerability

Designed to achieve **greater skeletal & cardiac muscle penetrance;** extensive portfolio of product candidates for the treatment of **multiple neuromuscular diseases (NMD)**

Rare disease focus, lead assets target a potentially **large market opportunity** in US/EEA/JP:
PGN-EDO51: ~6k Duchenne muscular dystrophy (DMD) exon 51 patients*
PGN-EDODM1: ~130k myotonic dystrophy type 1 (DM1) patients

PGN-EDO51 treatment resulted in the **highest levels of oligonucleotide delivery & exon 51 skipping** in a clinical trial following a single dose

DMD & DM1 patient POC anticipated in 2024

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*DMD patient numbers: 15k US + 25k EEA + 5k JP whole population (range used: Crisafulli et al 2020 – 7.1/100k males; Orphanet 2021– 4.78/100k pop). Exon 51 population 13% of total. DM1 patient numbers: 1 in 8,000 (Johnson et al); 40k US + 75k EEA + 15k JP.
**Reported in Ph1 trial. Based on cross-trial comparisons with publicly-available data for other exon skipping approached that have been assessed following a single dose.

PEPGEN: EXPERIENCED TEAM OF COMPANY BUILDERS, SCIENTISTS, AND CLINICIANS

Management team

JAMES MCARTHUR, PhD
(CEO & President)

imara · RACAPITAL · Cydan · nightstar THERAPEUTICS · Vtesse

JAYA GOYAL, PhD
(EVP Research & Preclinical Development)

WAVE LIFE SCIENCES · Biogen

NIELS SVENSTRUP, PhD
(SVP Chemistry & Manufacturing)

BAYER · ascendis pharma · Cydan · Lundbeck

NOEL DONNELLY
(CFO)

EIP PHARMA · Takeda · Shire

MICHELLE MELLION, MD
(SVP Clinical Development)

Fulcrum Therapeutics · Biogen · VERTEX

SONIA BRACEGIRDLE, DPhil
(SVP Strategy & Operations)

BCG · Syncona · McKinsey & Company

Board of Directors*

LAURIE KEATING, JD
(Chair)

Immuneering · Alnylam · MILLENNIUM PHARMACEUTICALS, INC · IMAGO BioSciences

JOSH RESNICK, MD
(Director)

RACAPITAL

HABIB DABLE
(Director)

BAYER · ACCELERON PHARMA

CHRIS ASHTON, PhD
(Director)

SOCIETE ENTERPRISES

HEIDI HENSON
(Director)

Pardes Biosciences

* Plus Dr. McArthur (Director).

WE ARE BUILDING ON FDA-APPROVED EXON 51 SKIPPING MODALITIES TO DEVELOP THE NEXT GENERATION OF OLIGO TX

APPROVED EXON 51 PMO

Drug	Sponsor	Exon	Dystrophin restoration*
EXONDYS 51® *(eteplirsen)*	Sarepta Therapeutics	Exon 51	0.44%

2021 sales: $454M
*(US & Israel)***

PEPGEN'S STEP CHANGE

- **Enhanced delivery** to skeletal muscle (inc. diaphragm), cardiac muscle and the CNS
- In DMD Ph1 clinical study in healthy normal volunteers, the **highest levels of exon 51 skipping** were observed following a single dose***
- Potential for **greater dystrophin production**
- **Enhanced balance between activity and tolerability** compared to early delivery peptides
- **Robust & scalable manufacturing**

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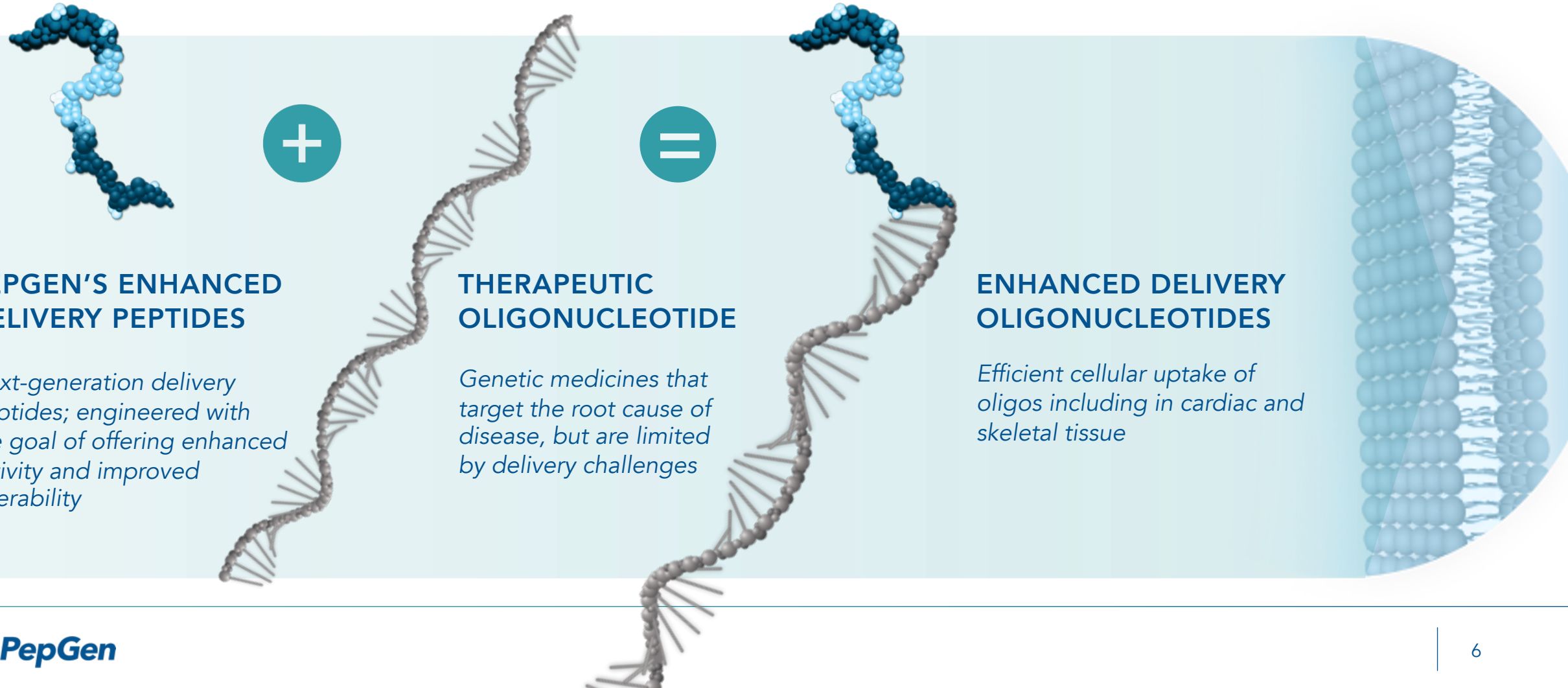
* Clinical data included in drug label (FDA). **Source: Sarepta 2021 10K filing.
*** Based on cross-trial comparisons with publicly-available data for other exon skipping approaches that have been assessed following a single dose.

THE POWER OF EDOs

Enhanced Delivery Oligonucleotides are well-characterized therapeutic PMO oligonucleotides conjugated to proprietary delivery-enhancing peptides



PEPGEN'S ENHANCED DELIVERY PEPTIDES

Next-generation delivery peptides; engineered with the goal of offering enhanced activity and improved tolerability

THERAPEUTIC OLIGONUCLEOTIDE

Genetic medicines that target the root cause of disease, but are limited by delivery challenges

ENHANCED DELIVERY OLIGONUCLEOTIDES

Efficient cellular uptake of oligos including in cardiac and skeletal tissue

SCALABLE EDO TECHNOLOGY DESIGNED TO ENABLE BROAD PORTFOLIO

PROGRAM	INDICATION *TARGET*	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT ANTICIPATED MILESTONE
PGN-EDO51	Duchenne muscular dystrophy *Exon 51*						**1H23** *Ph2a patient clinical trial initiation*
PGN-EDODM1	Myotonic dystrophy type 1 *DMPK*						**1H23** *Ph1/2 patient clinical trial initiation*
PGN-EDO53	Duchenne muscular dystrophy *Exon 53*						**2H22** *NHP exon skipping data*
PGN-EDO45	Duchenne muscular dystrophy *Exon 45*						**2H22** *Candidate nomination*
PGN-EDO44	Duchenne muscular dystrophy *Exon 44*						**2H22** *Candidate nomination*

FUTURE PIPELINE OPPORTUNITIES

Additional neuromuscular indications

Neurologic indications

PGN-EDO51 FOR DUCHENNE MUSCULAR DYSTROPHY

DUCHENNE MUSCULAR DYSTROPHY IS A DEBILITATING, PROGRESSIVE MUSCLE-WASTING DISEASE

ROOT CAUSE OF DISEASE

- Caused by mutations in the dystrophin gene
- Absence of dystrophin leads to muscle degeneration

SYMPTOMATOLOGY & NATURAL HISTORY

- Progressive loss of function, including ambulation
- Cardiac & respiratory conditions
- Lifespan ~25 years

EXON 51 PATIENT POPULATION*

~2,000
(US)

~3,200
(EEA)

~700
(JP)

EXON 51 THERAPEUTIC LANDSCAPE

- Exondys51® approved in US on the basis of <1% dystrophin restoration
- Not approved in EEA or JP

*DMD patient numbers: 15k US + 25k EEA + 5k JP whole population (range used: Crisafulli et al 2020 – 7.1/100k males; Orphanet 2021 – 4.78/100k pop). Exon 51 population 13% of total.

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PRECLINICAL DATA

THE ACTIVITY OF OUR EDO PLATFORM IN DMD HAS BEEN EVALUATED IN MULTIPLE PRECLINICAL MODELS

		Species	Study design	Key readouts observed
Non-GLP pharmacology studies	Patient cells *PGN-EDO51*	*DMD patient*	*Hour:* 0 96	• High levels of exon 51 skipping
	Single dose *PGN-EDO23*	*mdx*	*Week:* 0 1	• Normalization of serum creatine kinase • High levels of exon 23 skipping and dystrophin restoration
	Single dose *PGN-EDO51*	*WT*	*Week:* 0 1	• High levels of exon 51 skipping
	Repeat dose *PGN-EDO51*	*WT*	*Week:* 0 1 2 3 4 5	• High levels of exon 51 skipping • Accumulation of exon skipping levels with repeat dosing

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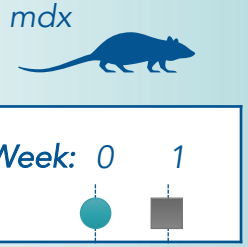
● PGN-EDO dose ■ Tissue / serum analysis

MDX MICE: A SINGLE DOSE OF PGN-EDO23 WAS OBSERVED TO NORMALIZE CREATINE KINASE, A MARKER OF MUSCLE DAMAGE

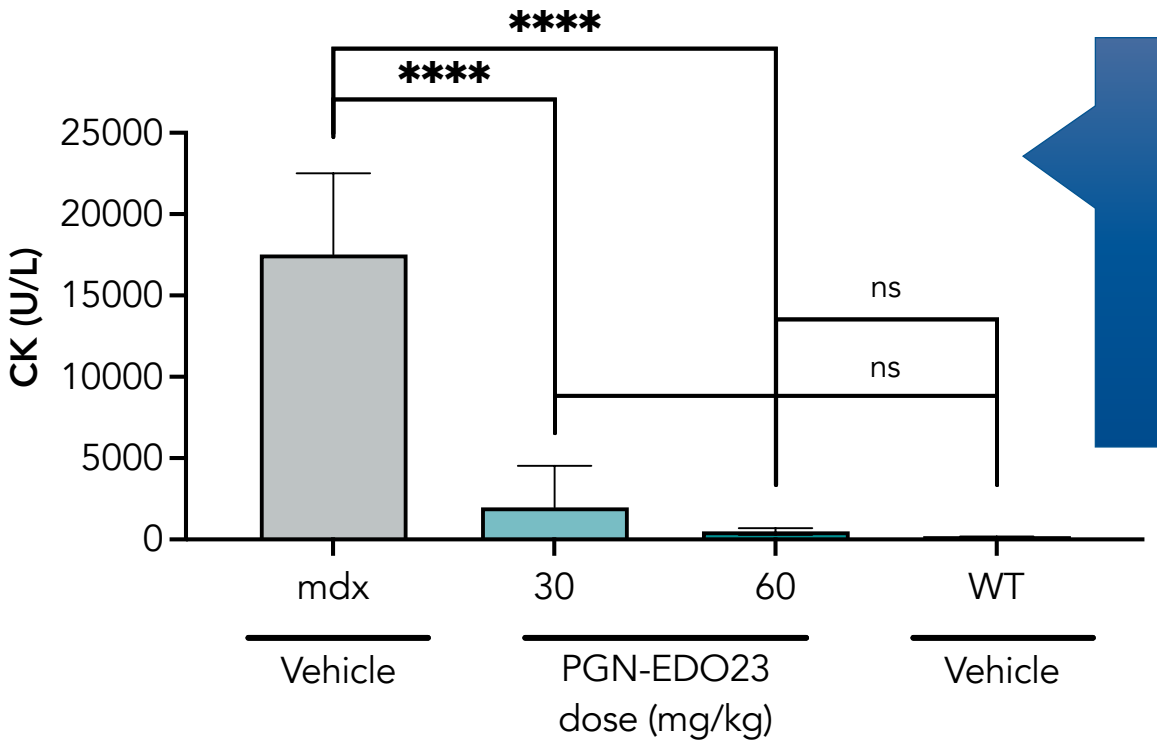
PGN-EDO23
(murine analogue of PGN-EDO51)



PGN-EDO dose

Serum analysis

SERUM CREATINE KINASE



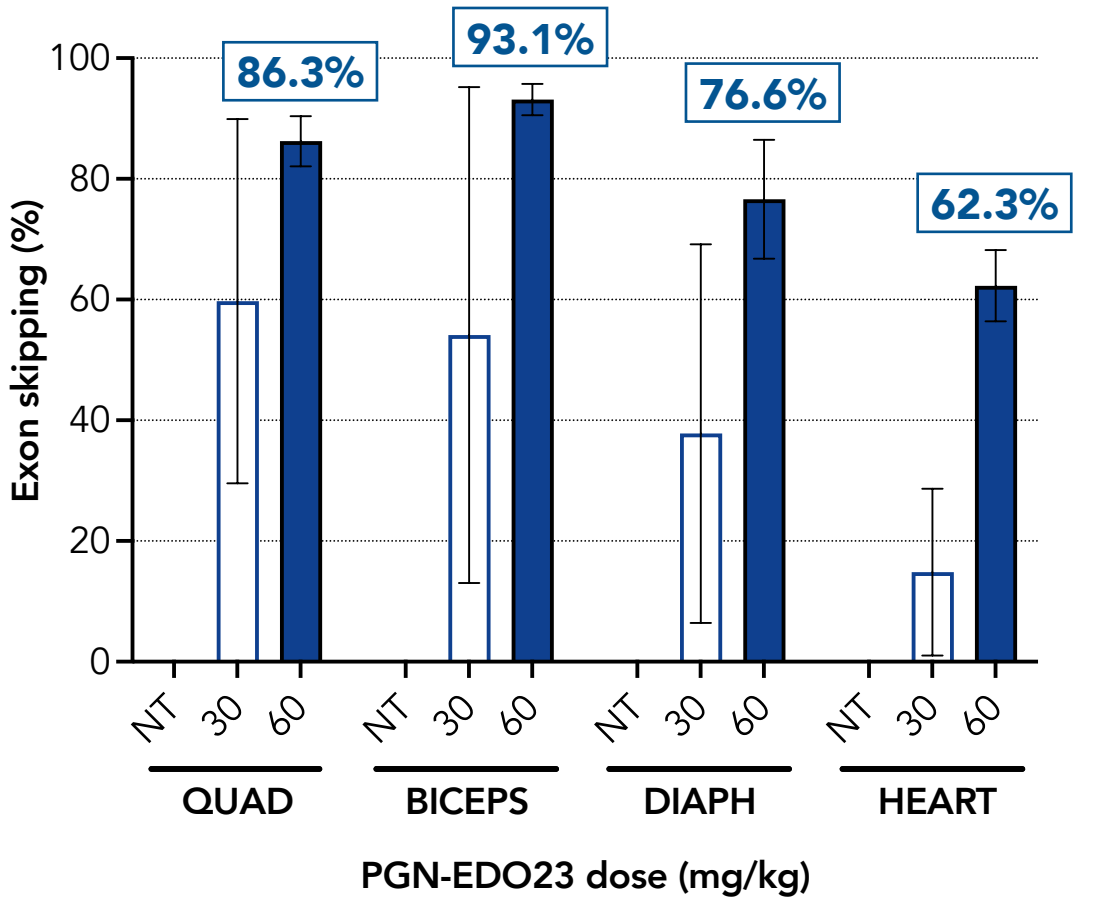
This result suggests that PGN-EDO23 potentially **restored muscle cell integrity** following a single dose at tolerable levels

PGN-EDO23 utilizes the **same EDO delivery peptide** as our clinical candidate

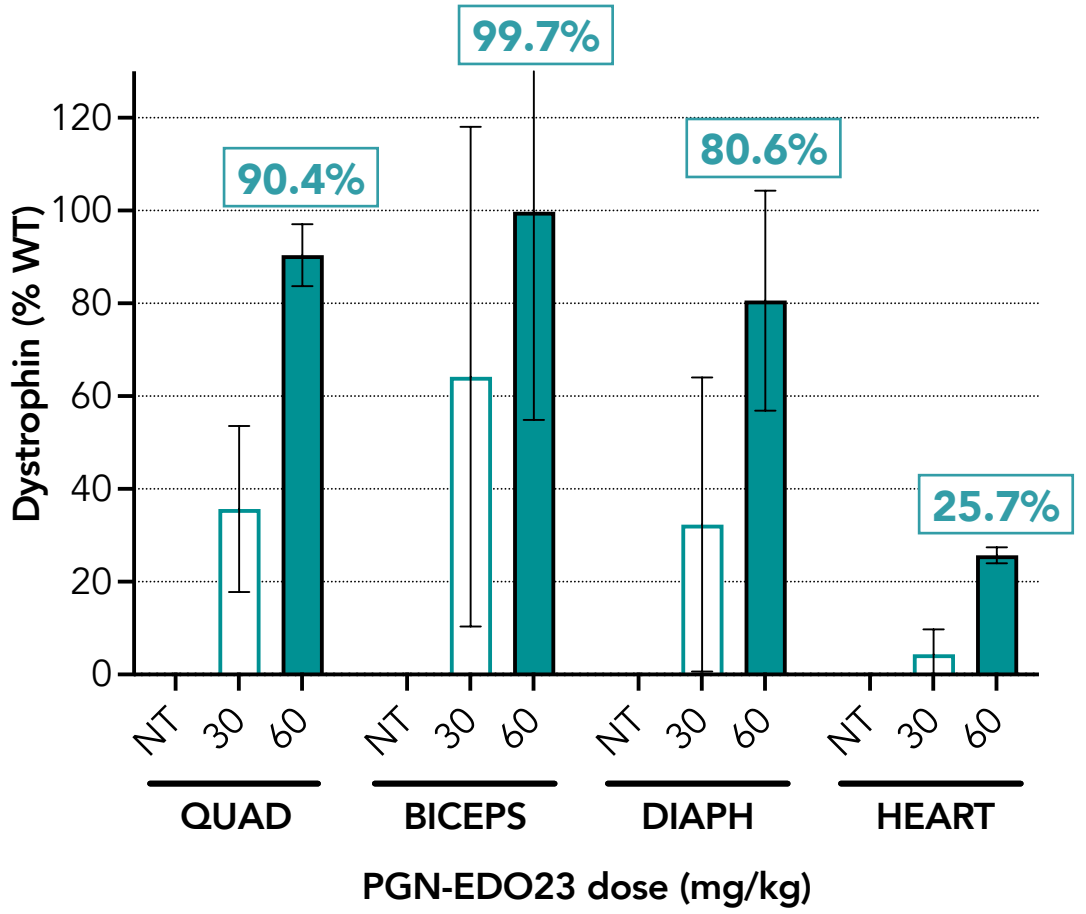
Protocol: peptide-PMO conjugate and a saline control were administered intravenously (IV) to *mdx* and WT mice; serum creatine kinase measured 7 days after injection. Mean ± SD; **** = p≤0.0001; **ns** = p≥0.05; n = 3 for control groups and 5 for treated group.

MDX MICE: ROBUST DYSTROPHIN RESTORATION OBSERVED 7 DAYS AFTER A SINGLE, GENERALLY WELL-TOLERATED DOSE OF PGN-EDO23

EXON SKIPPING



DYSTROPHIN



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Protocol: peptide-PMO conjugate and a saline control were administered intravenously (IV) to *mdx* and WT mice; exon skipping and dystrophin restoration measured 7 days after injection. Mean ± SD; n = 3 for control groups and 3 for treated groups. NT = not treated.

NHP: BIODISTRIBUTION DATA EXHIBITED ROBUST EDO DELIVERY ACROSS KEY NEUROMUSCULAR TISSUE TYPES

PGN-EDO51

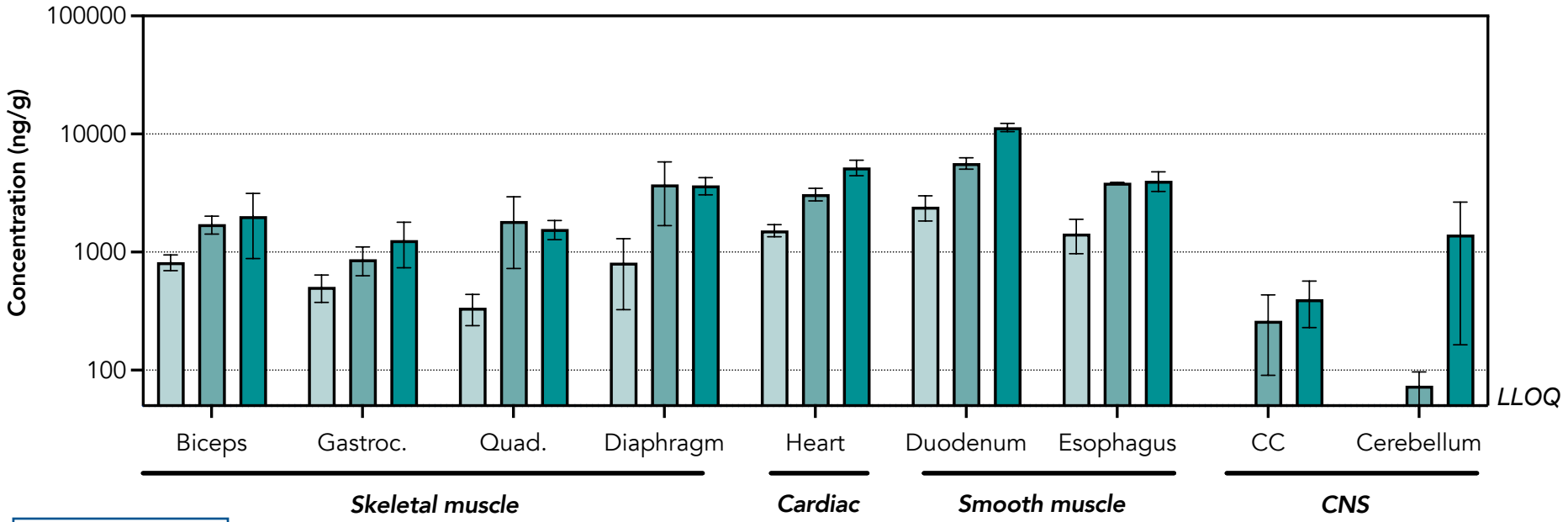
WT

Week: 0 1

PGN-EDO51 dose

Tissue analysis

TISSUE PMO QUANTIFICATION



DOSE
- 20 mg/kg
- 40 mg/kg
- 60 mg/kg

Delivery to hard-to-reach cardiac tissue

Delivery across the **blood-brain barrier**

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Protocol: NHPs received one slow bolus IV infusion on Day 1, study was terminated on Day 8 and PMO levels were quantified in key tissues. Shown as mean ± SEM; n = 2 per group. CC = cerebral cortex; LLOQ = lower limit of quantification.

NHP: 10 MG/KG OF PGN-EDO51 WAS APPROXIMATELY AS POTENT AS 30 MG/KG OF R_6G-PMO IN QUADS & BICEPS

PGN-EDO51
R_6G-PMO51

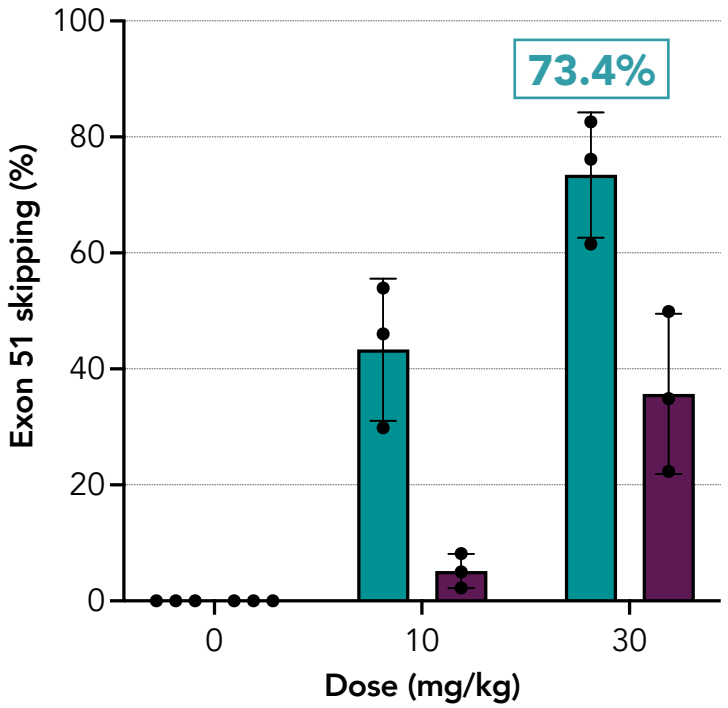
PGN-EDO51

WT

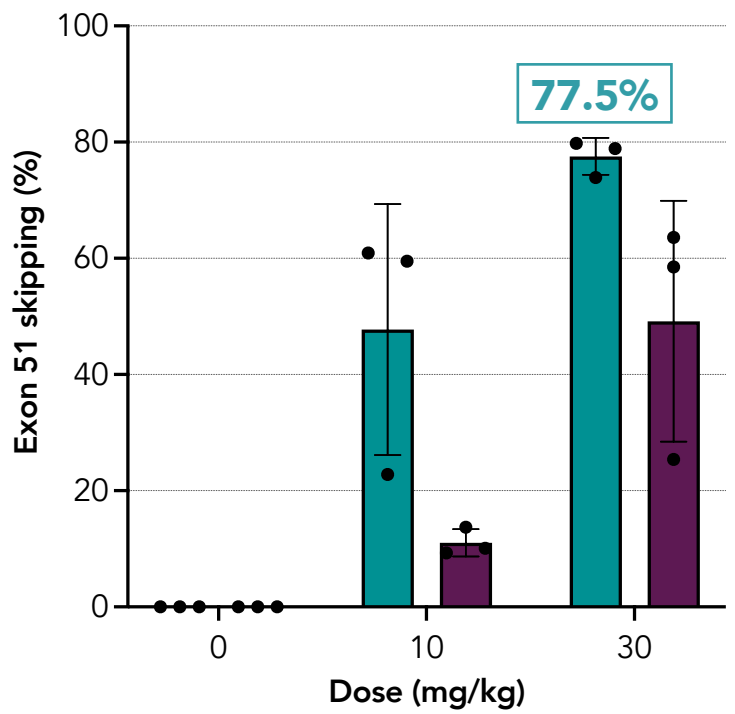
Week: 0 1 2 3 4 5

PPMO dose
Tissue analysis

QUADRICEPS



BICEPS



Exon skipping levels of >70% observed in skeletal muscles at 30 mg/kg for PGN-EDO51

Protocol: PGN-EDO51 and R_6G-PMO were administered to NHP by IV infusion over 30 min at the doses indicated (n=3). Q2W, three doses administered, saline control. Tissues were harvested 7 days after final administration. Shown as mean ± SD; n = 3 per group. Study was not powered for statistical significance. R_6G-PMO is believed to be structurally equivalent to SRP-5051.

NHP: 10 MG/KG OF PGN-EDO51 WAS APPROXIMATELY AS POTENT AS 30 MG/KG OF R_6G-PMO IN DIAPHRAGM

PGN-EDO51
R_6G-PMO51

PGN-EDO51

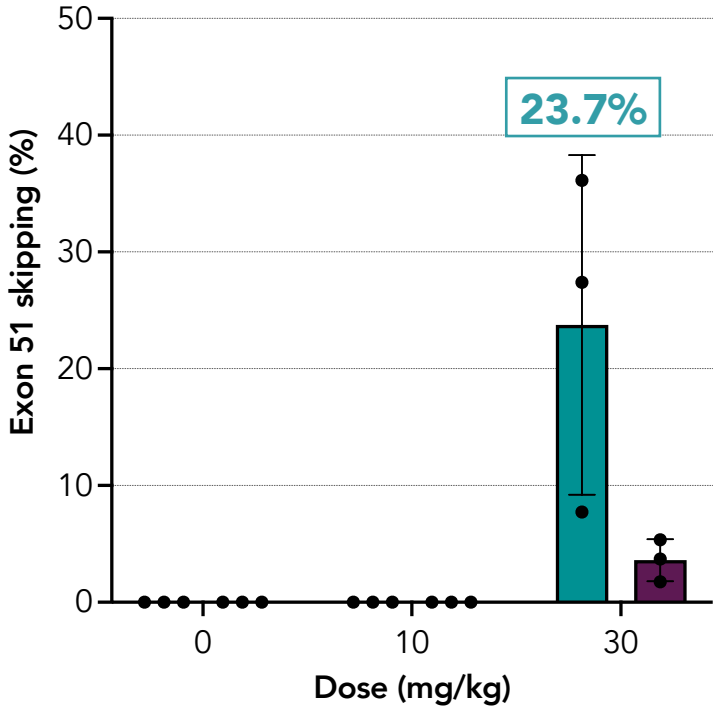
WT

Week: 0 1 2 3 4 5

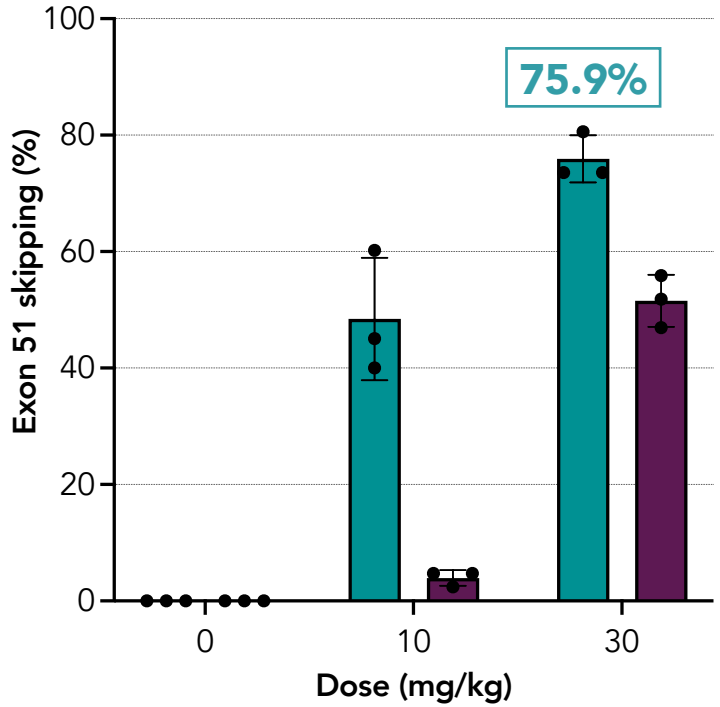
PPMO dose

Tissue analysis

CARDIAC LEFT VENTRICLE



DIAPHRAGM



A single dose of 20 mg/kg of PGN-EDO51 afforded 19% exon 51 skipping in whole heart

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Protocol: PGN-EDO51 and R_6G-PMO were administered to NHP by IV infusion over 30 min at the doses indicated (n=3). Q2W, three doses administered, saline control. Tissues were harvested 7 days after final administration. Shown as mean ± SD; n = 3 per group. Study was not powered for statistical significance. R_6G-PMO is believed to be structurally equivalent to SRP-5051.

NHP: EXON SKIPPING LEVELS ACCUMULATED WITH REPEAT DOSE ADMINISTRATION OF PGN-EDO51

PGN-EDO51
R_6G-PMO51

PGN-EDO51

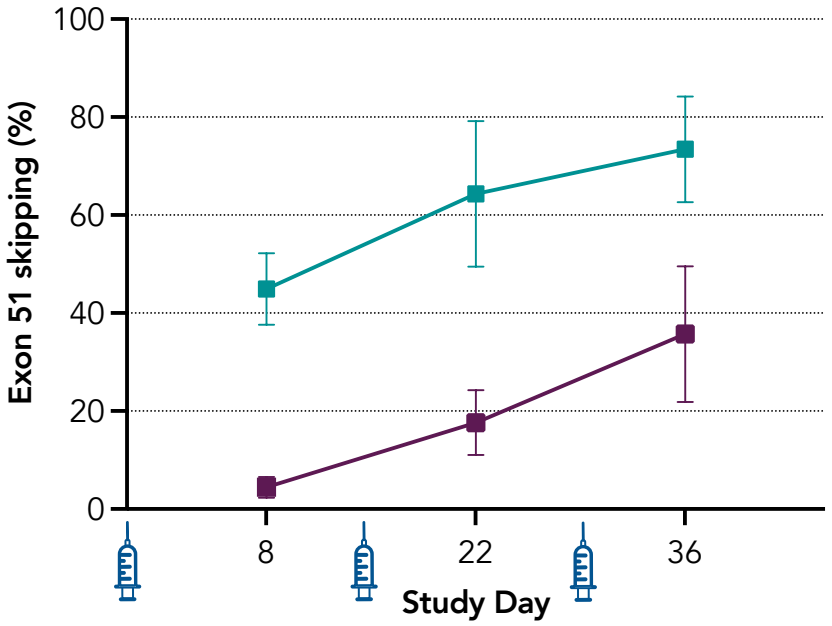
WT

Week: 0 1 2 3 4 5

PPMO dose
Tissue analysis

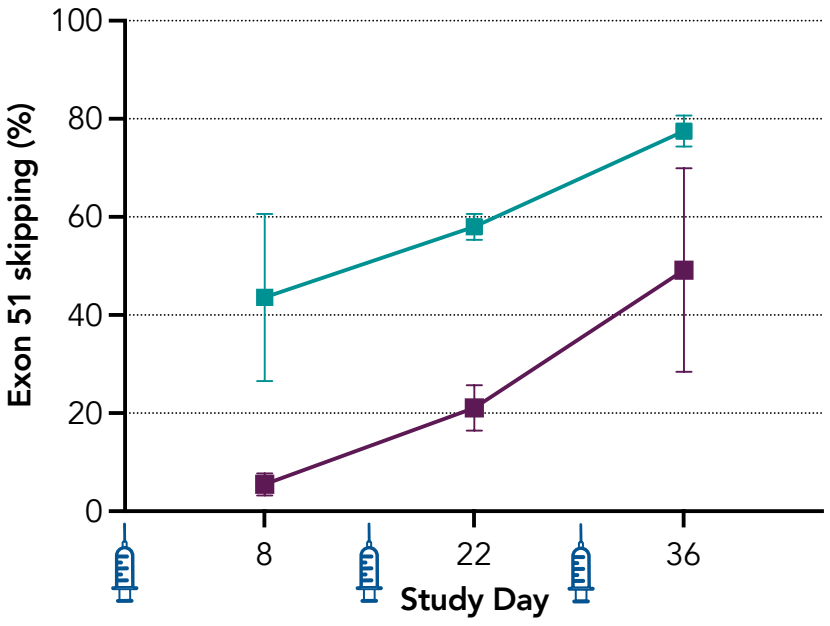
QUADRICEPS

30 mg/kg



BICEPS

30 mg/kg



Q2W regimen employed in this study; differential with R_6G-PMO may increase with monthly dosing

Protocol: PGN-EDO51 and R_6G-PMO were administered to NHP by IV infusion over 30 min at the doses indicated (n=3). Q2W, three doses administered, saline control. Biopsies taken 7 days after each 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_6G-PMO is believed to be structurally equivalent to SRP-5051.

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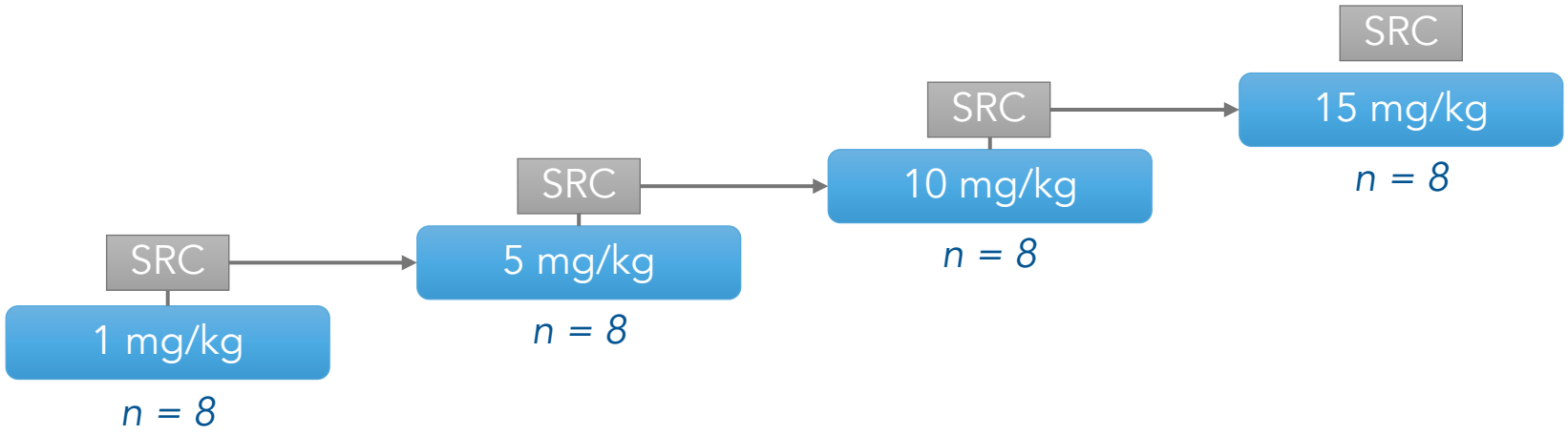
CLINICAL DATA

HNV: WE HAVE COMPLETED A SINGLE ASCENDING DOSE PH1 TRIAL OF PGN-EDO51 IN HEALTHY NORMAL VOLUNTEERS

PH1 HEALTHY NORMAL VOLUNTEER (HNV) TRIAL SUMMARY

Overview	• **Study population:** Healthy adult males (n = 32, 3:1 PGN-EDO51:placebo) • **Dosing:** Single dose, i.v. administration • **Placebo control** • Biceps biopsies conducted on **Day 10 and Day 28**
Trial summary	

SRC = safety review committee.

HNV: HIGHEST LEVELS OF OLIGO DELIVERY & EXON 51 SKIPPING OBSERVED, SUPPORTING FURTHER DEVELOPMENT OF PGN-EDO51

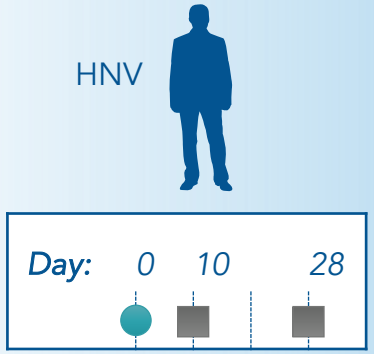
PH1 ENDPOINTS	READOUTS OBTAINED
Target engagement *Exon skipping (biceps)*	**Highest level of DMD exon 51 skipping** observed following a single dose in humans
Pharmacokinetics *Tissue concentration (biceps)*	**Highest level of oligonucleotide delivery** observed for a DMD therapeutic following a single dose in humans
Safety & tolerability	**Generally well-tolerated**

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.

HNV: HIGHEST LEVELS OF EXON 51 SKIPPING OBSERVED IN HUMANS FOLLOWING A SINGLE DOSE

PGN-EDO51

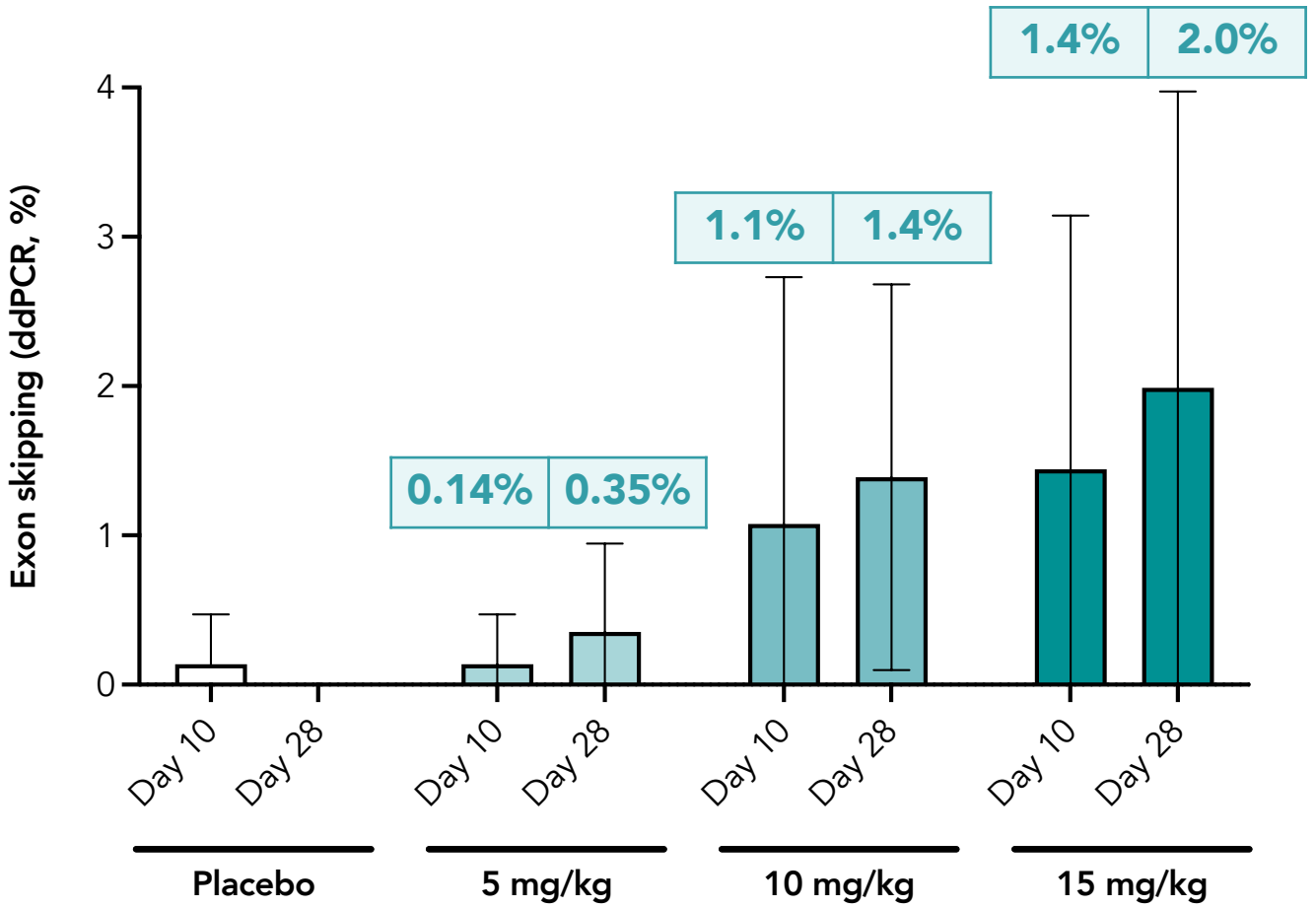
HNV



PGN-EDO51 dose

Biceps biopsy

EXON SKIPPING (BICEPS)

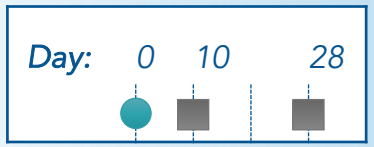


Protocol PGN-EDO51-101: Phase 1, first in human, randomized double blind, placebo controlled single ascending dose study in healthy adult volunteers. Single dose of either PGN-EDO51 or Placebo were administered by IV infusion at doses indicated. Participants were followed for 28 day period following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

HNV: HIGH, PERSISTENT TISSUE CONCENTRATIONS OF OLIGONUCLEOTIDE WERE OBSERVED

PGN-EDO51

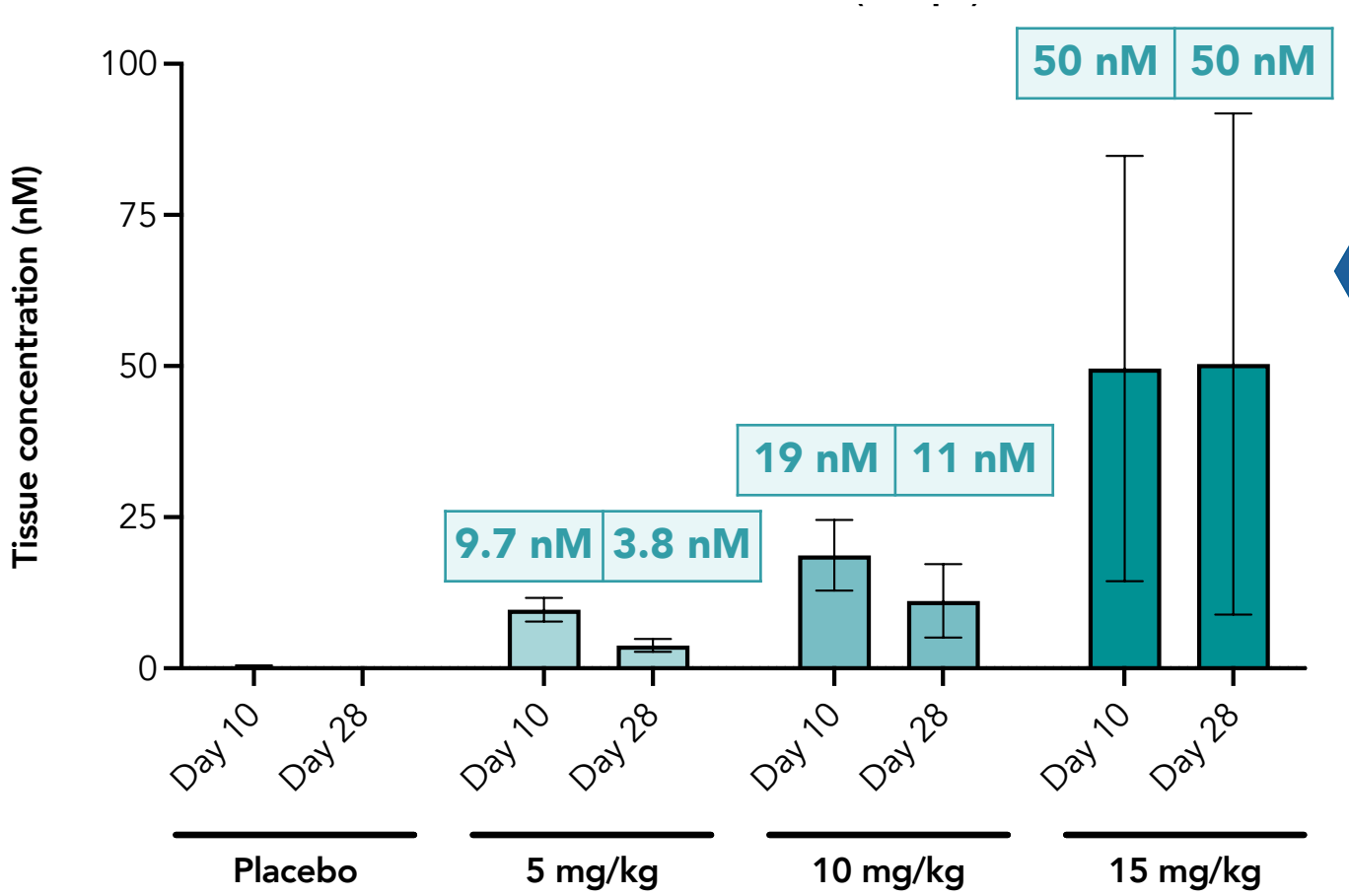
HNV



PGN-EDO51 dose

Biceps biopsy

TISSUE CONCENTRATION (BICEPS)



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

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).

HNV: PGN-EDO51 WAS GENERALLY WELL-TOLERATED AT DOSES ASSESSED IN PH1 SAD TRIAL

SAFETY & TOLERABILITY SUMMARY

- All participants completed the study; there were **no discontinuations**.
- The majority of treatment-emergent adverse events (TEAEs) were assessed as **mild and resolved without any intervention**. At 10 mg/kg there were **only Grade 1 (mild)** AEs .
- At 15 mg/kg there were **transient, reversible** changes in kidney biomarkers that **resolved in all subjects**.
- At 15 mg/kg there was one non-life threatening serious adverse event (SAE) related to changes in kidney biomarkers that were **transient and reversible**. This HNV was admitted to the hospital for less than 24 hours, received hydration and then was re-admitted to the Phase 1 unit and completed the study.
- Transient mild (Grade 1) to moderate (Grade 2) hypomagnesemia was observed in two participants at the 15 mg/kg dose and **did not require any intervention**.
- Serum cystatin C, the recommended biomarker to assess renal function in DMD, showed **minimal change at the highest dose**.

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In light of higher than anticipated oligo levels and exon skipping levels in muscle observed at 5 mg/kg and 10 mg/kg , further does escalation was not deemed necessary by sponsor. Under this Phase 1 protocol any non-life-threatening SAE was considered a dose-limiting toxicity (DLT), however study was not halted by the SRC nor put on hold by Health Canada.

HNV: MAJORITY OF TEAEs MILD AND RESOLVED WITHOUT INTERVENTION; SUPPORTS PROGRESSION TO PH2a PATIENT TRIAL

PH1 TRIAL SAFETY & TOLERABILITY SUMMARY

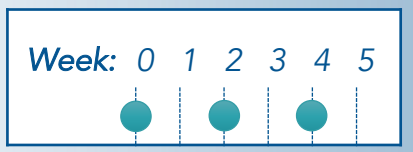
Healthy Normal Volunteers (HNV) with ≥1 AE, n (%)	Placebo (n=8)	Cohort A: 1 mg/kg (n=6)	Cohort B: 5 mg/kg (n=6)	Cohort C: 10mg/kg (n=6)	Cohort D: 15 mg/kg (n=6)	PGN-EDO51 Total (n=24)
Any AE	4 (50)	4 (66.7)	2 (33.3)	5 (83.3)	6 (100)	17 (70.8)
Related to study drug	1 (12.5)	2 (33.3)	0	4 (66.7)	6 (100)	12 (50)
Serious AE related to study drug	0	0	0	0	1 (16.7)	1 (4.2)
AE leading to discontinuation	0	0	0	0	0	0
AE leading to death	0	0	0	0	0	0
Number of Related TEAEs by CTCAE v5.0 grading*						
Grade 1 (Mild)	1	1	0	7	12	20
Grade 2 (Moderate)	0	1	0	0	3	4
Grade 3 (Severe)	0	0	0	0	1	1

* No Grade 4 or 5 recorded; 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.

HNV: IN NHP REPEAT DOSE STUDY, KIDNEY BIOMARKER ELEVATIONS WERE REDUCED AFTER FIRST DOSE OF PGN-EDO51

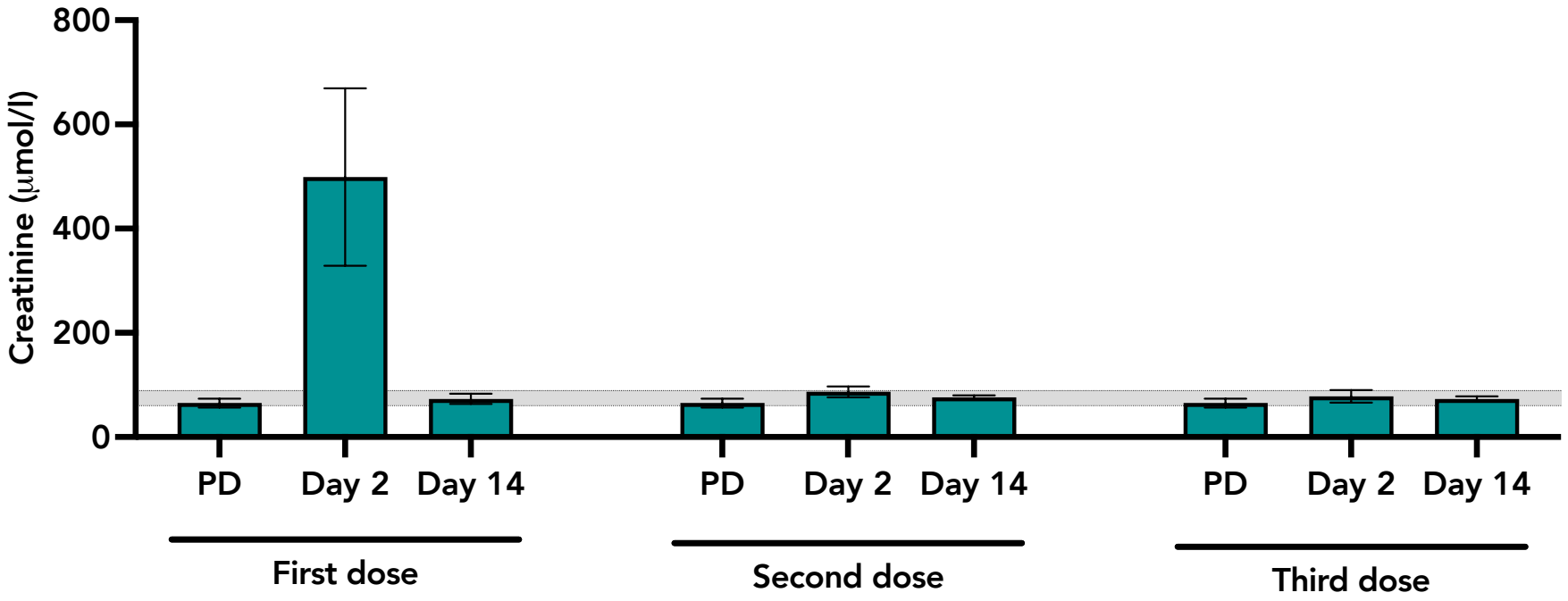
PGN-EDO51

WT



PPMO dose

REPEAT-DOSE SERUM CREATININE LEVELS *(HIGH-DOSE COHORT)*



These results support the potential tolerability of PGN-EDO51 with repeat dosing

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PD = pre-dose. Protocol: PGN-EDO51 was administered to NHP by IV infusion over 30 min at a given dose level (n=3). Q2W, three doses administered, saline control. Tissues were harvested 7 days after final administration. Shown as mean ± SD; n = 3 per group. Study was not powered for statistical significance. Grey bar shows normal range.

PEPGEN HAS COMPLETED A PH1 HNV TRIAL FOR PGN-EDO51; ON TRACK TO INITIATE DMD PATIENT CLINICAL TRIAL IN 1H23

	2022	2023	2024
Anticipated milestones	• **2Q:** First HNV dosed in Ph1 trial ✓ • **3Q: Ph1 clinical safety, oligo delivery & exon skipping data** ✓ • **4Q:** Completion of Ph2a-enabling tox studies	• **1H: Initiation of Ph2a DMD patient clinical trial**	• Safety and **dystrophin data** in DMD patients (Ph2a)
Overview	• Ph1 trial showed highest single-dose levels of exon skipping & oligo delivery • PGN-EDO51 was generally well-tolerated • We believe readouts support progression to Ph2a	• Trial will assess safety and tolerability, exon skipping and dystrophin in DMD patients • Safety readouts from HNV trial anticipated to support MAD initiation at higher dose levels • Precedents suggest that exon skipping readouts will be higher in patients than in HNVs at the same dose level • Anticipate trial will be conducted in multiple geographies, including U.S.	

PGN-EDODM1 FOR MYOTONIC DYSTROPHY TYPE 1 (DM1)

MYOTONIC DYSTROPHY TYPE 1 IS A PROGRESSIVE, DEBILITATING NEUROMUSCULAR DISORDER WITH GREAT UNMET NEED

ROOT CAUSE OF DISEASE

- Due to a CTG repeat expansion mutation in the *DMPK* gene
- Leads to downstream dysregulation of a broad set of proteins

SYMPTOMATOLOGY & NATURAL HISTORY

- Myotonia, muscle weakness, GI issues
- CNS symptoms*, cardiac & respiratory abnormalities
- Wide range in age of onset, life expectancy 45 – 60 years

PATIENT POPULATION**

~40,000 *(US)*

~75,000 *(EEA)*

~15,000 *(JP)*

THERAPEUTIC LANDSCAPE

- No approved disease-modifying therapeutics
- Standards of care focused on symptom management

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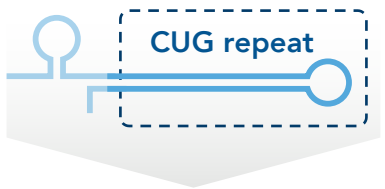
* CNS symptoms include cognitive deficits, excessive daytime sleepiness and behavioral impairments.
** Johnson et al 2021, NORD (1 in 8,000 prevalent population)

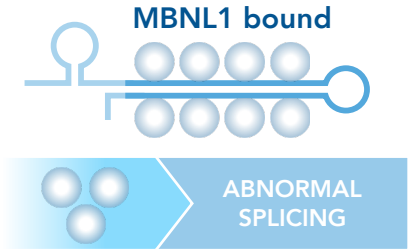
PEPGEN'S PLATFORM DELIVERS STERIC BLOCKING ASOs TO RESTORE CELLULAR FUNCTION IN DM1

DM1 CAUSED BY CUG TRIPLET EXPANSION HAIRPIN LOOP IN *DMPK* RNA SEQUESTERING MBNL1 PROTEIN

WITHOUT TREATMENT

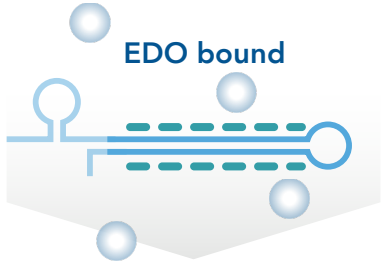


CUG repeats form 'hairpin loops' in the *DMPK* RNA, which sequester a key RNA processing protein (MBNL1)



Downstream mis-splicing events and aberrant protein expression gives rise to disease phenotypes

WITH PGN-EDODM1 TREATMENT



PGN-EDODM1 binds toxic CUG repeats in *DMPK* RNA and blocks MBNL1 binding

Downstream splicing patterns are restored

PGN-EDODM1 is designed to **restore MBNL1 functions and correct downstream mis-splicing events**

THE PHARMACOLOGY OF PGN-EDODM1 HAS BEEN EVALUATED IN MULTIPLE PRECLINICAL MODELS

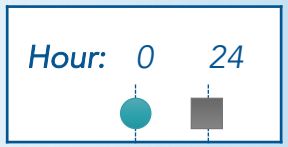
		Species	Study design	Key readouts observed
Non-GLP pharmacology studies	Patient cells *PGN-EDODM1*	*DM1 patient*	*Hour:* 0 24	• Reduction in nuclear foci • Correction of downstream transcript mis-splicing
	Single dose *PGN-EDODM1*	*HSA^{LR}*	*Week:* 0 1 2	• Correction of downstream transcript mis-splicing • Normalization of myotonia
	Duration of effect *PGN-EDODM1*	*HSA^{LR}*	*Week:* 0 12 24	• Correction of downstream transcript mis-splicing for at least 24 weeks post-dose
Non-GLP dose-range finding (DRF) studies	Single dose *PGN-EDODM1*	*WT*	*Week:* 0 1	• *In progress*
	Repeat dose *PGN-EDODM1*	*WT*	*Week:* 0 1 2 3 4 5	• *In progress*

PepGen ● PGN-EDO dose ■ Tissue / serum analysis

PGN-EDODM1 REDUCED PATHOGENIC NUCLEAR FOCI AND CORRECTED DOWNSTREAM TRANSCRIPT MIS-SPLICING

PGN-EDODM1

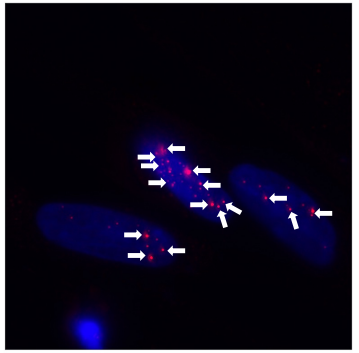
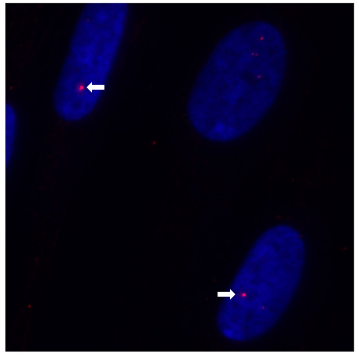
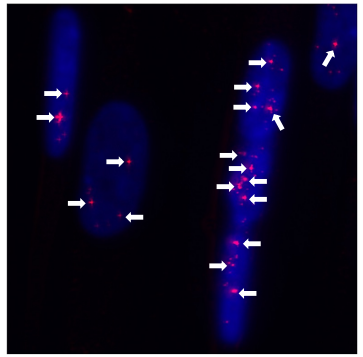
DM1 patient cells
(2,600 CTG repeats)



PGN-EDODM1 dose

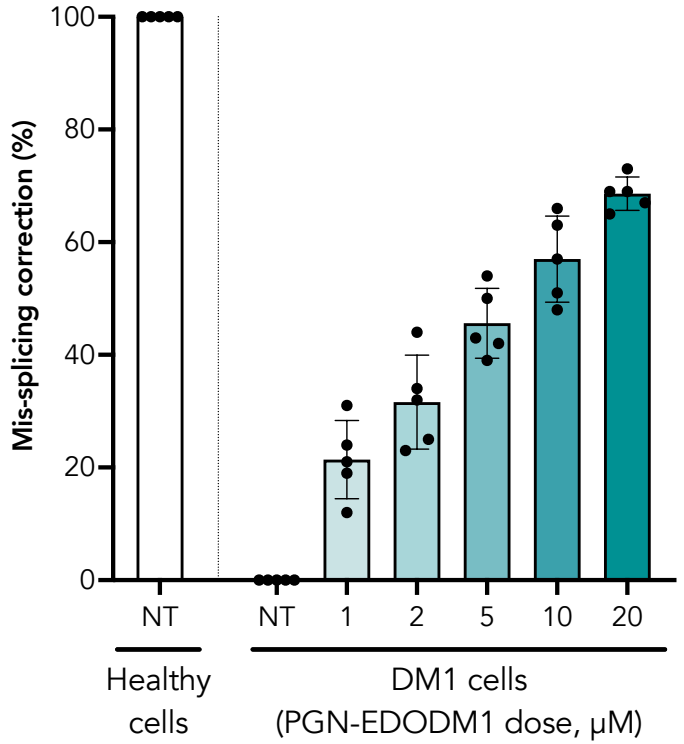
Analysis

FOCI REDUCTION

Not treated (NT)	PGN-EDODM1	PMO
		
Foci observable in patient cells	**Robust reduction** in number of foci following PGN-EDODM1 treatment	No foci reduction with unconjugated PMO

MIS-SPLICING CORRECTION

Across multiple transcripts



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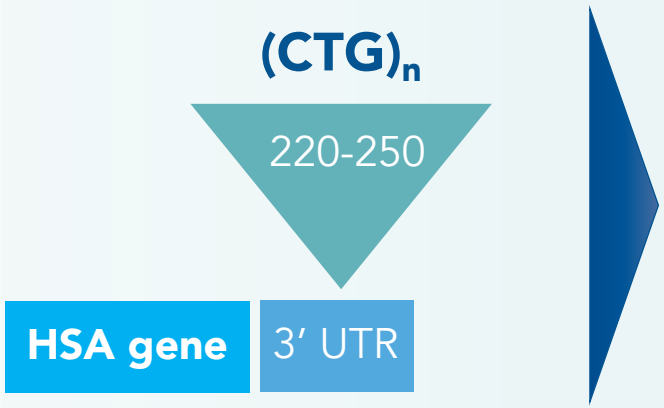
Immortalized myoblasts from healthy individual or DM1 patient with 2600 CTG repeats were cultivated then differentiated for 4 days. Treatment with PMO or peptide-PMO conjugates at concentrations given. Cells were harvested for analysis 24h after treatment. Visualisation with FISH and immunofluorescence.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

HSA^{LR} MOUSE DISPLAYS MOLECULAR AND FUNCTIONAL DM1 PHENOTYPE

REPEAT EXPANSION IN HSA GENE UTR



DM1 ASSOCIATED ABNORMALITIES

- Skeletal muscle specific CUGexp
- MBNL1 sequestration in the nucleus
- Downstream mis-splicing events
- Myotonia

HSA^{LR} mouse

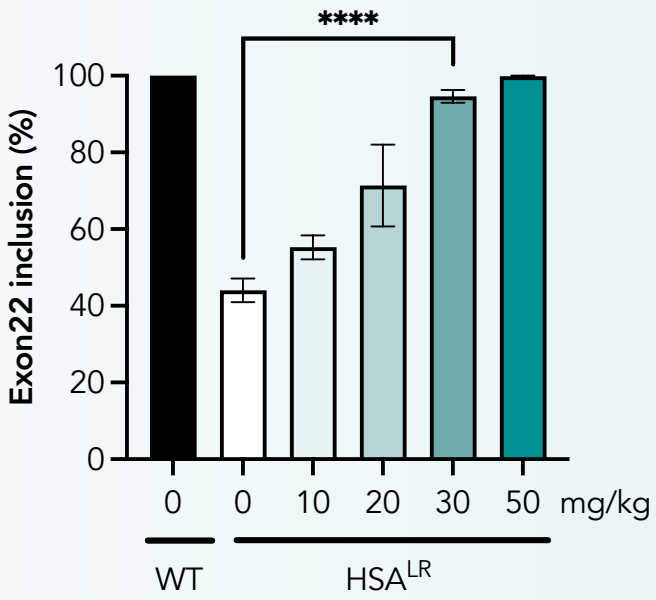
HSA^{LR} mouse

Source: Mankodi et al., SCIENCE 2000.

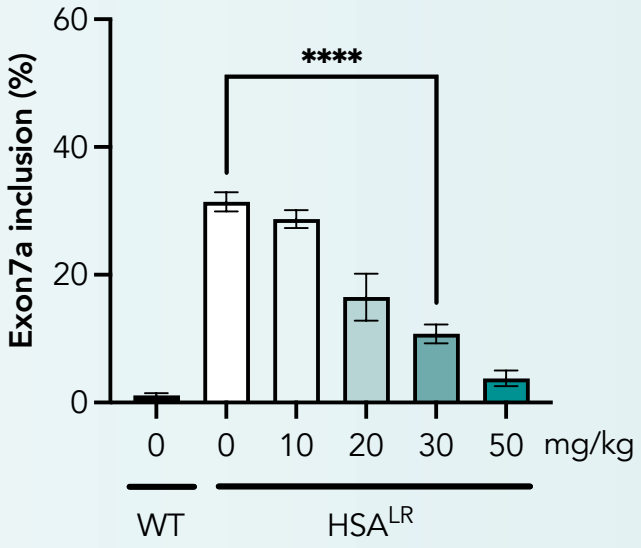
HSA^{LR}: PGN-EDODM1 CORRECTED MOLECULAR AND FUNCTIONAL DM1 PHENOTYPE AT GENERALLY WELL-TOLERATED DOSES

CORRECTION OF MIS-SPLICING

Atp2a1

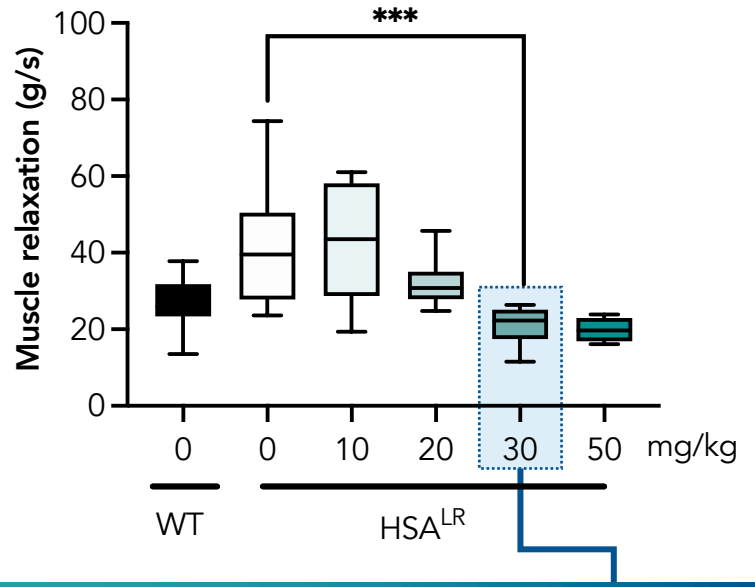


Clcn1



REVERSAL OF MYOTONIA

Rate of muscle relaxation



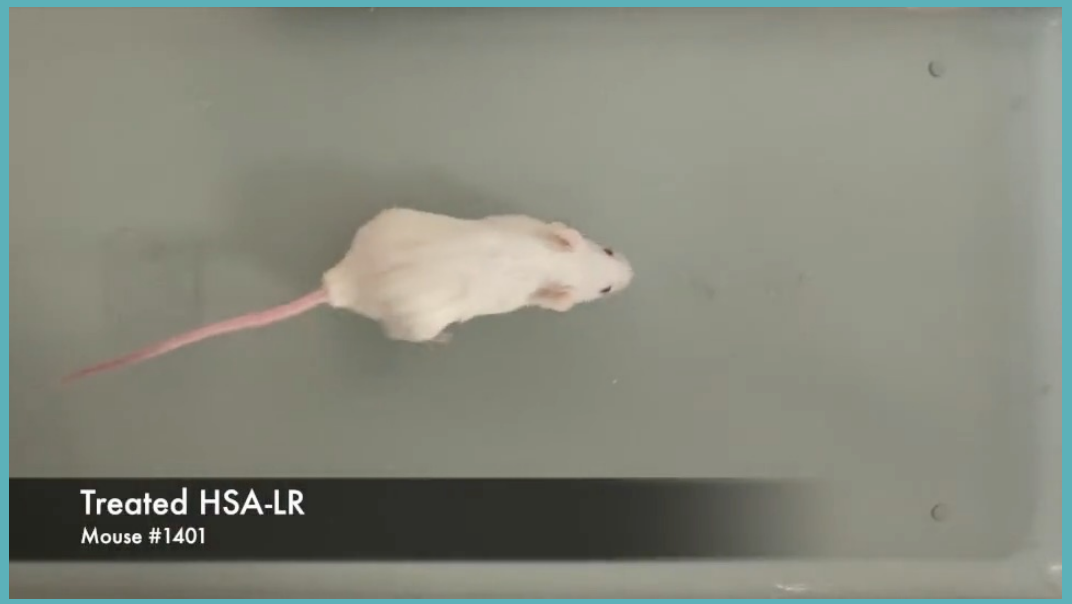
Correction of myotonia observed after a **single dose of 30 mg/kg**

Protocol: PGN-EDODM1 was administered IV to HSA^{LR} mice at doses (mg/kg): 10, 20, 30 (n=8), 50 (n=4) 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 ± SEM or min to max. **** = p≤0.0001; *** = p≤0.001.

HSA^{LR}: SPLICING CORRECTION TRANSLATED TO PHENOTYPIC IMPROVEMENT OF DM1 MICE TREATED WITH PGN-EDODM1

UNTREATED HSA^{LR}

TREATED HSA^{LR}

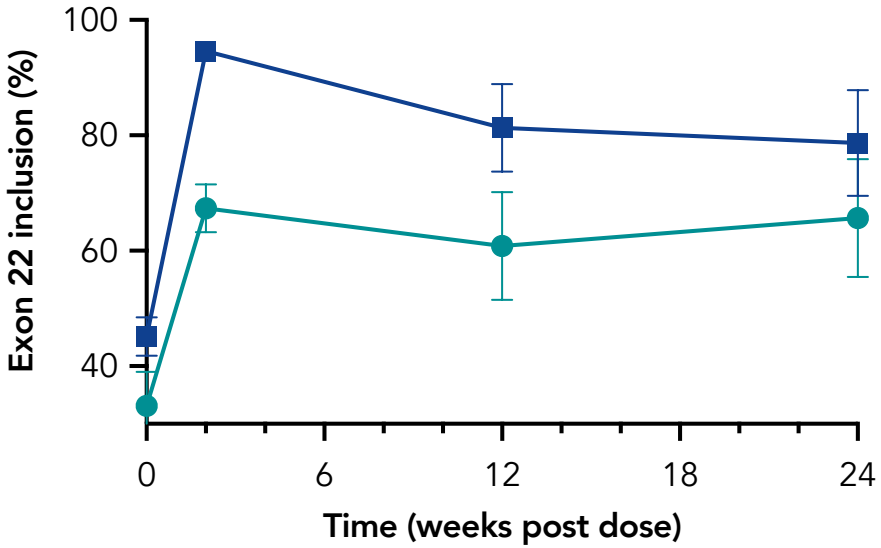


Protocol: PGN-EDODM1 was administered intravenously (IV) to WT and HSA^{LR} mice at 50 mg/kg (n=4-16); myotonia assessed two weeks post-administration.

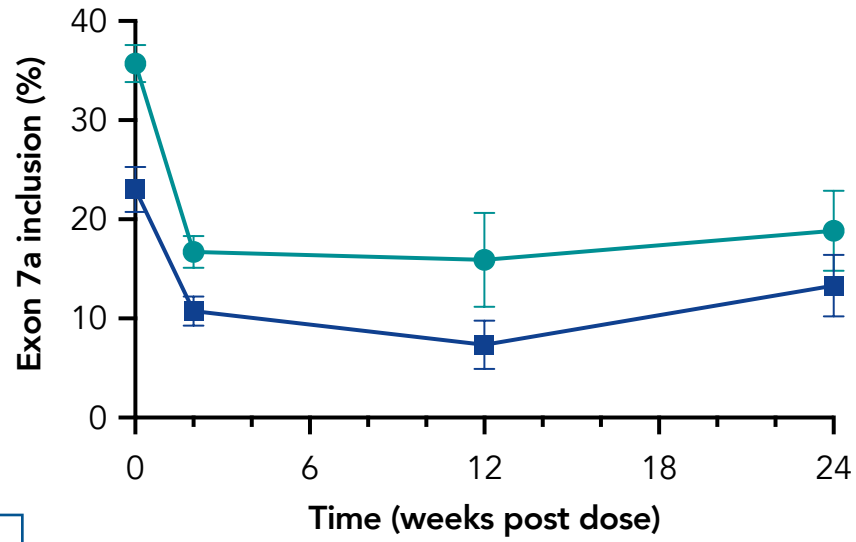
HSA^{LR}: SINGLE DOSE TREATMENT OF PGN-EDODM1 LED TO DURABLE IMPROVEMENTS IN SPLICING THROUGH 24 WEEKS

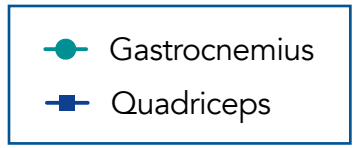
CORRECTION OF MIS-SPLICING

Atp2a1



Clcn1



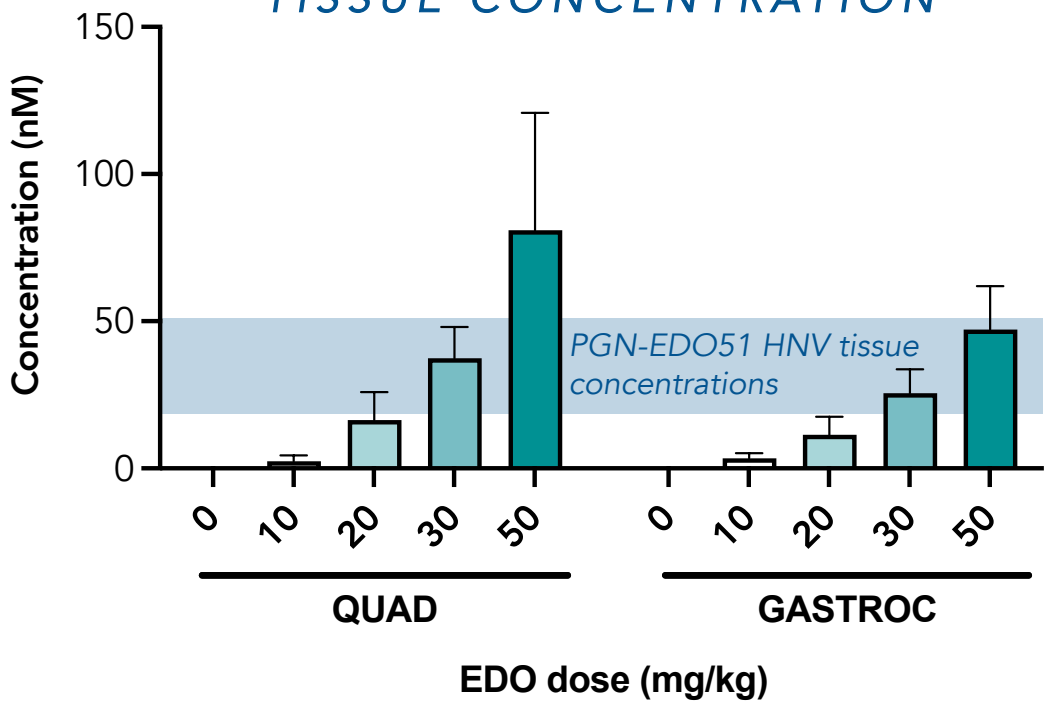


Protocol: PGN-EDODM1 was administered intravenously (IV) to WT and HSA^{LR} mice at 30 mg/kg; gastrocnemius muscle harvested 2 (n=8), 12 (n=8) or 24 (n=5) weeks post-administration; graph plotted as mean ±SEM; n = 7 for 0 timepoint, 8 for 2- and 12-week timepoints; 5 for 24-week timepoint.

HUMAN PGN-EDO51 TISSUE CONCENTRATIONS WERE COMPARABLE TO THOSE ACHIEVED IN HSA^{LR} MOUSE MODEL

HSA^{LR} MOUSE

Robust mis-splicing correction and reversal of myotonia were observed after a **single dose of 30 mg/kg**



PGN-EDO51 Ph1

Following a single 10 or 15 mg/kg dose of PGN-EDO51 in our Ph1 HNV trial, **tissue concentrations were similar** to those measured for PGN-EDODM1 at 30 mg/kg

We believe that PGN-EDODM1 has the potential to achieve concentrations in DM1 patients that could lead to **clinically-meaningful outcomes**, supporting further development of this candidate

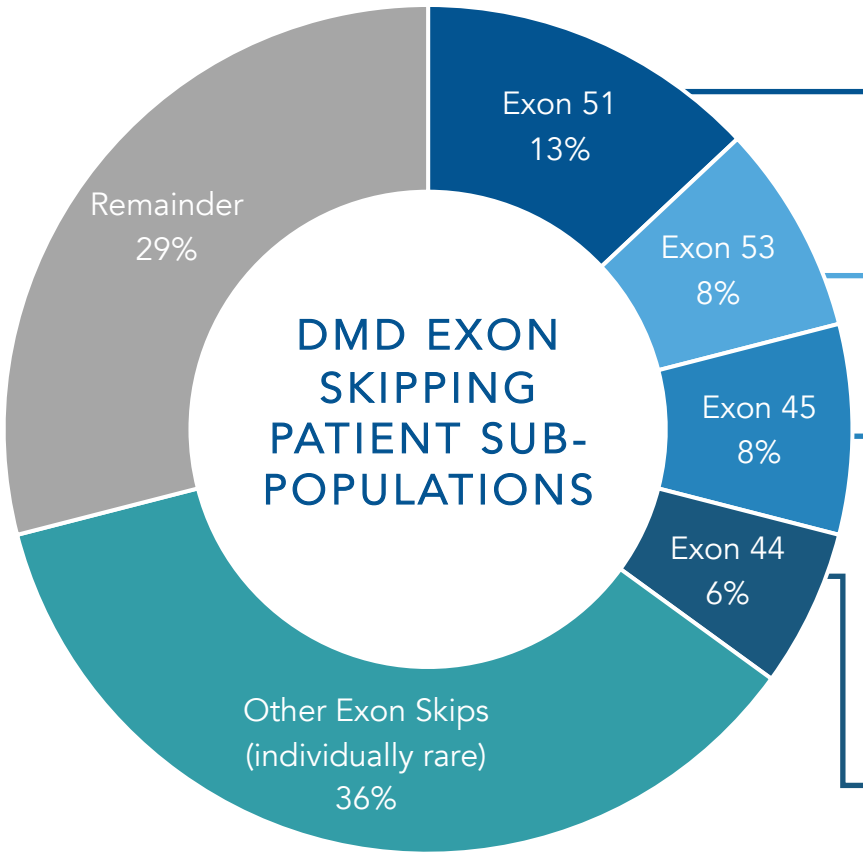
Protocol: PGN-EDODM1 was administered IV to HSA^{LR} mice at doses (mg/kg): 10, 20, 30 (n=8), 50 (n=4) against a wild-type (WT) saline control (n=8). Tissue concentration assessed by HPLC.

PEPGEN IS ON TRACK TO INITIATE A DM1 PATIENT CLINICAL TRIAL IN 1H23

	2022	2023	2024
Anticipated milestones	• **2Q:** NHP dose range-finding study ✓ • **2H: IND-enabling studies**	• **1H: Initiation of Ph1/2 DM1 patient clinical trial**	• Safety and **splicing data** in DM1 patients (Ph1/2)
Overview	• We believe oligonucleotide tissue concentration readouts from PGN-EDO51 Ph1 study support clinical potential of PGN-EDODM1	• Aim of clinical trials is to assess safety, tolerability and efficacy of PGN-EDODM1 in DM1 patients	

EDO PIPELINE

PEPGEN'S LEAD PROGRAM TARGETS LARGEST EXON SKIPPING PATIENT POPULATION IN DMD



PepGen's clinical program

Exon 51: PGN-EDO51

Next anticipated milestone: Ph2a patient trial initiation (1H23)

PepGen's discovery programs

Exon 53: PGN-EDO53

Next anticipated milestone: NHP exon skipping data (2H22)

Exon 45: PGN-EDO45

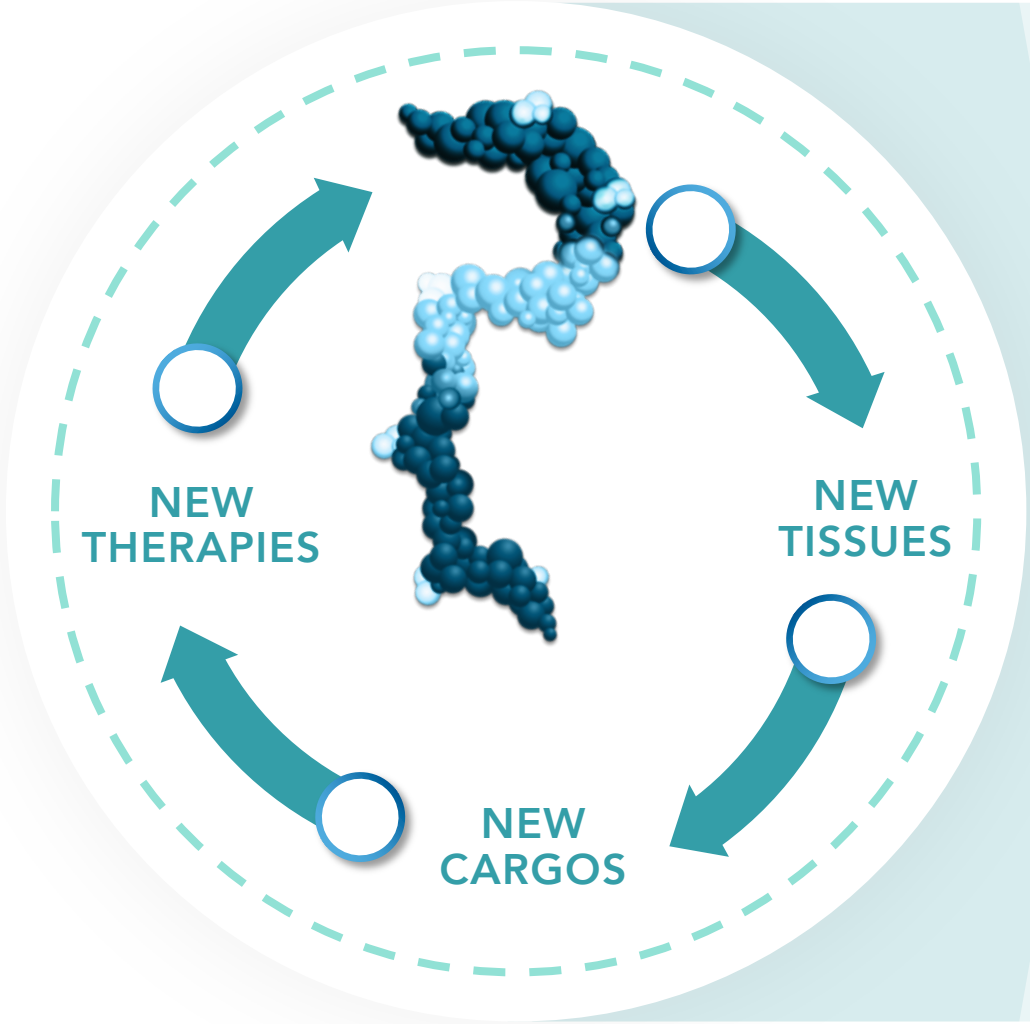
Next anticipated milestone: Candidate nomination (2H22)

Exon 44: PGN-EDO44

Next anticipated milestone: Candidate nomination (2H22)

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

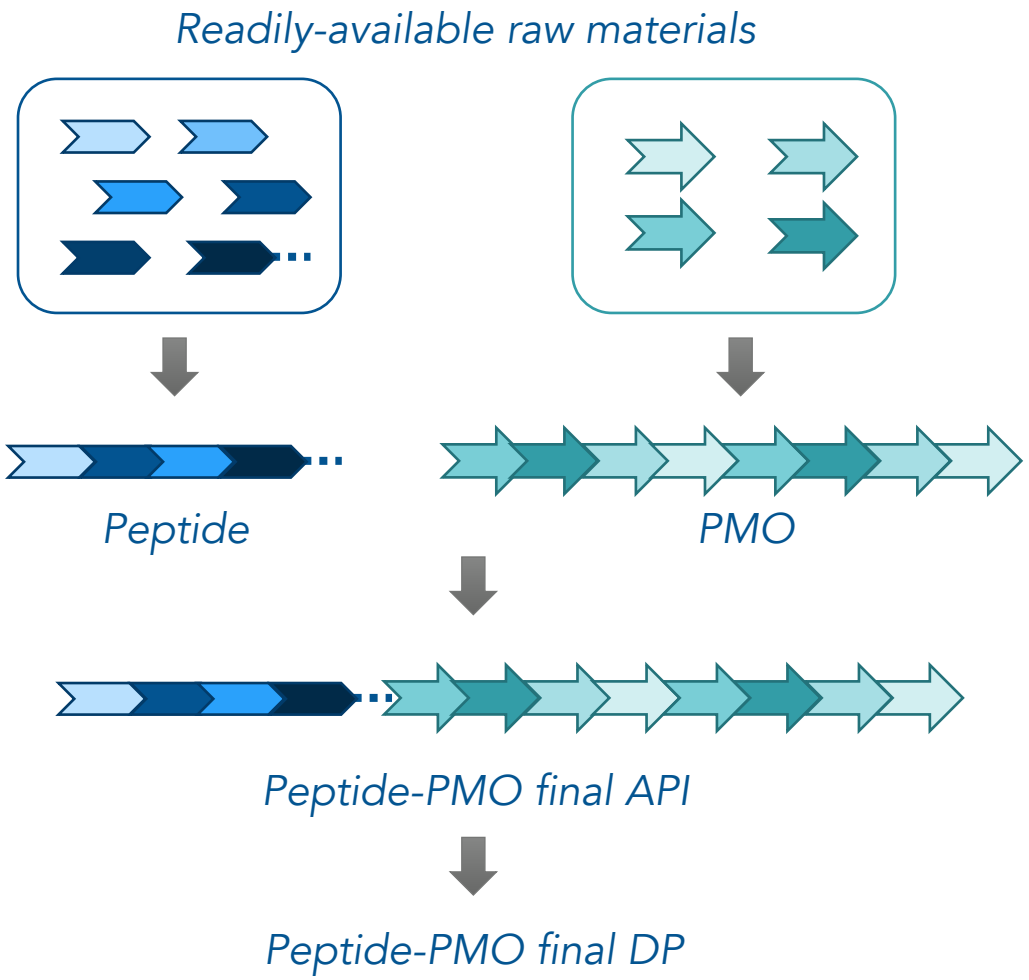
WE ARE HARNESSING THE POWER OF OUR EDO PLATFORM TO REACH NEW TISSUES, DELIVER NEW CARGOS, & DEVELOP NEW THERAPIES



WE WILL LEVERAGE OUR EDO PEPTIDE PLATFORM TO:

- *REACH NEW TISSUES*
  - Explore full potential of EDO platform across **multiple tissue types**, including:
    - Deep brain structures via IT administration
    - Peripheral nerves via IV administration
    - Other tissue and cell types
- *DELIVER NEW CARGOS*
  - Utilize **modular nature** of EDO platform to evaluate new cargo technologies
  - Explore potential for **non-PMO oligo** and small molecule delivery
- *DEVELOP NEW THERAPIES*
  - Identify opportunities for novel EDO therapeutics
  - Maximize EDO platform and pipeline value through **strategic collaborations**

CURRENT MANUFACTURING CAPABILITIES DESIGNED TO SUPPORT ALL PLANNED CLINICAL TRIALS AND COMMERCIALIZATION



HIGHLIGHTS:

- **Fully synthetic** manufacturing process; **no cell-based steps**
- Product and intermediates are **readily characterized**
- Research to date suggests product has **robust stability**
- **Multiple cGMP** DP batches have been **manufactured and released**

CONCLUSION

THE FUTURE OF PEPGEN

2022

PGN-EDO51 (DMD exon 51) Ph1 HNV trial showed:

- **Highest level of single-dose exon skipping and oligo delivery observed in a clinical trial***
- PGN-EDO51 was generally well-tolerated

2023

Anticipate **initiation of patient clinical trials** for DMD & DM1

2024

Anticipate **clinical POC in two indications:**

- Patient dystrophin data (DMD)
- Patient splicing data (DM1)

- 5 neuromuscular disease therapies in pipeline
- Work underway to **leverage EDO platform** to expand to new tissues & new indications

PepGen

* 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.

THANK YOU