PepGen™

Advancing the Use of Peptide-Conjugated Oligonucleotides to Target Neuromuscular Disorders: Enhanced Delivery Oligonucleotides for DMD and DM1

James McArthur, PhD

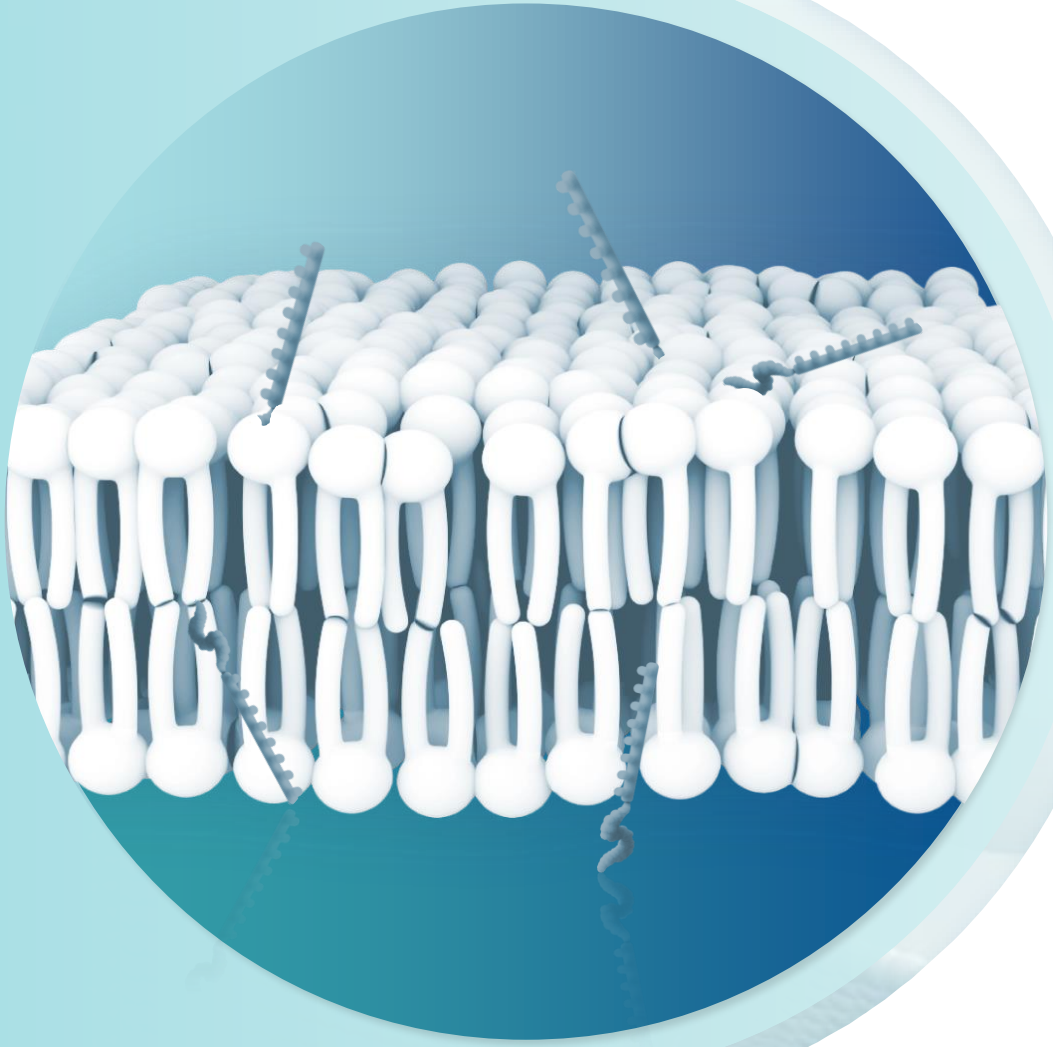
President and CEO

September 4, 2024

Forward-Looking Statements

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 presentation that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include, without limitation, statements regarding the potential of our EDO platform to deliver higher levels of oligonucleotide to the nuclei and retain the efficacy with an improved safety profile relative to other cell penetrating peptides, the therapeutic potential and safety profile of our product candidates, including PGN-EDODM1 and, based on early data, PGN-EDO51, the design, initiation and conduct of clinical trials, including expected timelines for our CONNECT2-EDO51 Phase 2 trial and FREEDOM2-DM1 Phase 2 trial, the expected timing for additional results from our CONNECT1-EDO51 Phase 2 trial and results from our FREEDOM-DM1 Phase 1 trial, ongoing and planned regulatory interactions, and the advancement of PGN-EDO53 in IND/CTA enabling studies.

Any forward-looking statements in this presentation are based on current expectations, estimates and projections only as of the date of this presentation 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: delays or failure to successfully initiate or complete our ongoing and planned development activities for our product candidates, including PGN-EDO51, PGN-EDODM1 and PGN-EDO53; our ability to enroll patients in our clinical trials, including CONNECT1-EDO51, CONNECT2-EDO51, FREEDOM-DM1 and FREEDOM2-DM1; that our interpretation of clinical and preclinical study results may be incorrect, or that we may not observe the levels of therapeutic activity in clinical testing that we anticipate based on prior clinical or preclinical results, including for PGN-EDO51 and PGN-EDODM1; our product candidates, including PGN-EDO51 and PGN-EDODM1, may not be safe and effective or otherwise demonstrate safety and efficacy in our clinical trials; adverse outcomes from our regulatory interactions, including delays in regulatory review, clearance to proceed or approval by regulatory authorities with respect to our programs, including clearance to commence planned clinical studies of our product candidates, or other regulatory feedback requiring modifications to our development programs, including in each case with respect to our including CONNECT1-EDO51, CONNECT2-EDO51, FREEDOM-DM1 and FREEDOM2-DM1 clinical trials; changes in regulatory framework that are out of our control; our ability to obtain, maintain and protect our intellectual property; our ability to enforce our patents against infringers and defend our patent portfolio against challenges from third parties; competition from others developing therapies for the indications we are pursuing; unexpected increases in the expenses associated with our development activities or other events that adversely impact our financial resources and cash runway; and our dependence 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 our most recent annual report on Form 10-K and quarterly report on Form 10-Q that are filed with the SEC. PepGen explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.



Driven by our proprietary Enhanced Delivery Oligonucleotide (EDO) platform, PepGen is creating a pipeline of disease-modifying therapeutics with the potential to safely and effectively target the underlying cause of serious genetic neuromuscular and neurological disorders.

Pipeline Enabled by EDO Technology

INVESTIGATIONAL CANDIDATES	CLINICAL PROGRAMS	INDICATIONS	PRECLINICAL	PHASE 1	PHASE 2	PIVOTAL
PGN-EDO51	Connect	DMD – *Exon 51*				
PGN-EDODM1	Freedom	DM1 – *DMPK*				
PGN-EDO53		DMD – *Exon 53*				

Research

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

Note: Clinical plans are subject to alignment with regulatory authorities.

Who We Are

Our mission

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

Proprietary delivery platform

- Enhanced Delivery Oligonucleotide platform
  - Increased cellular uptake
  - Increased nuclear uptake
  - Enhanced potency at tolerable doses

Clinical stage pipeline: readouts in 2024

- Duchenne muscular dystrophy (DMD): Initial readout (5 mg/kg) from multiple ascending dose study (Phase 2)
  - Data demonstrates EDO technology delivers high levels of oligonucleotides to the nucleus
- Myotonic dystrophy type 1 (DM1): Initial readout from single ascending dose study (Phase 1) expected Q4:2024

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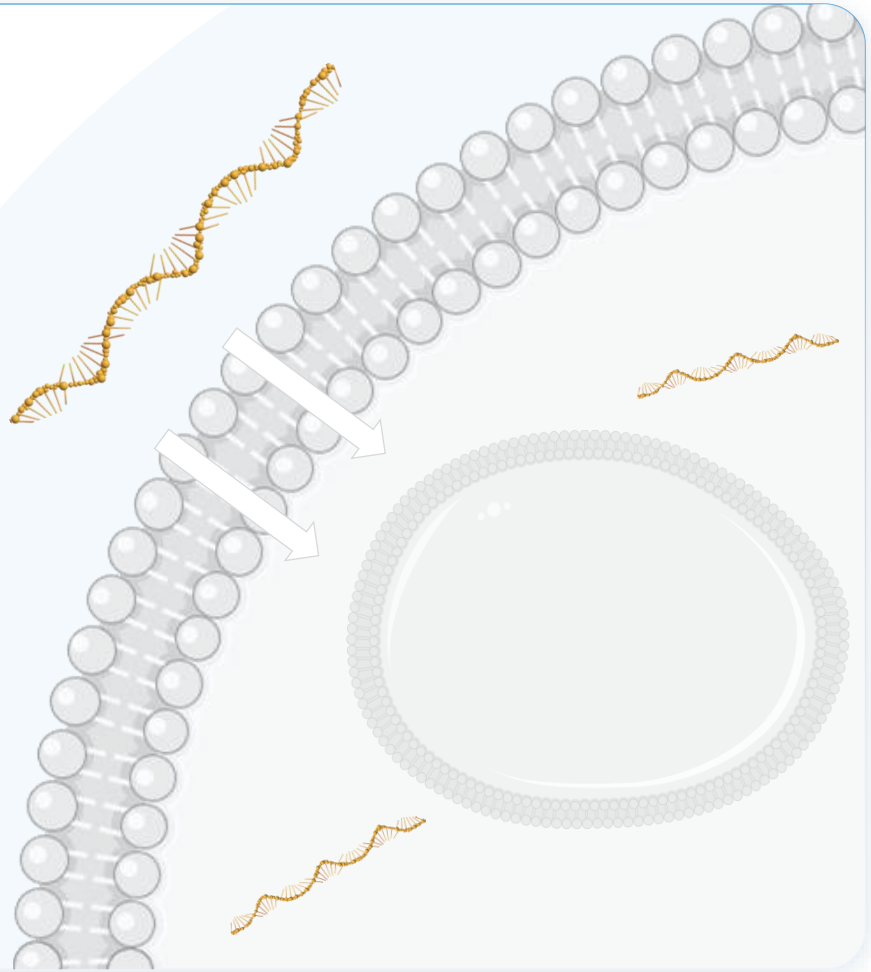
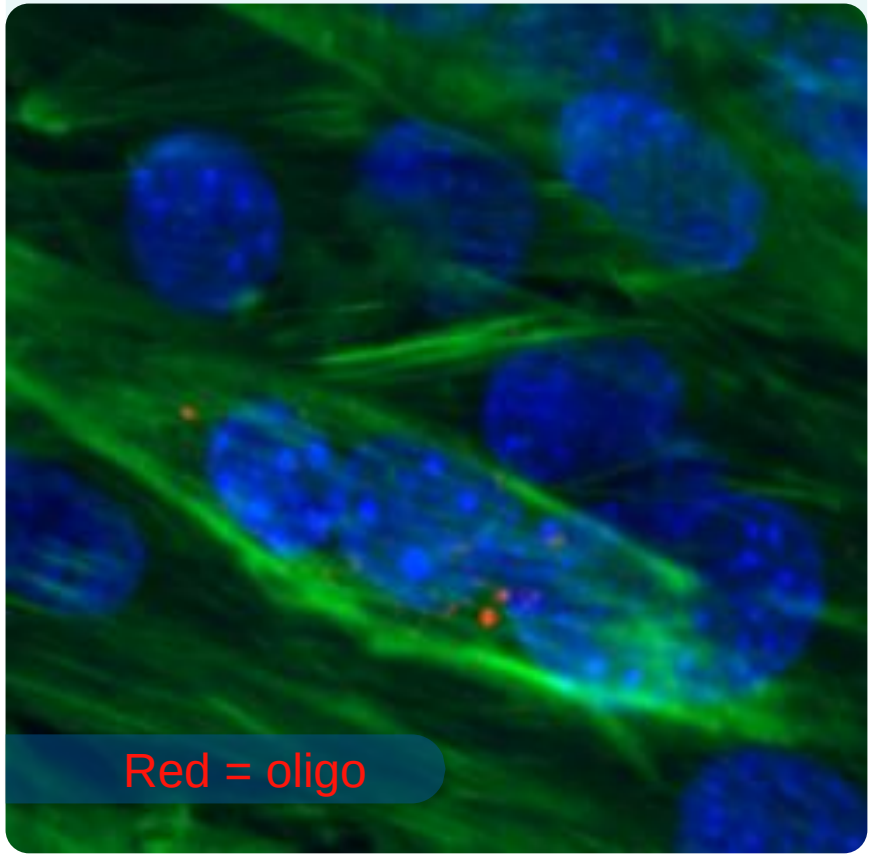
Enhanced Delivery Oligonucleotide Platform

The Challenge of Oligonucleotides

Naked oligonucleotides do not efficiently penetrate muscle cells and nucleus



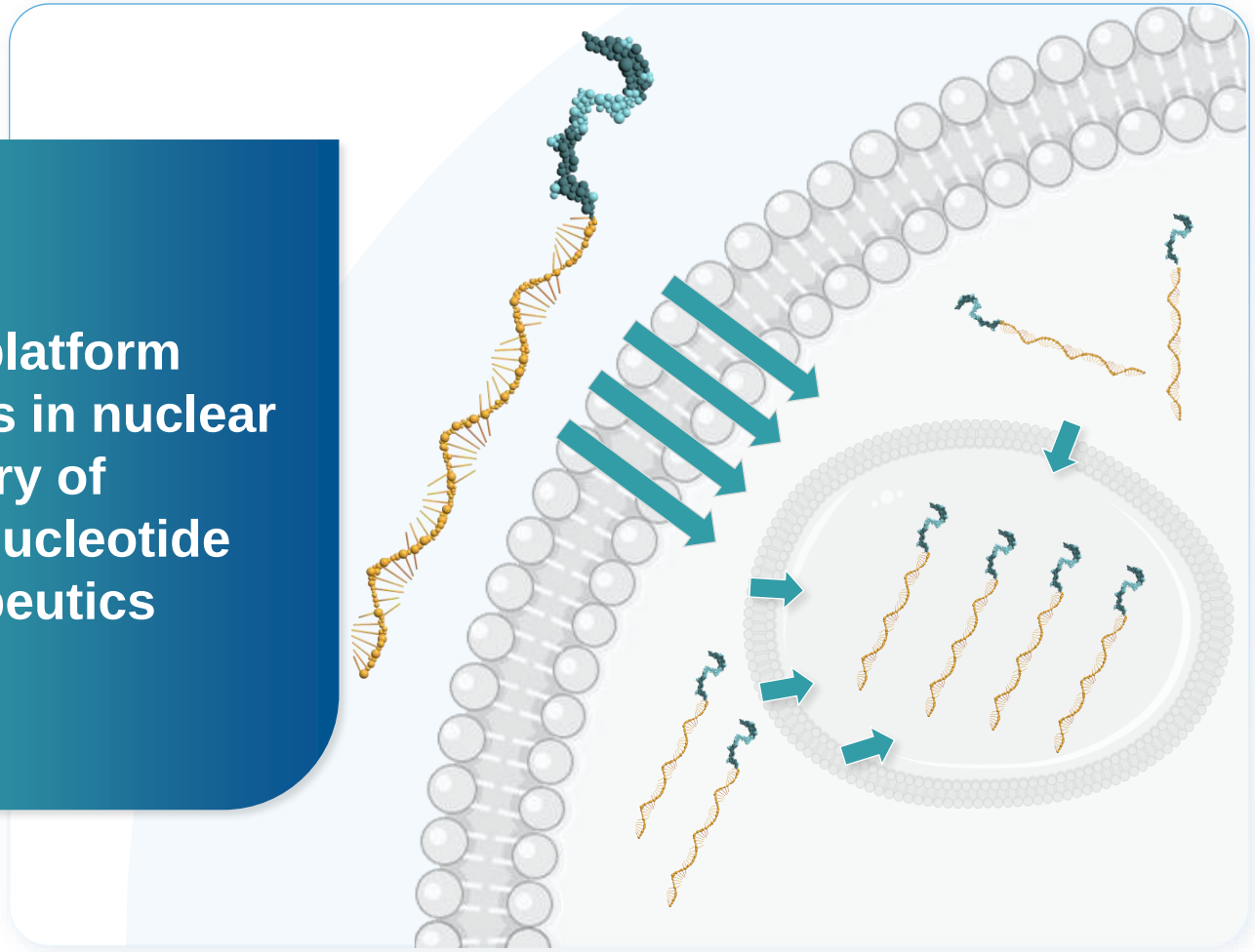
Naked Oligonucleotide (PMO)



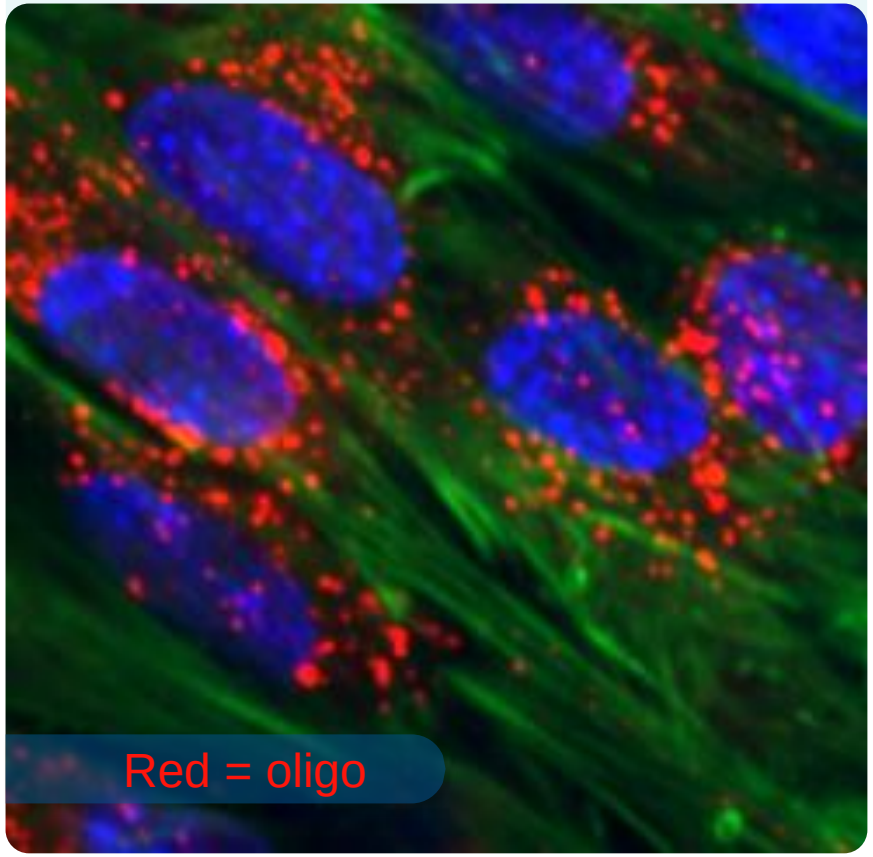
In vitro staining image is shown with 10µM concentration of PMO23 (naked oligonucleotide). C2C12 mouse cells were differentiated for 4 days into myotubes and treated with fluorescently tagged compounds for 24h. PMO: phosphorodiamidate morpholino oligomer

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 25X Higher Nuclear Uptake of Oligonucleotide



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

Evolution of Cell Penetrating Peptides

	“Naked” PMO	PiP Peptide	R6G
Amino acids	0	18-22	6
Arginines	0	8-10	6
Aminohexanoic acids	0	2-4	0
Hydrophobic core used in EDO	**No**	**No**	**No**

PMO: phosphorodiamidate morpholino oligonucleotide; PiP peptide: most frequently published peptide nucleic acid/phosphorodiamidate morpholino oligonucleotide internalizing peptide; R6G-PMO23 is believed to be structurally equivalent to the peptide component of vesleteplirsen conjugated to a murine exon 23 skipping oligonucleotide.

EDO's Construction is Distinct from Other Cell Penetrating Peptides

	"Naked" PMO	PiP Peptide	R6G	EDO
Amino acids	0	18-22	6	**<17**
Arginines	0	8-10	6	**5 or 6**
Aminohexanoic acids	0	2-4	0	**0**
Hydrophobic core used in EDO	No	No	No	**Yes**

EDO's hydrophobic core is distinct from those of PiP peptides

PMO: phosphorodiamidate morpholino oligonucleotide; PiP peptide: most frequently published peptide nucleic acid/phosphorodiamidate morpholino oligonucleotide internalizing peptide; R6G-PMO23 is believed to be structurally equivalent to the peptide component of vesleteplirsen conjugated to a murine exon 23 skipping oligonucleotide.

EDO Technology Increases Endosomal Escape and Cellular Uptake of Oligonucleotides

PMO Delivery in Cells

HeLa cells

HOURS:

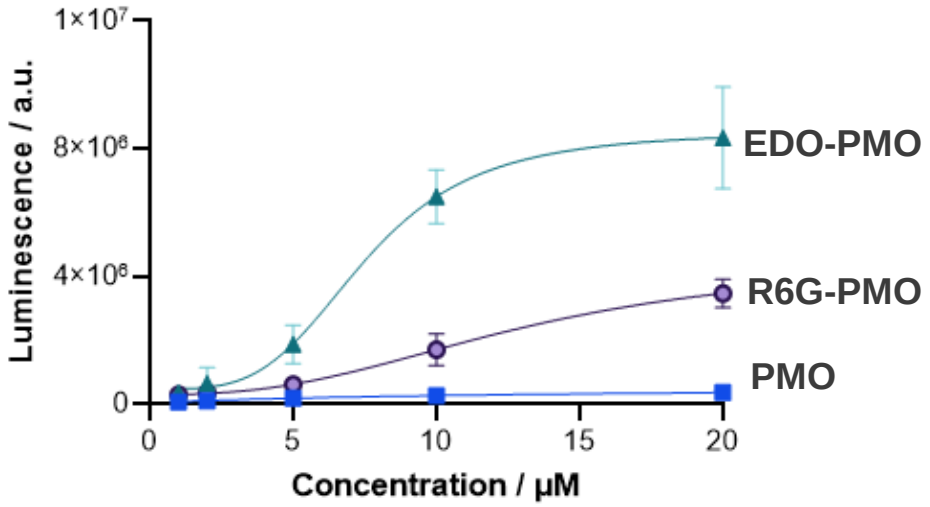
0 24

PMO or PPMO dose

Tissue analysis

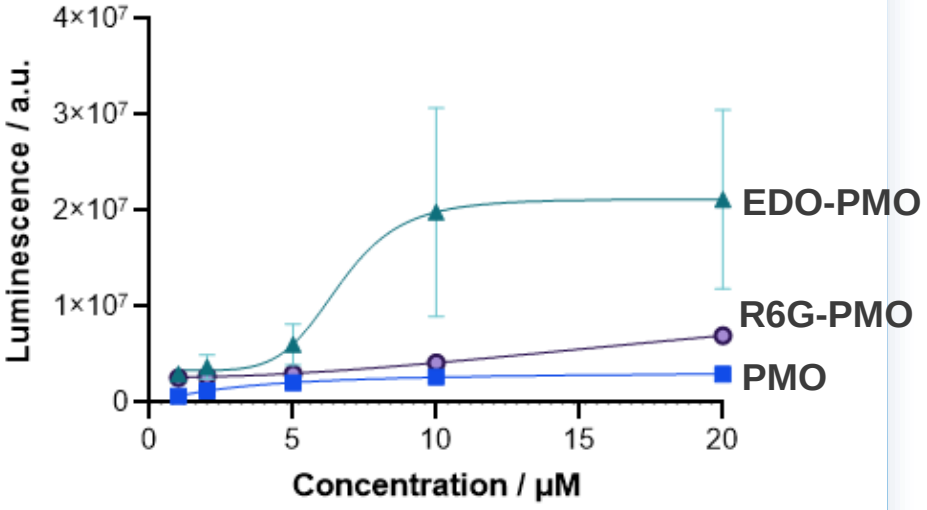
ENDOSOMAL ESCAPE

>30x more escape than PMO or R6G-PMO



TOTAL CELLULAR UPTAKE

>24x more uptake than PMO or R6G-PMO



Cells were treated with 0.1 to 20 µM HiBiT-conjugate for 24 h. Following live cell measurement, 0.01% digitonin was added and cells were incubated for 30 min at 37°C. Mean luminescence is shown relative to HiBiT peptide at matched concentration (± s.d., n=3). PMO: phosphorodiamidate morpholino oligonucleotide; R6G-PMO23 is believed to be structurally equivalent to the peptide component of vesleteplirsen conjugated to a murine exon 23 skipping oligonucleotide

PepGen's Unique EDO Peptides Retain the Efficacy of Previous Generations with Improved Safety Profile Observed to Date

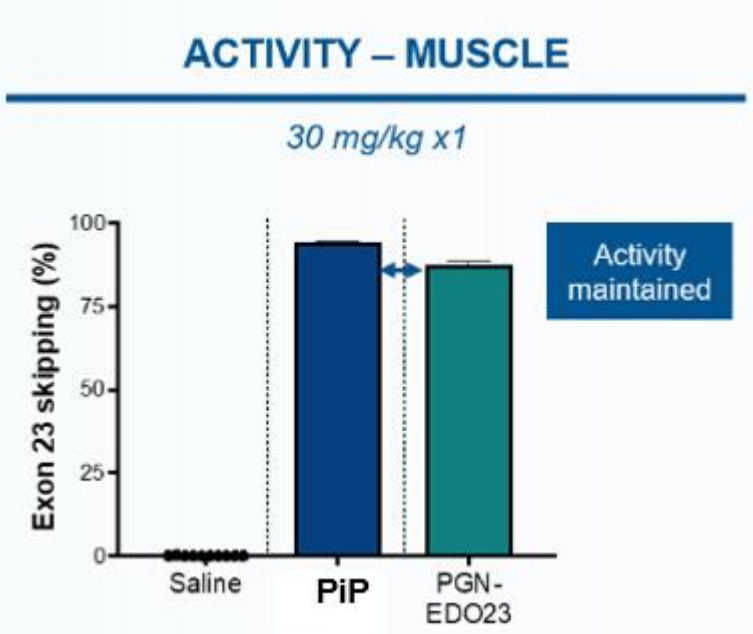
PGN-EDO23
(murine analogue of PGN-EDO51)

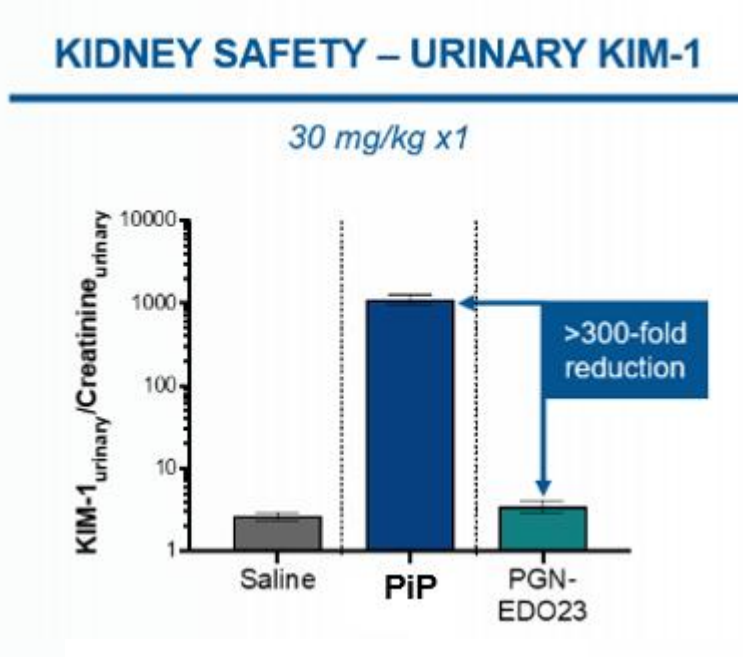
WT

Day:

0 2 7

- Peptide-PMO dose
- Urinary analysis
- Tissue analysis





EDO peptides are structurally distinct from PiP delivery peptides. Combined, EDO peptides have demonstrated comparable activity and improved kidney safety profiles in WT mice after a single dose.

ACTIVITY:	EDO peptide-conjugates result in similar exon skipping profiles as PiP peptide-conjugates in muscle
KIDNEY SAFETY:	EDO peptide-conjugates resulted in significantly lower KIM-1 urinary safety profiles than PiP peptide-conjugates

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PiP peptide: most frequently published peptide nucleic acid/phosphorodiamidate morpholino oligonucleotide internalizing peptide; PiP-peptide conjugate and PGN-EDO23 were administered I.V. to WT mice with a saline control. Tissues harvested 7 days post single dose, exon skipping was measure by qPCR in the tibialis anterior muscle. Urine was collected 2-days post dose, kidney injury molecule-1 (KIM-1) levels were measured and normalized to creatinine in urine. Graphs plotted as mean ± SD, *n* = 3-10.

EDO Platform Has Potential to Increase the Potency of Exon Skipping Oligonucleotides *In Vivo*

PGN-EDO23
(murine analogue of PGN-EDO51)

WT

Week:

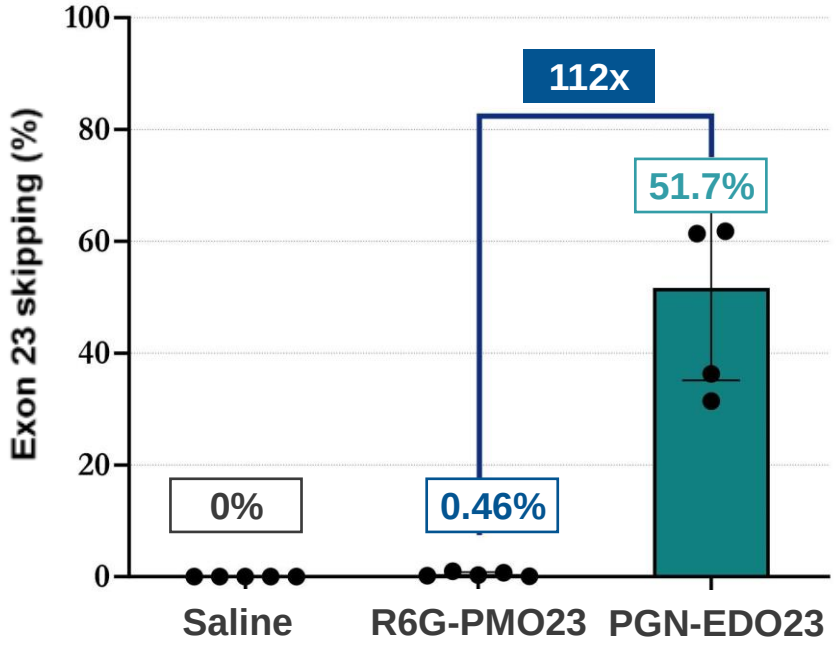
0 1

PMO or PPMO dose

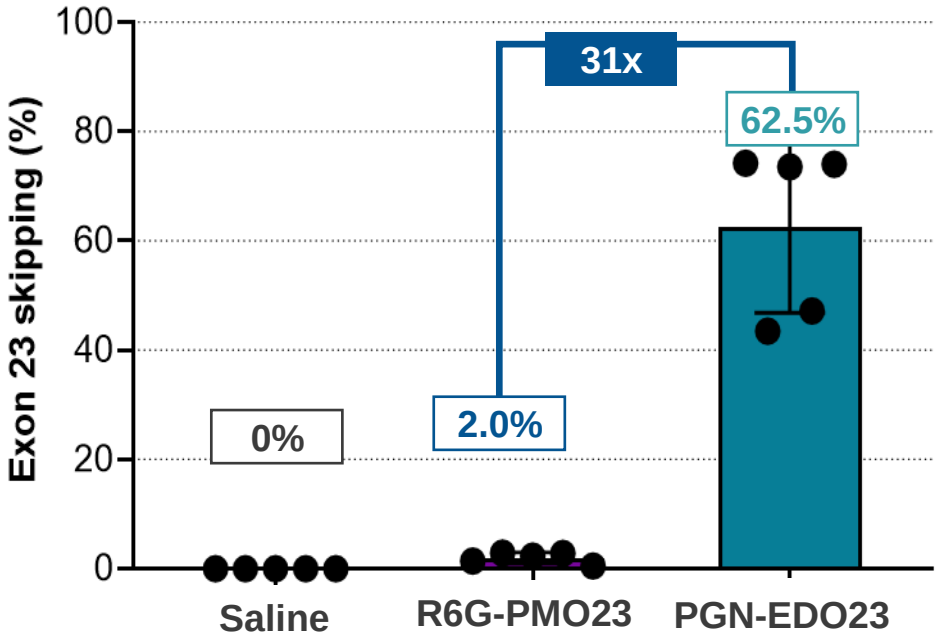
Tissue analysis

EXON SKIPPING

Biceps, 10 mg/kg (qPCR)



Quadriceps, 10 mg/kg (qPCR)



R6G-PMO23 is believed to be structurally equivalent to the peptide component of vesleteplirsen conjugated to a murine exon 23 skipping oligonucleotide. Protocol: R6G-PMO23 or PGN-EDO53 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.

EDO Platform: Broad Distribution Across Muscle Groups Impacted in Neuromuscular Diseases

PGN-EDO51

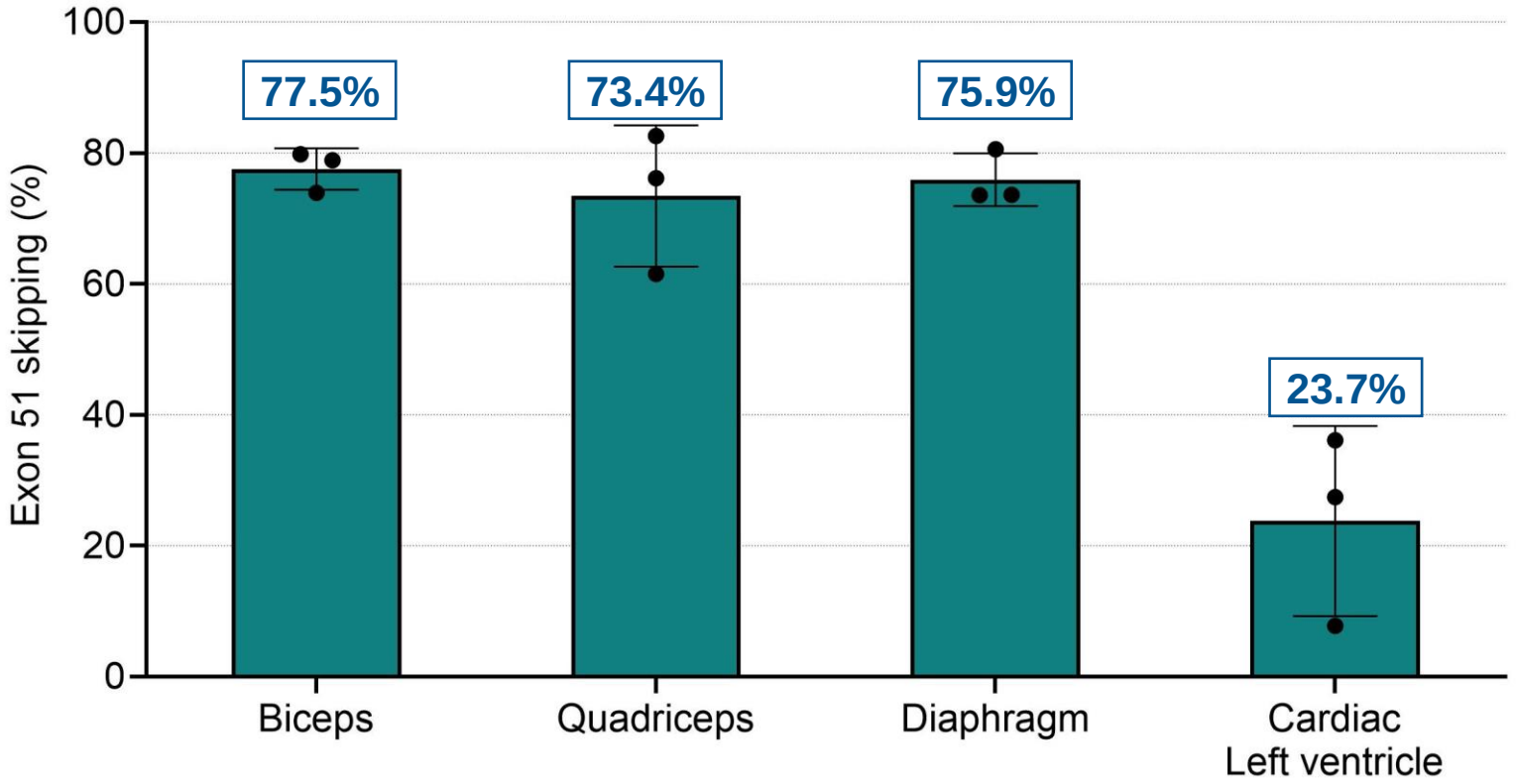
WT

Week:

PPMO dose

Tissue analysis

EXON SKIPPING



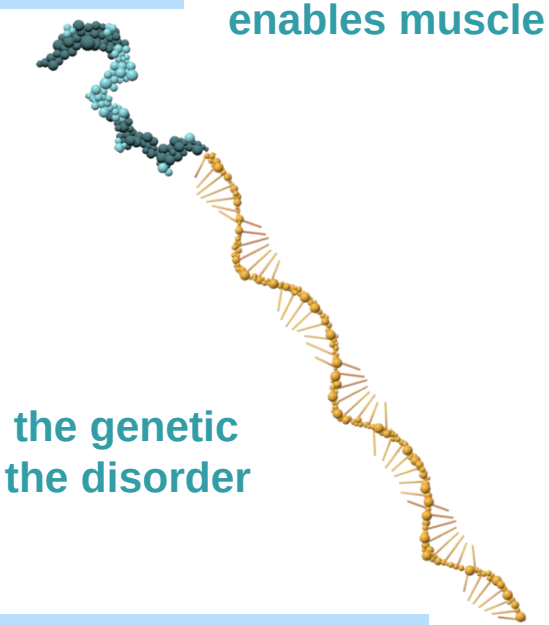
Protocol: Three doses of 30 mg/kg PGN-EDO51 were administered by IV over 30 min every two weeks (n=3). Tissues were harvested 7 days after final administration. Shown as mean ± SD; n = 3 per group. Study was not powered for statistical significance.

PepGen's EDOs Have Potential to Reach Multiple Muscle Groups

PGN-EDO51

Neuromuscular EDO peptide

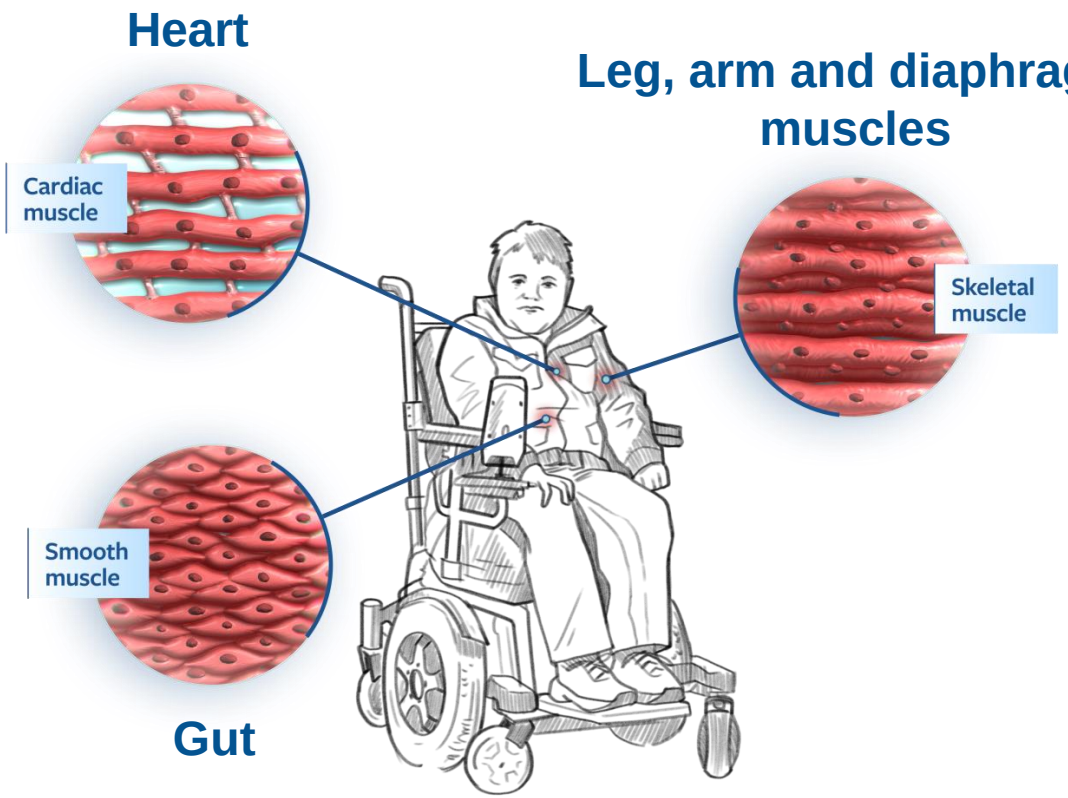
Proprietary EDO peptide enables muscle delivery



Oligo targets the genetic cause of the disorder

Exon 51 skipping antisense oligonucleotide

Delivery



PGN-EDO51: P1 Demonstrated Acceptable Safety Profile Supporting Further Study; P2 Demonstrated Favorable Safety Profile in Indicated Population

Phase 1 Healthy Volunteer (HV) Trial (N=32)

- Volunteers were dosed with 1, 5, 10 or 15 mg/kg of PGN-EDO51 or placebo
- All TEAEs resolved
  - At 10 mg/kg, there were only mild adverse events
  - At 15 mg/kg, the majority of TEAEs were mild, transient, reversible changes in kidney biomarkers
    - 1 HV received <24hrs IV hydration for a related, non-life-threatening SAE, which completely resolved
- Transient mild to moderate hypomagnesemia was observed in 2 participants at 15 mg/kg
- No discontinuations or clinical symptoms of acute kidney injury
- No hematologic, CV or hepatic signs or symptoms

CONNECT1 Phase 2 Trial 5 mg/kg Cohort (N=3)[1]

- All 3 TEAEs were mild and resolved
- 1 patient had 2 related mild TEAEs: (abdominal pain, flatulence)
- No SAEs
- No discontinuations, dose modifications or dose interruptions
  - All participants rolled over to the long-term extension study
- No sustained elevation in kidney biomarkers
- No changes in electrolytes
  - No hypomagnesemia or hypokalemia
- No changes in hepatic function
- No anemia or thrombocytopenia

1. As of May 31, 2024. TEAEs: treatment emergent adverse events; IV: intravenous; SAE: serious adverse event; CV: cardiovascular

EDO Platform: Differentiated Construction with Strong Potency and Improved Safety Profile Observed to Date

	"Naked" PMO	PiP Peptide	R6G	EDO
Amino acids	0	18-22	6	**<17**
Arginines	0	8-10	6	**5 or 6**
Aminohexanoic acids	0	2-4	0	**0**
Hydrophobic core used in EDO	No	No	No	**Yes**
Potency	Weak	Strong	Moderate	**Strong**
Safety: Kidney Kim1 Mice	No	Yes	No	**No**
Safety: Severe Hypomag Human	No	N/A	Yes	**No[1]**

1. As of CONNECT1 PGN-EDO51 5 mg/kg update on July 30, 2024.

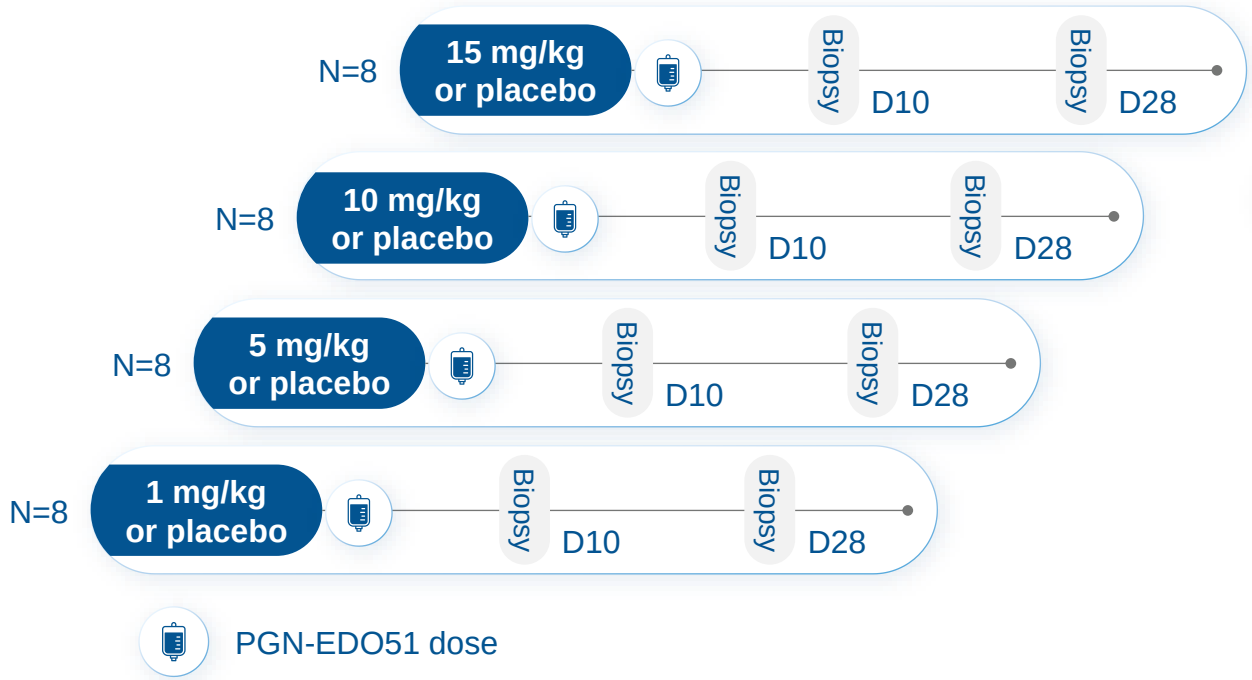
PMO: phosphorodiamidate morpholino oligonucleotide; PiP peptide: most frequently published peptide nucleic acid/phosphorodiamidate morpholino oligonucleotide internalizing peptide; R6G-PMO23 is believed to be structurally equivalent to the peptide component of vesleteplirsen conjugated to a murine exon 23 skipping oligonucleotide; Kim-1: kidney injury marker-1.

PGN-EDO51: Phase 1 Healthy Volunteers Trial

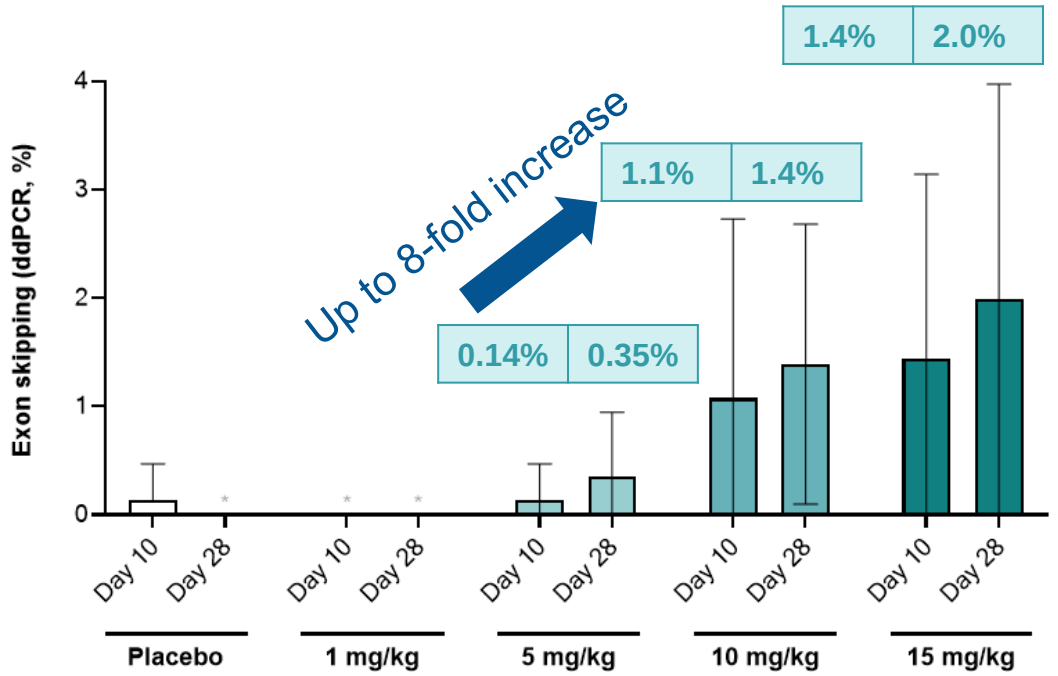
Healthy Volunteer Trial Results Led to CONNECT1: Highest Levels of Exon 51 Skipping in Humans Following Single Dose of PGN-EDO51[1]

Phase 1 Healthy Volunteer (HV) 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: Exon Skipping (Biceps)

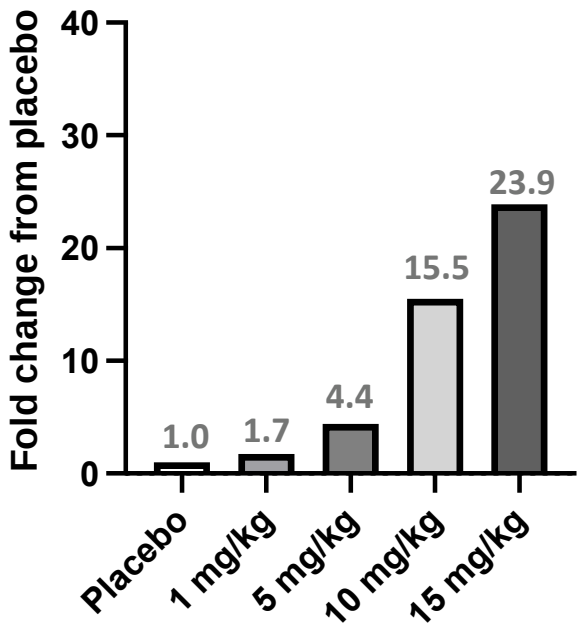


Protocol PGN-EDO51-101: Phase 1, first in human, randomized double blind, placebo controlled single ascending dose study in healthy adult volunteers. Single dose of either PGN-EDO51 or placebo administered by IV infusion at doses indicated. Participants were followed for 28-day period following dose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

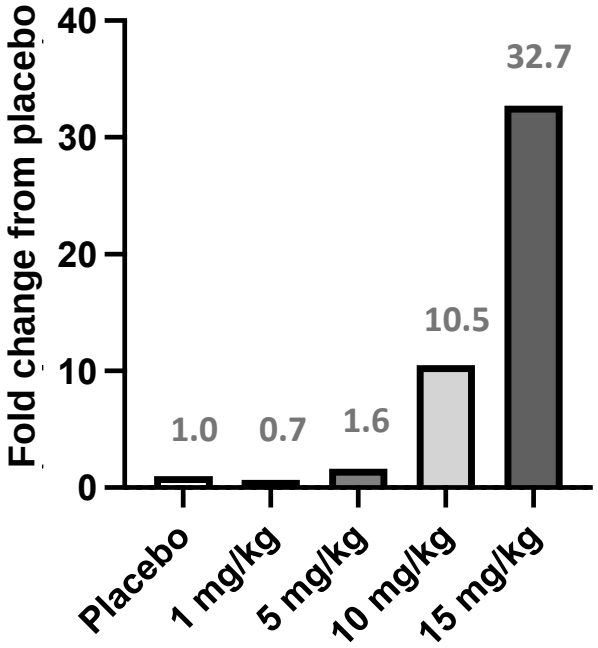
Substantial PMO Signal Observed in Bicep Myocytes and Nuclei Following a Single PGN-EDO51 Dose in Healthy Volunteers

MYOCYTES

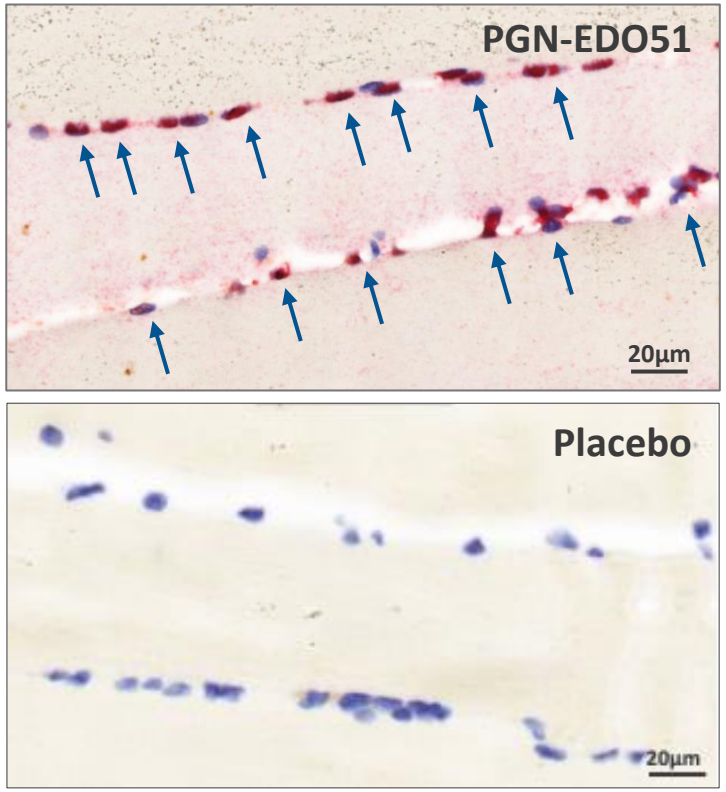


Note: Myocyte signal = nuclear signal + cytoplasmic signal

NUCLEI



Dose-dependent uptake of EDO51 in nucleus



Red-PMO **Blue-Nuclei**

Image from 10 mg/kg dosed group

Healthy volunteers were dosed with placebo or 1, 5, 10, 15 mg/kg PGN-EDO51 via iv infusion. Biceps samples collected at day 10 and assessed for PGN-EDO51 levels in post hoc in situ hybridization analysis using a probe targeting the PMO sequence. Image analysis and quantification was done using Halo imaging software. N=5-8/group.

EDO Technology Demonstrates Highest Level of Skipping in Cross-Trial Comparisons of Exon 51 Skipping Oligonucleotides in Healthy Volunteers

		EXON SKIPPING	DYSTROPHIN
		1 dose (HV)	*>3 doses (DMD patients)*
PGN-EDO51 • Potential for greater dystrophin production • Generally well tolerated in single dose study through 15 mg/kg	**10 mg/kg**	**1.1%[3]**	**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). 3. Day 10 post dose

PGN-EDO51: CONNECT1 Phase 2 Trial

CONNECT1: Designed to Establish Proof-of-Concept

Study Design and Population

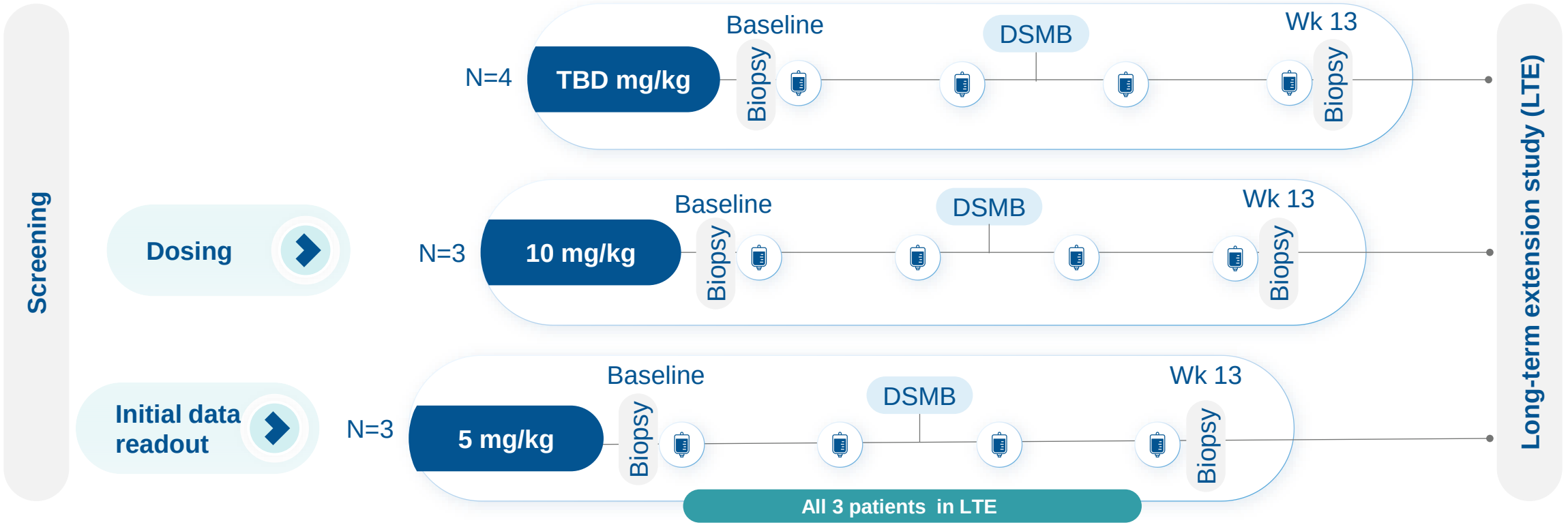
- Open label clinical trial in Canada
- DMD patients (n=10) with exon 51 skippable mutation
- Ages ≥ 8 years
- Ambulatory and non-ambulatory

Endpoints

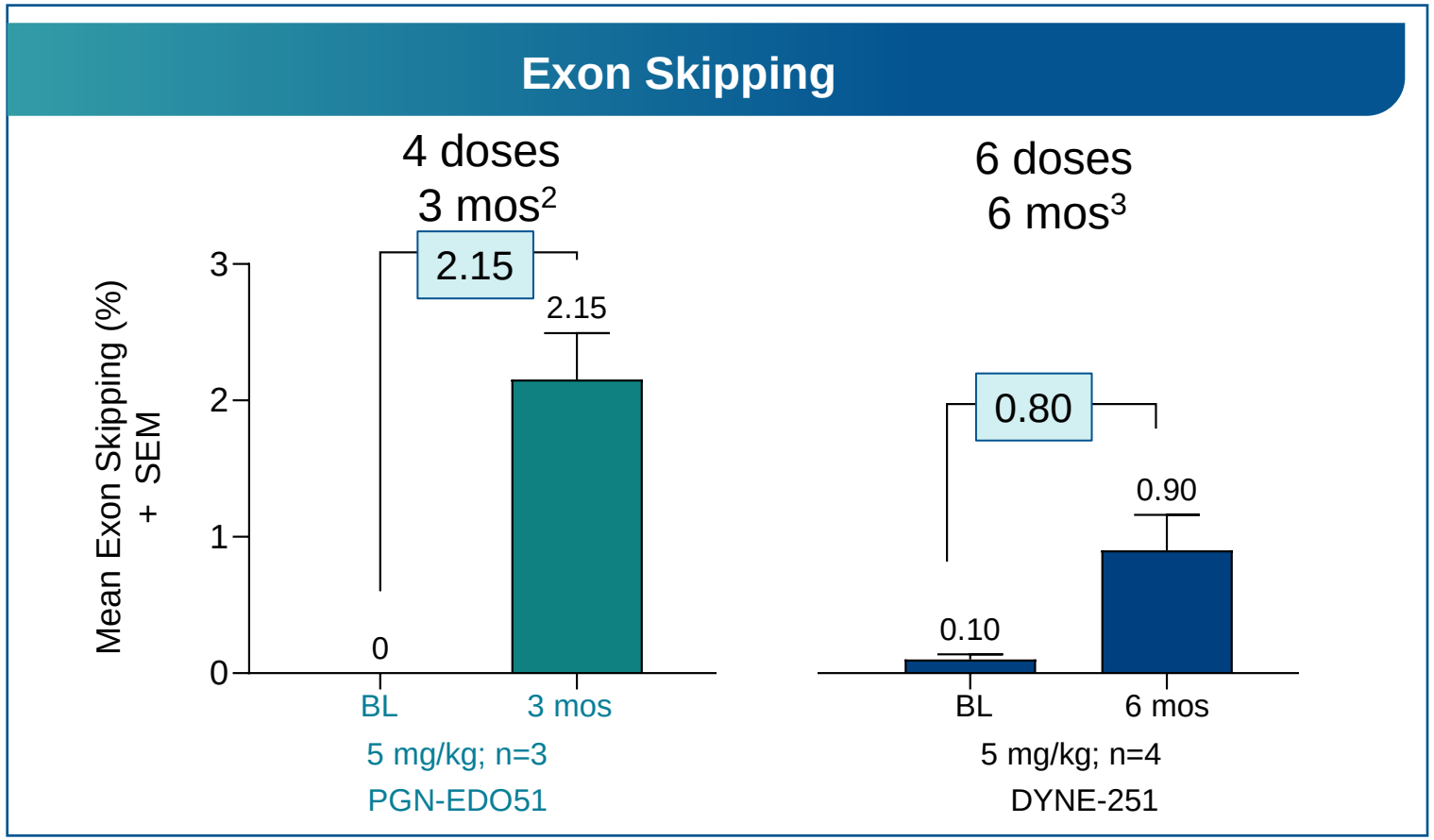
- Safety and tolerability
- Dystrophin
- Muscle tissue concentration of PGN-EDO51
- Exon skipping

CONNECT1 Trial Design

Open Label Study in Patients with DMD Amenable to Exon 51 Skipping Therapy



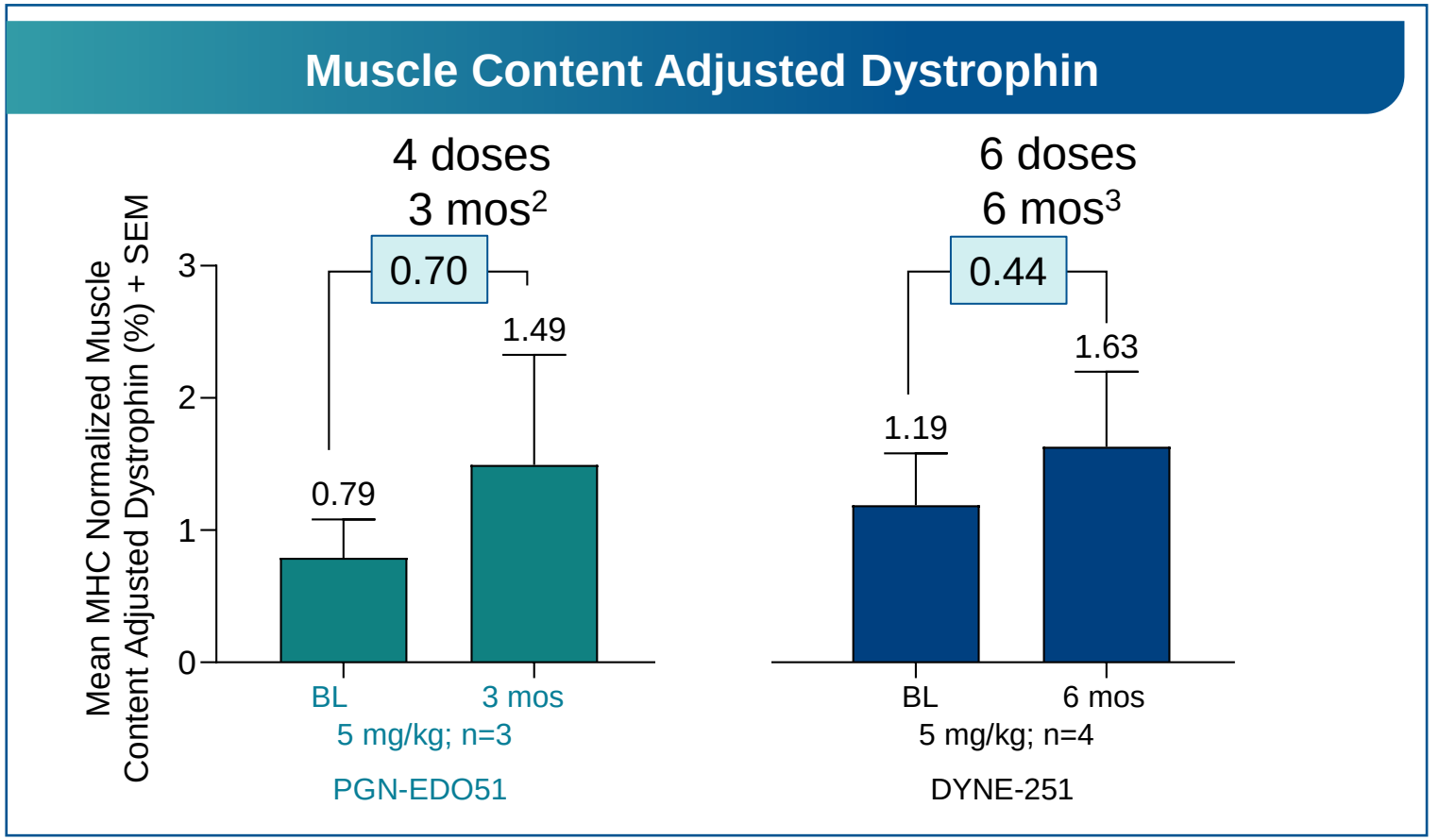
PGN-EDO51 Showed High Levels of Mean Exon Skipping at Low Dose



2. PGN-EDO51 muscle biopsy taken approximately 7 days after last dose. 3. DYNE-251 muscle biopsy taken approximately 28 days after last dose.

1. No head-to-head trials have been conducted comparing PGN-EDO51 to DYNE-251. Data from studies of these clinical candidates may not be directly comparable due to differences in molecule composition, trial protocols, dosing regimens, and patient populations and characteristics. Accordingly, cross-trial comparisons may not be reliable.DYNE-251 DELIVER clinical Data update, May 20, 2024. Note: DYNE-251 error bars estimated based on public presentations.

PGN-EDO51 Produced Greater Muscle Content Adjusted Dystrophin Increase in Half the Treatment Duration and Fewer Doses[1]



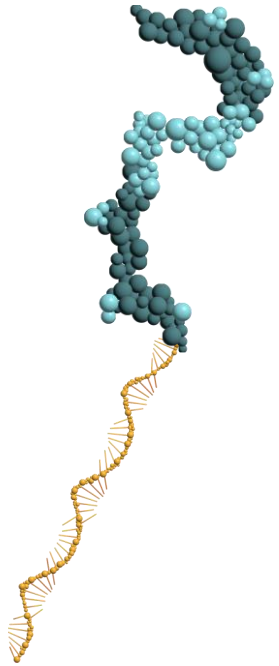
2. PGN-EDO51 muscle biopsy taken approximately 7 days after last dose. 3. DYNE-251 muscle biopsy taken approximately 28 days after last dose.

1. No head-to-head trials have been conducted comparing PGN-EDO51 to DYNE-251. Data from studies of these clinical candidates may not be directly comparable due to differences in molecule composition, trial protocols, methodologies for calculating muscle content adjusted dystrophin, dosing regimens, and patient populations and characteristics. Accordingly, cross-trial comparisons may not be reliable.DYNE-251 DELIVER clinical Data update, May 20, 2024. Note: Dyne-251 error bars estimated based on public presentations.

Looking Ahead

Building Therapeutic Area Leadership in Neuromuscular and Neurological Diseases

Cellular and nuclear delivery of EDOs



Our goal is to deliver best-in-class transformative therapies for DMD and DM1 patients

- PGN-EDO51: Mean exon 51 skipping and dystrophin production seen at initial low dose that was well tolerated
- PGN-EDODM1: Specific modulation of mutant DMPK transcript in the nucleus
- PGN-EDO53: 7X higher exon skipping than R6G-PMO53 comparator in NHPs

Potential multi-billion dollar opportunity

Expand EDO platform to other neuromuscular and neurological diseases

Long-term multi-billion dollar opportunity

PepGen™

R6G-PMO53 is believed to be structurally equivalent to the peptide component of vesleteplirsen conjugated to a murine exon 53 skipping oligonucleotide

Anticipated Upcoming Milestones

	2H: 2024	1H: 2025
DM1	• FREEDOM-DM1 initial clinical results in Q4 2024 • Initiate dosing in FREEDOM2-DM1 in 2H:2024	
DMD	• CONNECT2-EDO51 to open in US by year-end[1]	• CONNECT1 10 mg/kg dose cohort results in early 2025

1. Subject to regulatory clearance from FDA

Thank you!

Preclinical collaborators

Clinical site staff and investigators

Community and clinical advisors

Clinical study participants and their families