Nonclinical Data Demonstrate the Potential of the Enhanced Delivery Oligonucleotide (EDO) PGN-EDO51 for the Treatment of Duchenne Muscular Dystrophy

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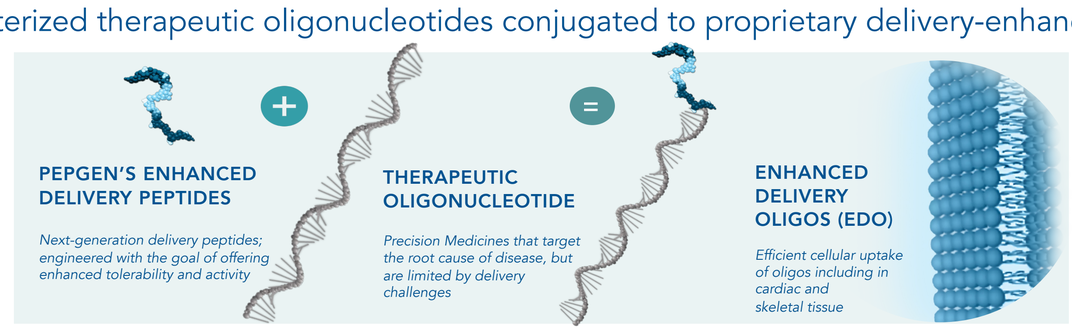
INTRODUCTION

PGN-EDO51 is PepGen's clinical-stage EDO candidate for the treatment of people with Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping. It is the first of a series of investigational therapies based on our EDO platform. PepGen has evaluated the potential of PGN-EDO23 (mouse equivalent) in the *mdx* mouse model of DMD and PGN-EDO51 in non-human primates (NHP) and showed robust exon skipping both following single- and repeat-dosing in both models and robust dystrophin production in *mdx* mice.

ENHANCED DELIVERY OLIGONUCLEOTIDES

THE POWER OF EDOs:

Well-characterized therapeutic oligonucleotides conjugated to proprietary delivery-enhancing peptides



PepGen's EDO technology is engineered to optimize cellular uptake and nuclear delivery of oligonucleotide therapeutic candidates. EDOs consist of a phosphorodiamidate morpholino oligonucleotide (PMO) attached to a delivery peptide to make a PPMO that increases delivery of the oligo into the nucleus.

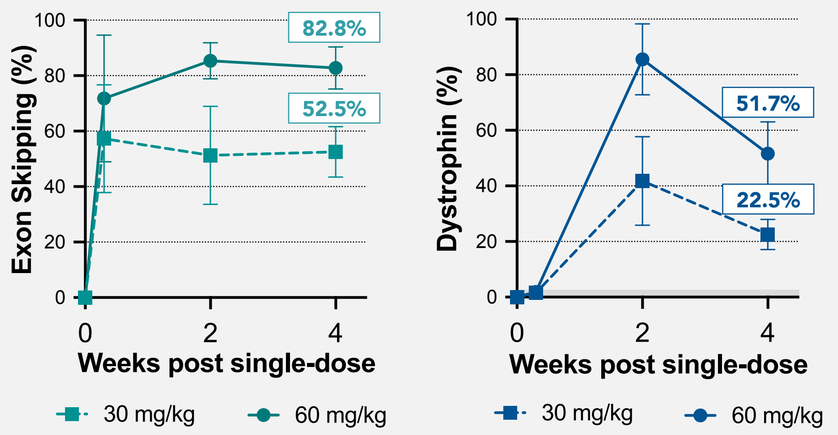
MDX MOUSE MODEL

NonGLP Pharmacology Studies			
	Species	Study design	Key readouts observed
Single-dose *PGN-EDO23 vs R_6G-PMO23**	*mdx*	Week: 0, 0.4, 2, 4	• High levels of exon 23 skipping and dystrophin production 4 weeks postdose • *Improved pharmacology with PGN-EDO23 vs R_6G-PMO23*
Repeat-dose *PGN-EDO23*	*mdx*	Week: 0, 4, 8, 12, 13	• Increased exon 23 skipping and dystrophin production following repeat-dosing every 4 weeks

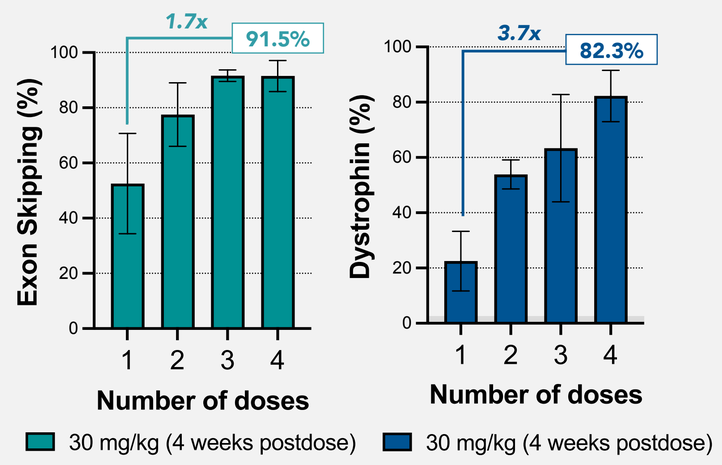
PGN-EDO dose ■ Tissue analysis

**R_6G-PMO23 is R_6G peptide conjugated to murine exon 23-skipping sequence.*

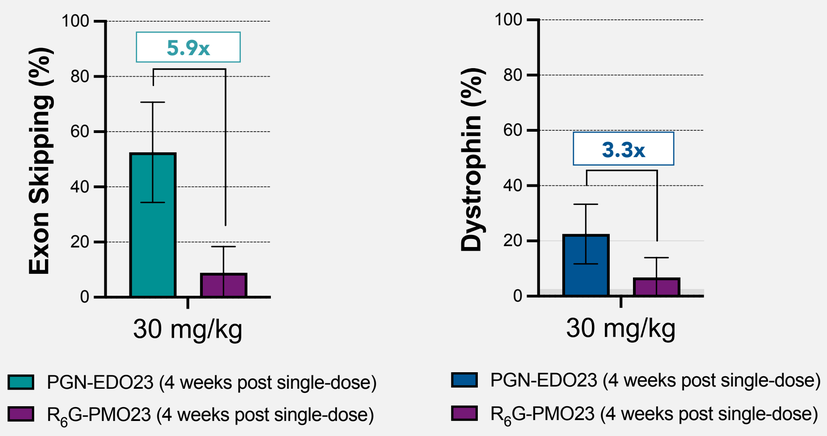
SUSTAINED EXON SKIPPING AND DYSTROPHIN AFTER A SINGLE-DOSE OF PGN-EDO23 - BICEPS



ACCUMULATION OF EXON SKIPPING AND DYSTROPHIN FOLLOWING REPEAT-DOSE - BICEPS



IMPROVED PHARMACOLOGY OBSERVED IN PGN-EDO23 IN *MDX MODEL* - BICEPS



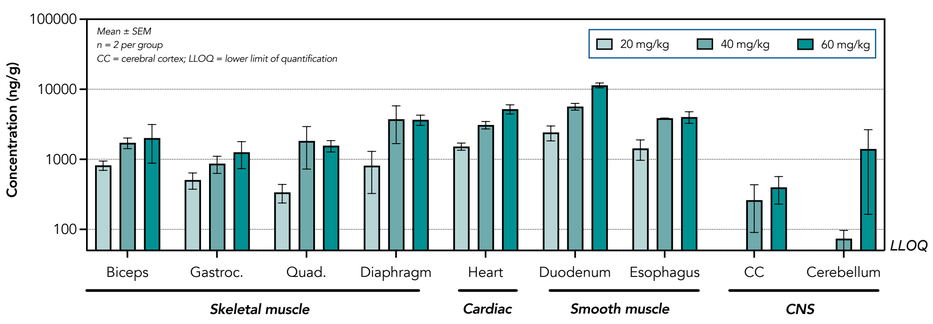
- Single-dose of PGN-EDO23 in *mdx* mice resulted in high levels of exon 23 skipping (RT-PCR) and dystrophin in biceps.
- Improved pharmacology was observed in *mdx* biceps with PGN-EDO23 in comparison to R_6G-PMO23.
- Sustained duration of exon 23 skipping (RT-PCR) and dystrophin in *mdx* biceps post single-dose supports dosing every 4 weeks.
- Repeat-dosing with PGN-EDO23 in *mdx* mice every four weeks for a total of four doses resulted in the highest exon 23 skipping levels (RT-PCR) and dystrophin production compared to single-dose.
- **Data support our belief that repeat dosing with PGN-EDO51 every 4 weeks has the potential to result in meaningful clinical benefit.**

NON-HUMAN PRIMATES

NonGLP Pharmacology Studies			
	Species	Study design	Key readouts observed
Single-dose *PGN-EDO51*	*WT*	Week: 0, 1	• High levels of exon 51 skipping
Single-dose *PGN-EDO51*	*WT*	Week: 0, 1	• Efficient delivery of oligonucleotide to skeletal, smooth and cardiac muscle and CNS
Repeat-dose *PGN-EDO51*	*WT*	Week: 0, 4, 8, 12, 13	• High levels of exon 51 skipping • Accumulation of exon skipping with repeat dosing every 4 weeks

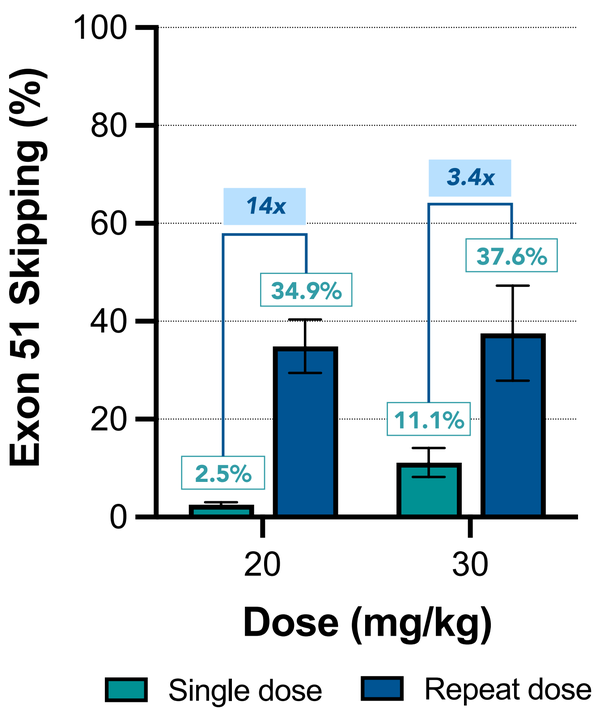
PGN-EDO dose ■ Tissue analysis

DELIVERY OF PGN-EDO51 TO KEY NEUROMUSCULAR TISSUES AFTER A SINGLE-DOSE



PepGen's EDO technology was observed to efficiently deliver oligo to skeletal and smooth muscle, and challenging tissues such as cardiac muscle and CNS.

DOSE DEPENDENT ACCUMULATION OF EXON SKIPPING (ddPCR) FOLLOWING REPEAT-DOSE - BICEPS



ACCUMULATION OF EXON SKIPPING

- Single-dose of PGN-EDO51 in male NHPs resulted in dose dependent exon 51 skipping (by ddPCR) in biceps.
- Repeat-dose resulted in dose dependent accumulation of exon 51 skipping (by ddPCR) in biceps.
- The lower levels of exon 51 skipping (by ddPCR) in biceps observed after a single-dose, significantly increased by **14-fold at 20 mg/kg and 3.4-fold at 30 mg/kg** with repeat-dosing.
- **Data support our belief that repeat-dosing with PGN-EDO51 every 4 weeks has the potential to result in meaningful clinical benefit.**

TOLERABILITY

- Clinical trial-enabling toxicology studies have been completed and supported the initiation of a Phase 1 Healthy Volunteer study for PGN-EDO51.
- PGN-EDO51 was observed to be well tolerated at clinically relevant dose levels in GLP single-dose intravenous mouse and NHP toxicology studies.

CONCLUSIONS & NEXT STEPS

These data demonstrate that single- and repeat-dose of PGN-EDO23/PGN-EDO51 resulted in high levels of exon skipping and dystrophin production in the models shown and were observed to be well tolerated at clinically relevant doses. The totality of evidence from these studies supports continued development of PGN-EDO51 for the treatment of people with DMD amenable to exon 51 skipping. A Phase 1 clinical trial assessing the tolerability of PGN-EDO51 in Healthy Volunteers is complete. A Phase 2 multiple ascending dose clinical trial in people living with DMD amenable to exon 51 skipping is planned for 2023.

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