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Three Novel Enhanced Delivery Oligonucleotide (EDO) Candidates for Duchenne Muscular Dystrophy Mediated High Levels of Exon 53, 45, and 44 Skipping

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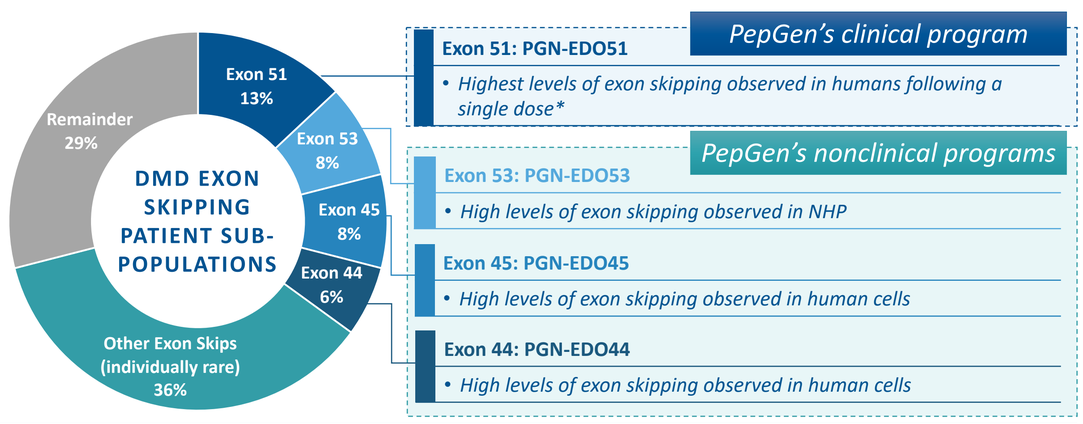
INTRODUCTION

PepGen is a clinical-stage company advancing the next generation of oligonucleotide therapies with the goal of transforming the treatment of severe neuromuscular diseases including Duchenne muscular dystrophy (DMD). PGN-EDO51 is PepGen's clinical-stage EDO candidate for the treatment of people with Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping (**Posters 25, 26 and 44**). It is the first of a series of investigational therapies based on our EDO platform. PepGen is also developing additional EDO programs for DMD exon 53 skipping, exon 45 skipping and exon 44 skipping. PepGen has demonstrated the potential of EDO53, EDO54 and EDO44 *in vitro* in human myotubes. In addition, in the *mdx* mouse model of DMD, PGN-EDO23 (mouse equivalent applicable to all DMD programs) showed superior exon skipping and robust dystrophin production over a comparator compound. In non-human primates (NHP) PGN-EDO53 showed robust exon skipping following single- and repeat-dosing.

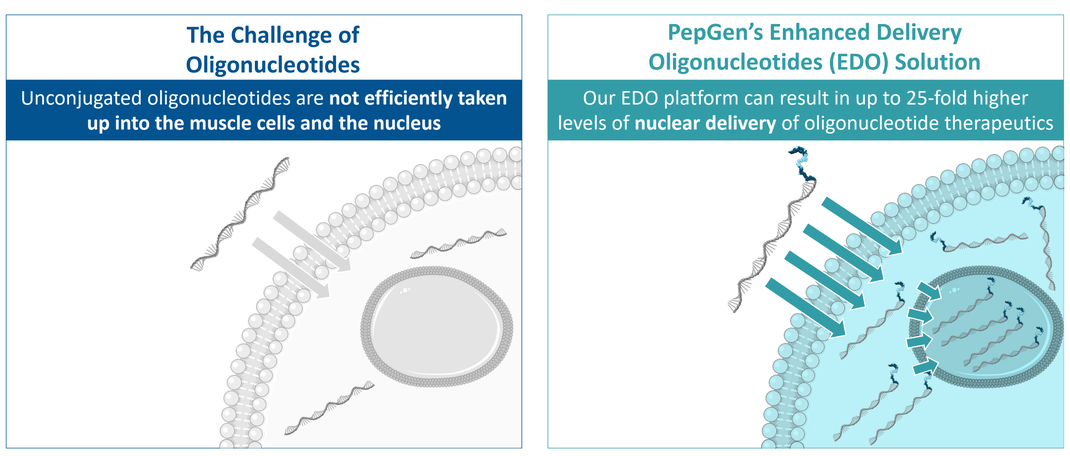
PEPGEN'S LEAD PROGRAM TARGETS LARGEST EXON SKIPPING PATIENT POPULATION IN DMD



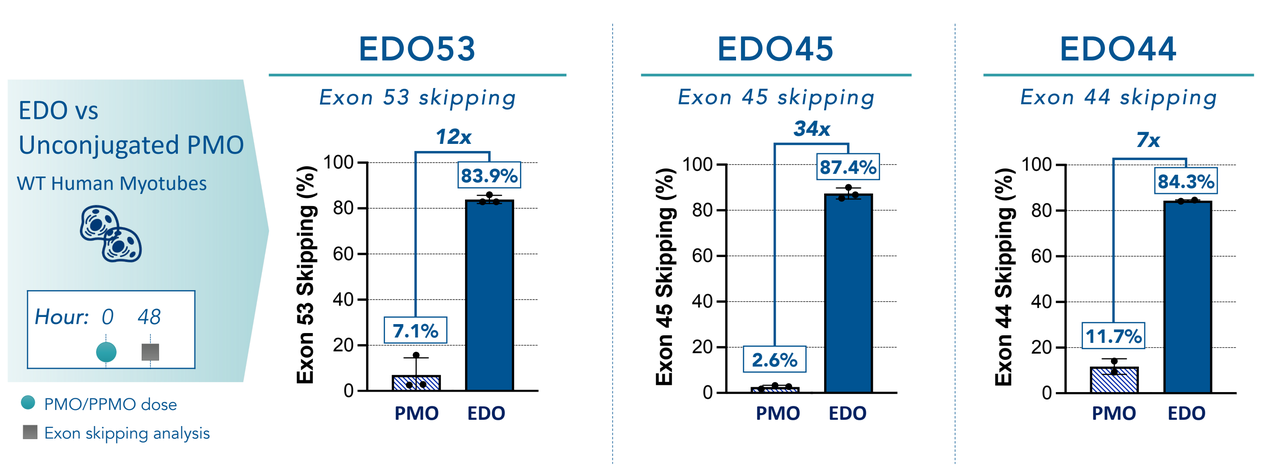
We believe we have potential to address at least 35% of total DMD patient population amenable to exon skipping

THE POWER OF ENHANCED DELIVERY OLIGONUCLEOTIDES

PEPGEN'S EDO PLATFORM IS DESIGNED TO ADDRESS THE DELIVERY CHALLENGES THAT LIMIT OLIGONUCLEOTIDE THERAPEUTICS



EDO INCREASED THE POTENCY OF DMD EXON SKIPPING OLIGOS OVER UNCONJUGATED PMO HUMAN IN MYOTUBES



- EDOs showed a **12x, 34x and 7x increase** in **exon 53, 45 and 44 skipping**, respectively, in human myotubes when compared to unconjugated phosphorodiamidate morpholino oligonucleotide (PMO) at the same concentration.
- EDOs showed a dose-response with consistent levels of exon skipping seen across exon 53, 45 and 44 skipping in human myotubes.
- The EDO platform has demonstrated significant potential over unconjugated PMO *in vitro*.

EVALUATION OF EDO IN MDX MOUSE MODEL AND NON-HUMAN PRIMATE

Species	Study	Study design	Study information
mdx	Single-dose *PGN-EDO23 vs* R_6*G-PMO23*	Week: 0 4	• PGN-EDO23 contains a murine exon 23-skipping sequence (PMO23) • R_6G-PMO23* is a comparator PPMO molecule, that uses an R_6G peptide conjugated to PMO23.

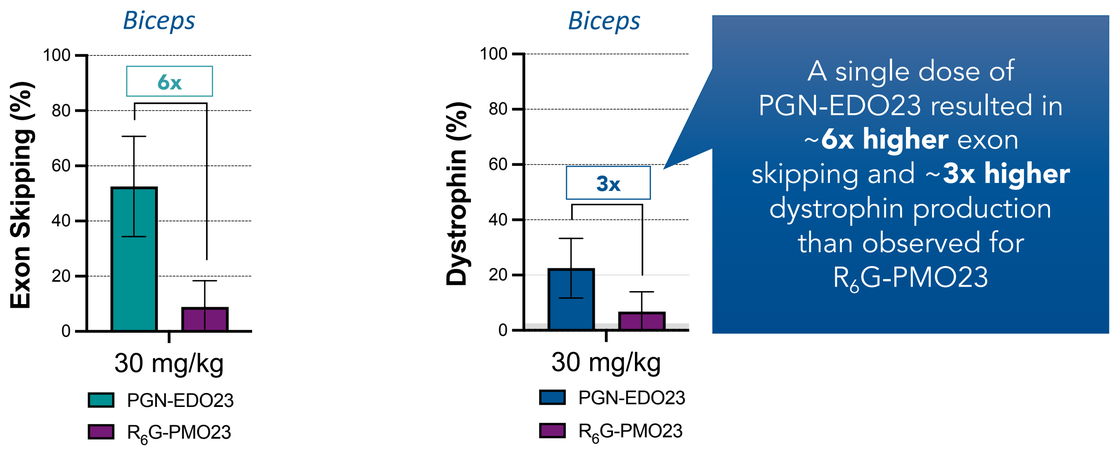
PGN-EDO dose ■ Exon skipping/dystrophin analysis

*R_6G-PMO23 is believed to be structurally equivalent to the peptide component of SRP-5051 conjugated to a murine exon 23 skipping oligonucleotide.

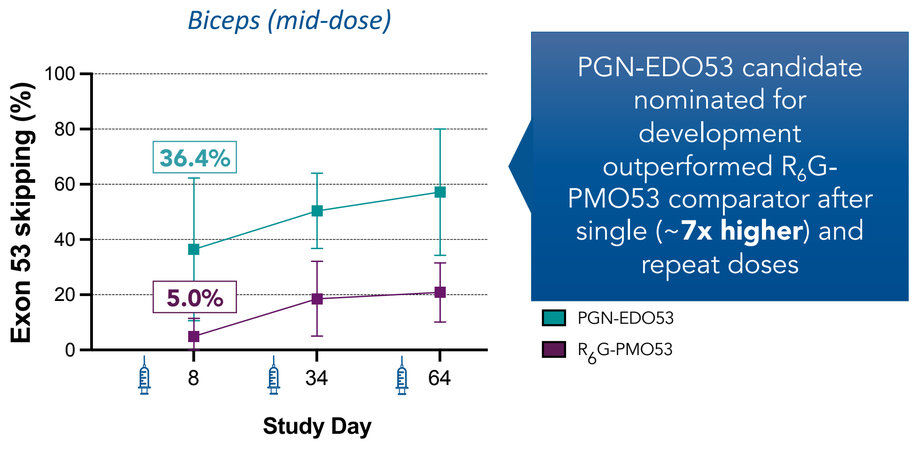
Species	Study	Study design	Study information
WT	Repeat-dose *PGN-EDO53vs* R_6*G-PMO53*	Day: 1 8 29 34 57 64	• R_6G-PMO53* is a comparator PPMO molecule, that uses R_6G peptide conjugated to a PMO53 sequence

PGN-EDO dose ■ Exon skipping analysis

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



DOSE-DEPENDENT ACCUMULATION OF EXON 53 SKIPPED TRANSCRIPTS FOLLOWING REPEAT DOSING



SUMMARY AND CONCLUSIONS

- We believe the EDO platform has the potential to address at least 35% of the total DMD patient population amenable to exon skipping.
- EDOs showed up to a 12x, 34x and 7x increase in exon 53, 45 and 44 skipping, respectively, in human myotubes when compared to unconjugated PMO.
- In a DMD mouse model, the *mdx* mouse, a single dose of PGN-EDO23 (mouse equivalent EDO applicable to all DMD programs) resulted in high levels of exon skipping and dystrophin production which were more than 3-fold better than for a comparator compound.
- In NHP, a single dose of PGN-EDO53 resulted in ~7x higher levels of exon skipping than a comparator compound.
- We believe the *in vitro* and *in vivo* data support the continued development of the EDO platform and development of EDO53, EDO45 and EDO44 programs.

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

* Comparative statements are based on cross-trial comparisons with publicly-available data for other exon skipping approaches that have been assessed following a single dose in humans.