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Single- and Repeat-Dose Nonclinical Data for PGN-EDO51 Demonstrated Favorable Pharmacology and Safety Profiles for the Treatment of DMD

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INTRODUCTION

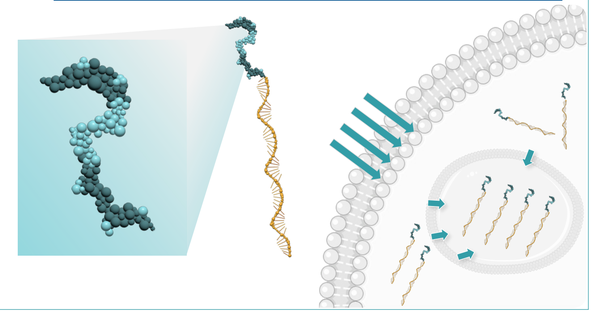
PGN-EDO51 is PepGen's Phase 2 clinical-stage Enhanced Delivery Oligonucleotide (EDO) candidate for the treatment of people with Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping. It is the first of a series of investigational therapies based on our EDO platform. PepGen has evaluated the potential of PGN-EDO23 (mouse equivalent) in the *mdx* mouse model of DMD and PGN-EDO51 in non-human primates (NHPs) and showed robust exon skipping both following single- and repeat-dosing in both models and robust dystrophin production in *mdx* mice.

ENHANCED DELIVERY OLIGONUCLEOTIDES

PEPGEN'S EDO PEPTIDES
Modified for enhanced uptake and improved tolerability

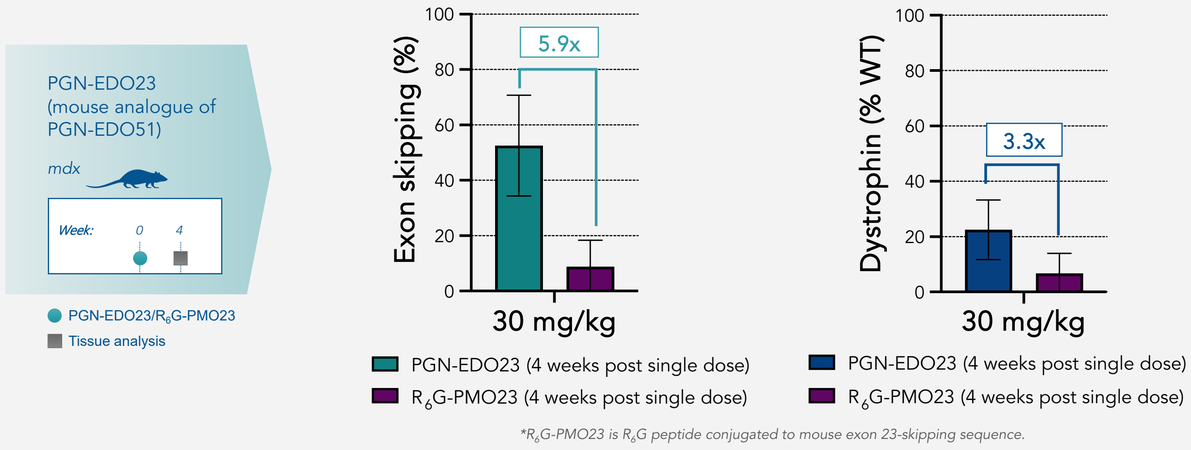
- Two poly-Arg domains where the number of arginines have been minimized are interspersed with non-natural amino acids to confer greater peptide stability
- Hydrophobic core coupled with poly-Arg domains contributes to endosomal escape
- Peptide sequence is linear with a length of less than 20 amino acids and is designed to be non-immunogenic

ENHANCED DELIVERY OLIGONUCLEOTIDES (EDOs)
Designed to increase nuclear uptake of oligos in muscle tissue



MDX MOUSE MODEL USING MOUSE EQUIVALENT OF PGN-EDO51 (PGN-EDO23)

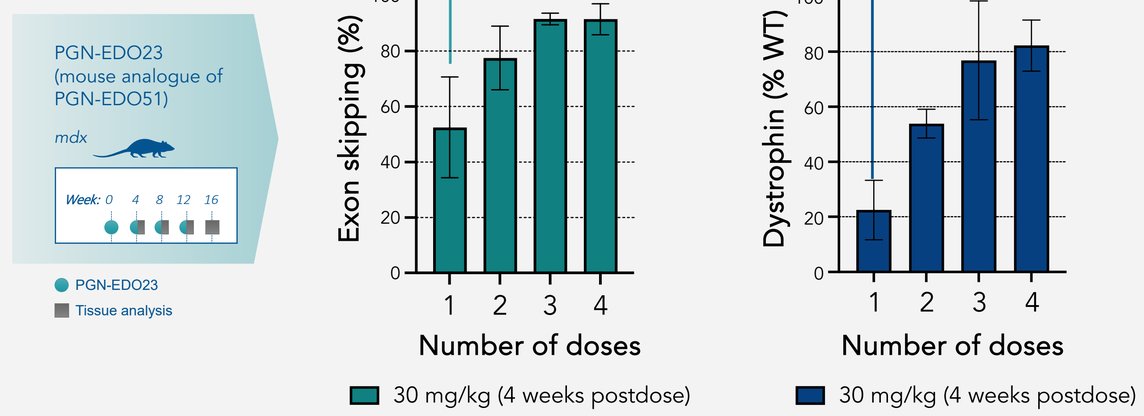
IMPROVED PHARMACOLOGY OBSERVED WITH PGN-EDO23 IN *MDX* MODEL - BICEPS



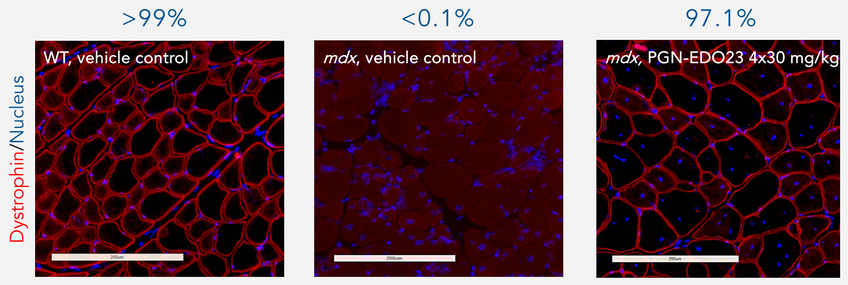
*R_6G-PMO23 is R_6G peptide conjugated to mouse exon 23-skipping sequence.

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

ACCUMULATION OF EXON SKIPPING AND DYSTROPHIN FOLLOWING REPEAT DOSING - BICEPS

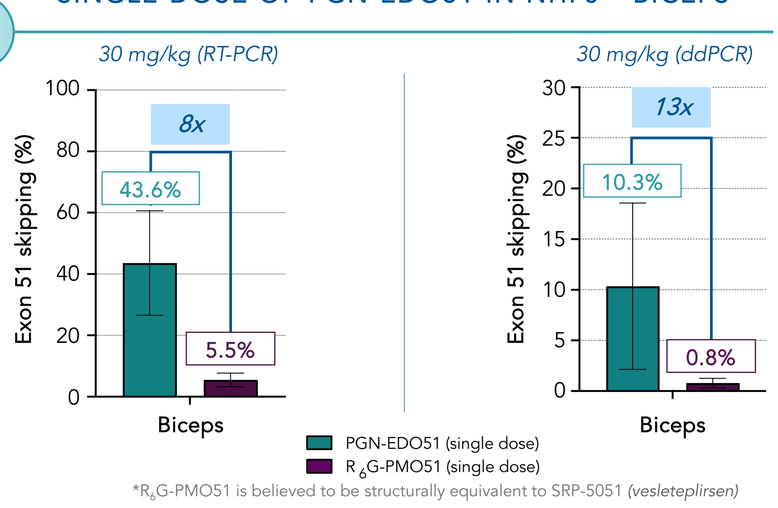


UNIFORM DISTRIBUTION OF DYSTROPHIN FOLLOWING REPEAT DOSING: BICEPS



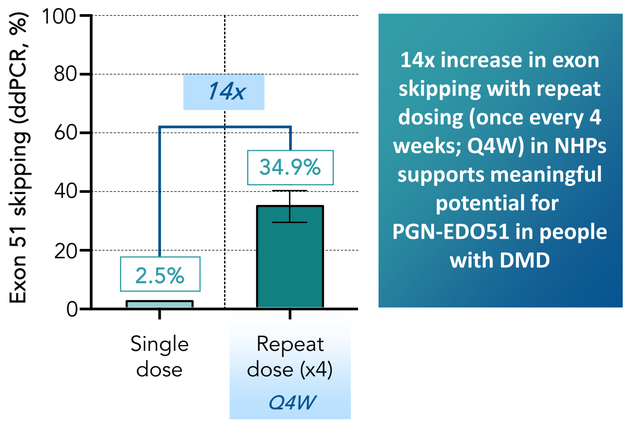
NON-HUMAN PRIMATE PHARMACOLOGY AND TOLERABILITY USING PGN-EDO51

IMPROVED PHARMACOLOGY OBSERVED WITH A SINGLE-DOSE OF PGN-EDO51 IN NHPs – BICEPS



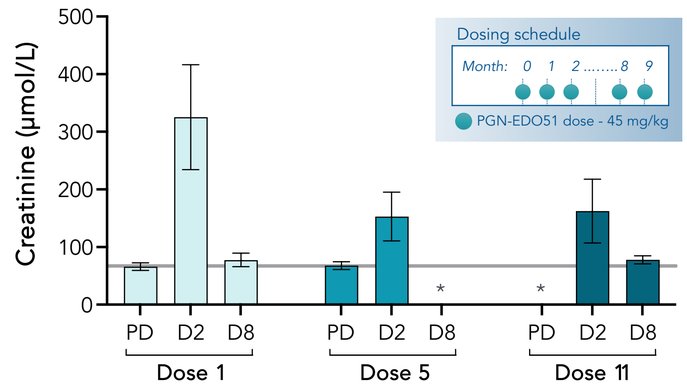
*R_6G-PMO51 is believed to be structurally equivalent to SRP-5051 *(vesleteplirsen)*

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



14x increase in exon skipping with repeat dosing (once every 4 weeks; Q4W) in NHPs supports meaningful potential for PGN-EDO51 in people with DMD

GLP NHP TOXICOLOGY STUDIES SUPPORT CONTINUED CLINICAL DEVELOPMENT OF PGN-EDO51



GLP = Good Laboratory Practice, PD = pre-dose, * Data not collected

SUPERIOR PHARMACOLOGY AND ACCUMULATION OF EXON SKIPPING FOLLOWING REPEAT DOSING

- Single dose of PGN-EDO51 in male NHPs resulted in significantly higher levels of exon 51 skipping in biceps over R_6G-PMO51 comparator peptide-conjugated phosphorodiamidate morpholino oligomer (PPMO).
- Repeat dosing 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 with repeat dosing in NHP.
- **Data support our belief that repeat dosing with PGN-EDO51 once every 4 weeks has the potential to result in meaningful levels of dystrophin production and clinical benefit.**

In a chronic NHP toxicology study (Q4W; 11 doses total):

- Through 45 mg/kg (highest dose tested), non-adverse, transient increases in serum creatinine were observed and were of lower magnitude with repeat dosing.
- Through 45 mg/kg, non-adverse minimal to moderate decreases in serum magnesium were observed.
- Through 45 mg/kg, no changes in serum potassium and no adverse renal, hematologic, cardiovascular or hepatic effects were observed.

CONCLUSIONS & NEXT STEPS

- These data demonstrate that single and repeat dosing of PGN-EDO23/PGN-EDO51 resulted in high levels of exon skipping and/or dystrophin production in the models shown and were observed to be well tolerated at clinically relevant doses.
- The totality of the activity and safety data from nonclinical and clinical studies to date supports the continued development of PGN-EDO51 for the treatment of people with DMD amenable to exon 51 skipping.
- The clinical development program includes a completed Phase 1 safety study in healthy volunteers, and the on-going CONNECT1 Phase 2 clinical program to investigate the effects of multiple doses of PGN-EDO51 in people with DMD amenable to exon 51 skipping (see Poster O74).

Disclosures: All authors are employees of PepGen Inc. and hold PepGen equity