404P

CONNECT2-EDO51: A Phase 2 placebo-controlled study to evaluate PGN-EDO51 safety and efficacy in people with Duchenne amenable to exon 51 skipping

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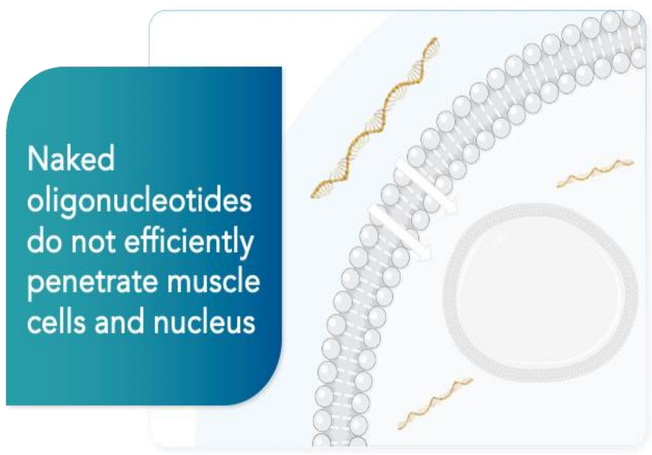
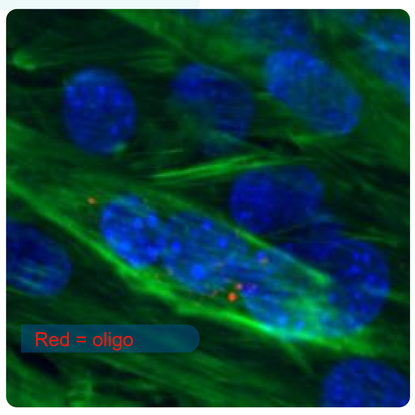
INTRODUCTION

THE CHALLENGE OF OLIGONUCLEOTIDE DELIVERY

Naked Oligonucleotide (PMO)

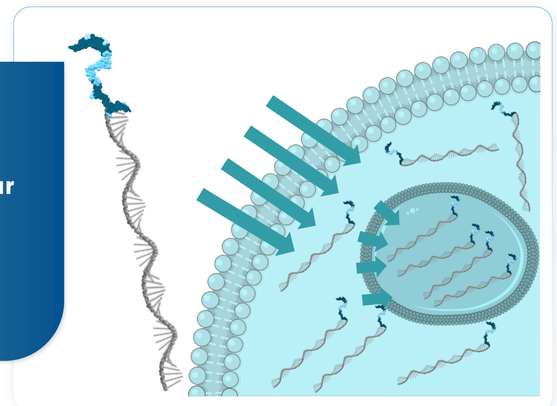




In vitro staining image is shown with 10 µM concentration of PGN-PMO23 (naked oligonucleotide). C2C12 mouse cells were differentiated for 4 days into myotubes and treated with fluorescently tagged compounds for 24h. PMO: phosphorodiamidate morpholino oligonucleotide

PEPGEN'S ENHANCED DELIVERY OLIGONUCLEOTIDES (EDO)

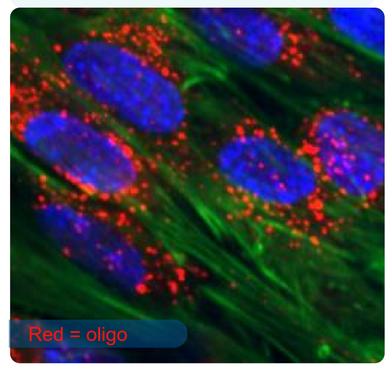
EDO platform results in nuclear delivery of oligonucleotide therapeutics



EDO cell-penetrating peptide technology is engineered to optimize tissue delivery and nuclear uptake of therapeutic oligonucleotides

PGN-EDO51 is PepGen's investigational clinical candidate for the treatment of Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping

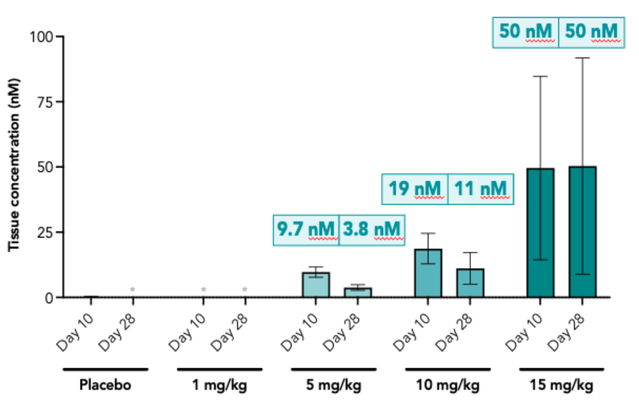
PepGen's EDO: Up to 25X Higher Nuclear Uptake of Oligonucleotide



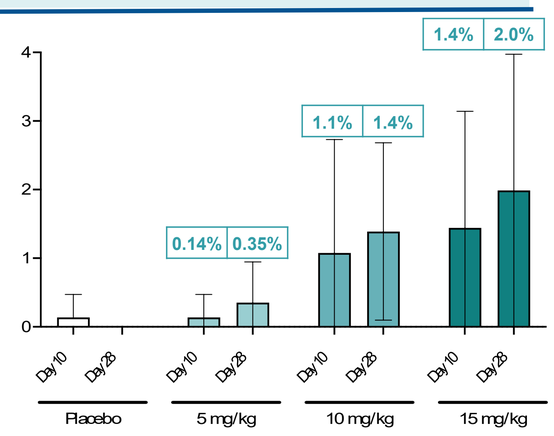
In vitro staining image is shown with 10 µM conc. of PGN-EDO23; C2C12 mouse cells were differentiated for 4 days into myotubes and treated with fluorescently tagged compounds for 24h.

PHASE 1 STUDY RESULTS[1]

TISSUE CONCENTRATION (BICEPS)[3]



EXON SKIPPING (BICEPS)[2]



Phase 1 Study in HV demonstrated effective delivery of PGN-EDO51 and high levels of exon skipping after a single dose

1. 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 was administered by IV infusion at the dose levels indicated. Participants were followed for a 28-day period following dosing to evaluate safety, tolerability, PK, and PD. Needle biopsies of biceps muscle were taken on Day 10 and Day 28.
2. 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).
3. 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). Asterix indicates that values were below the lower limit of quantitation.

PHASE 2 CLINICAL PROGRAM

CONNECT1-EDO51 AND CONNECT2-EDO51 STUDIES OVERVIEW

Connect 1 EDO51

Connect 2 EDO51

ONGOING

Phase 2: Open-label MAD trial in patients

Open in Canada

→ Fast path to proof-of-concept: dystrophin expression at 13 weeks

OPEN

Phase 2: Randomized, double-blind, placebo-controlled MAD trial in patients

Multinational trial; currently open in United Kingdom

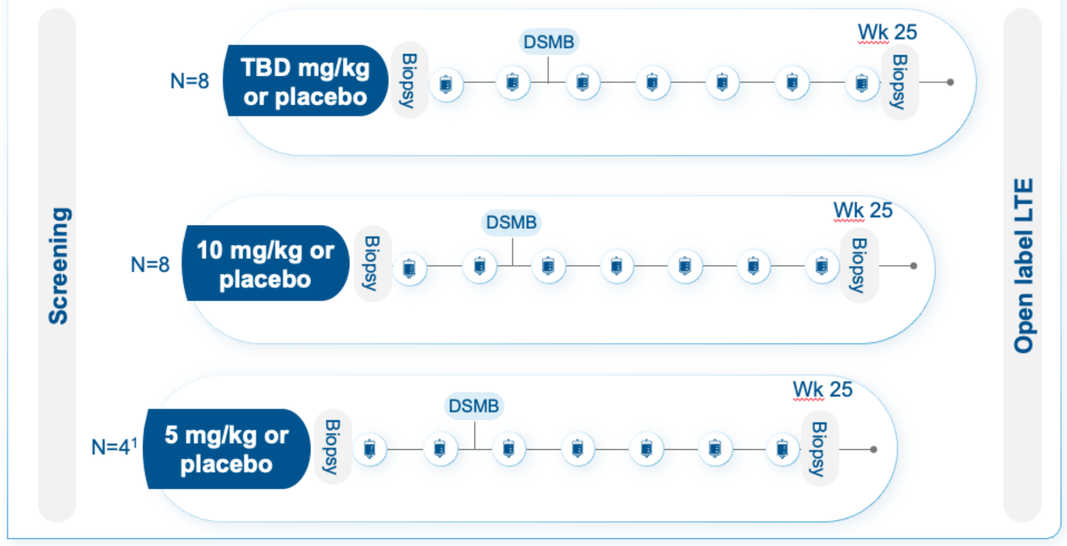
→ Potential to support accelerated approval[1]: dystrophin expression at 25 weeks

1. Subject to regulatory authority feedback

CONNECT2-EDO51 STUDY DESIGN, ELIGIBILITY AND OBJECTIVES

STUDY DESIGN

PGN-EDO51 Dosing Q4W for Treatment Period of 24 weeks Prior to Rolling over into LTE Trial (randomized 3:1)



1. Approved for n=8 in UK; amendment being submitted for the truncated cohort (n=4); truncated cohort planned for US and EU

Q4W: every 4 weeks; DSMB: data safety and monitoring board; IV: intravenous

KEY ELIGIBILITY CRITERIA

INCLUSION

- Males by birth age ≥6 years of age at the time of consent/assent
- Body weight ≥25 kg; Body Mass Index (BMI) ≤36 kg/m^2 at screening
- Diagnosis of DMD with exon 51 skippable mutation
- Performance of Upper Limb (PUL) 2.0 entry score of ≥ 3 at screening

EXCLUSION

- Initiation or change in doses of concomitant medications or herbal supplements (except for modifications to accommodate changes in weight)
- Left ventricle ejection fraction <45% as measured within 12 months of study start
- Forced vital capacity <40% predicted value

OBJECTIVES

PRIMARY

- To evaluate the safety and tolerability of PGN-EDO51 following multiple doses in male participants with DMD amenable to exon 51 skipping
- To evaluate the levels of dystrophin in skeletal muscle following multiple doses of PGN-EDO51

SECONDARY & EXPLORATORY

- To evaluate the concentration of PGN-EDO51 in skeletal muscle following multiple doses of PGN-EDO51
- To evaluate the pharmacokinetics (PK) of PGN-EDO51 in plasma following multiple doses of PGN-EDO51
- To evaluate *DMD* exon 51 skipping in skeletal muscle following multiple doses of PGN-EDO51

CONCLUSION

The CONNECT2-EDO51 multinational clinical study is designed to efficiently evaluate potential safety and efficacy of PGN-EDO51 in a population of people with DMD amenable to exon 51 skipping.

Connect 1 EDO51

CONNECT1-EDO51 clinical study cohort 1 (5 mg/kg) results were announced in July 2024. For details, you can visit poster 403P.

For details on PGN-EDO51 non-clinical data, you can visit poster 405P