403P CONNECT1-EDO51: A 12-week open-label Phase 2 study to evaluate PGN-EDO51 safety and efficacy in people with Duchenne amenable to exon 51 skipping

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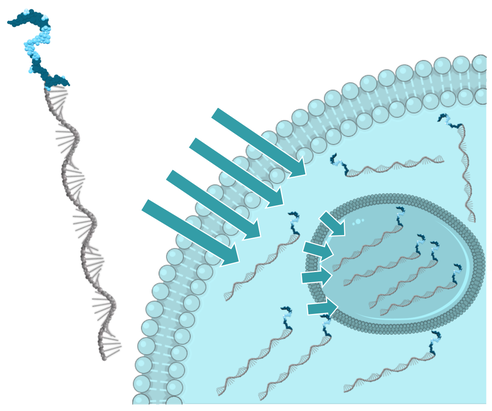
INTRODUCTION

PEPGEN'S ENHANCED DELIVERY OLIGONUCLEOTIDES (EDO)



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

PHASE 2 CLINICAL STUDIES (CONNECT)

CONNECT1and CONNECT2 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

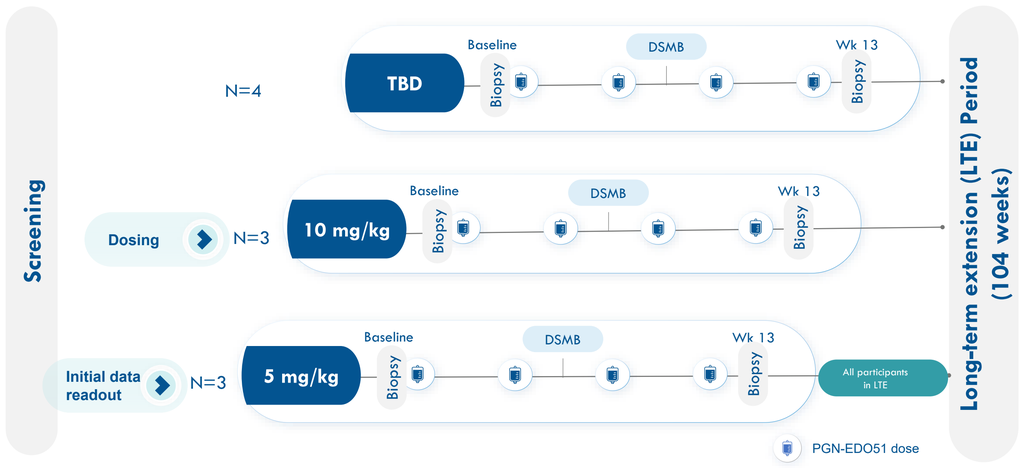
- Phase 2: Randomized, double-blind, placebo-controlled MAD trial in patients
- Multinational trial; currently open in the United Kingdom

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

1. Subject to regulatory authority feedback

CONNECT1-EDO51 STUDY DESIGN

Open-label study in people with DMD amenable to exon 51 skipping therapy



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

CONNECT1-EDO51 Study, Eligibility , Objectives and Baseline Characteristics

KEY ELIGIBILITY CRITERIA

INCLUSION

- Males by birth age ≥8 years of age at the time of consent/assent
- Body weight ≥25 kg; Body Mass Index (BMI) ≤32 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

SECONDARY & EXPLORATORY

- To evaluate the levels of dystrophin in skeletal muscle following multiple doses of PGN-EDO51
- To evaluate the concentration of PGN-EDO51 in skeletal muscle following multiple doses of PGN-EDO51
- To evaluate the pharmacokinetics (PK) of PGN-EDO51in plasma following multiple doses of PGN-EDO51
- To evaluate *DMD* exon 51 skipping in skeletal muscle following multiple doses of PGN-EDO51

CONNECT1 5 mg/kg: Baseline Characteristics of Participants (n=3)

	Mean (SD)
Age (years)	11.7 (1.5)
BMI (kg/m^2)	19.8 (2.7)
Height (cm)	132.0 (9.9)
Weight (kg)	34.4 (3.9)
Age of DMD genetic diagnosis (years)	6.3 (1.5)
Number of patients on daily corticosteroid dosing regimen	3
Number of ambulatory patients	3
Number of patients previously on DMD therapy	0

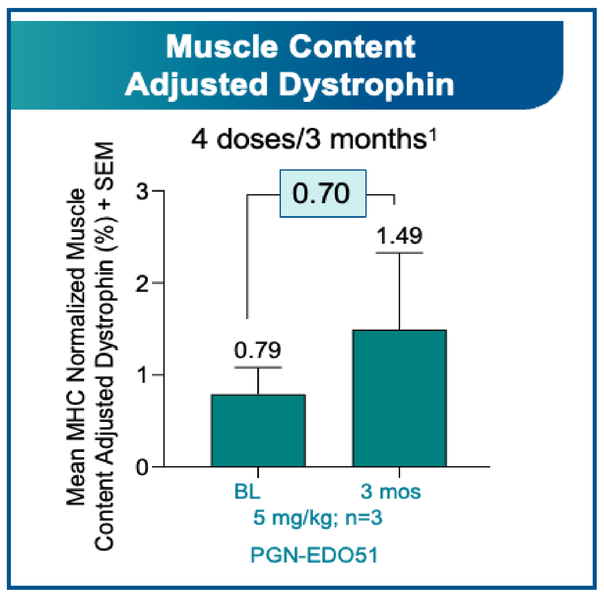
CONNECT1-EDO51 Study Results of First Cohort (5 mg/kg)

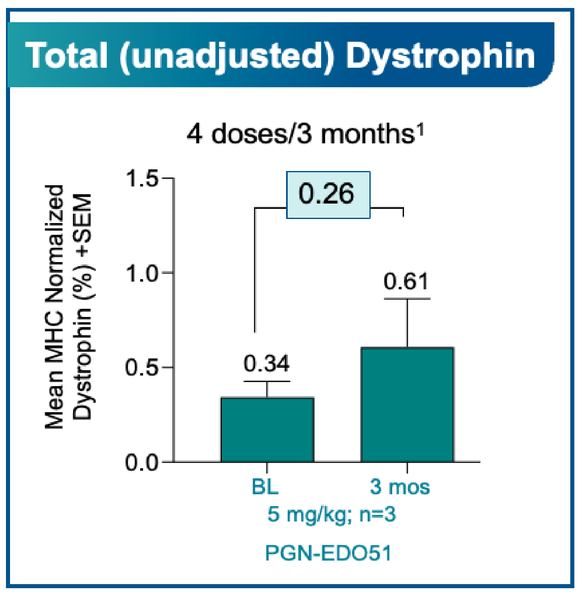
CONNECT1 5 MG/KG: PGN-EDO51 WAS WELL TOLERATED

	n (%)
Any TEAEs, n (%)	3 (100)
Related to study drug	1 (33.3)
• Mild	1 (33.3)
• Moderate	0
• Severe	0
Serious Adverse Events(AEs)	0
AEs leading to dose modification/ discontinuation/interruption	0
AEs leading to death	0

- All treatment emergent adverse events (TEAEs) were mild and resolved
- Related TEAE was mild (abdominal pain, flatulence)
- 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

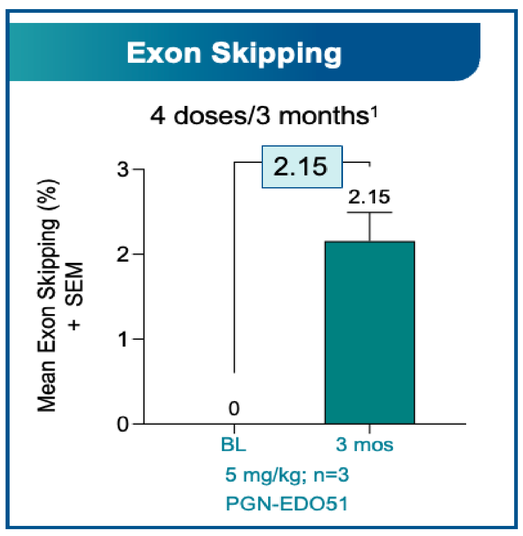
PGN-EDO51 PRODUCED DYSTROPHIN INCREASES OVER SHORT TREATMENT DURATION





1. PGN-EDO51 muscle biopsy taken approximately 7 days after last dose
MHC: Myosin Heavy Chain, BL: Baseline, SEM: Standard Error of the Mean

PGN-EDO51 SHOWED HIGH LEVELS OF MEAN EXON SKIPPING



1. PGN-EDO51 muscle biopsy taken approximately 7 days after last dose
BL: Baseline, SEM: Standard Error of the Mean

CONCLUSIONS

- PGN-EDO51 was well tolerated at 5 mg/kg, currently dosing at 10 mg/kg
- All patients dosed at 5 mg/kg demonstrated increased exon skipping and dystrophin production and have continued into the long-term extension study
- PGN-EDO51 generated high levels of mean exon 51 skipping (2.15%)
- Dystrophin production is encouraging at just 3 months and 4 doses of 5 mg/kg
- Initial results support that EDO technology delivers high levels of oligonucleotides to the nucleus
- Potentially higher levels of dystrophin production are expected with higher doses of PGN-EDO51 over longer treatment periods which will be assessed in CONNECT2; see poster
  - 404P CONNECT2-EDO51: A Phase 2 placebo-controlled study to evaluate PGN-EDO51 safety and efficacy in people with DMD amenable to exon 51 skipping

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

ACKNOWLEDGEMENTS

We sincerely thank all patients, families and clinical investigators for their participation in, and contributions to, the CONNECT1 study.