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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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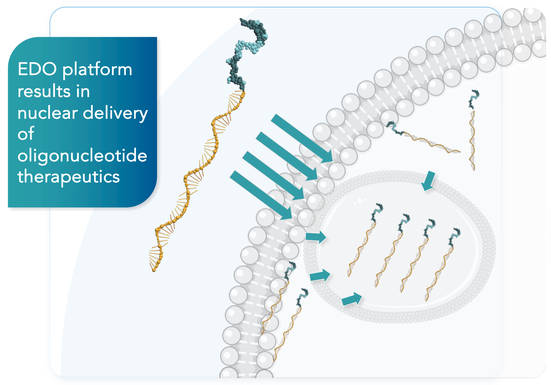
INTRODUCTION

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)

CONNECT1 and CONNECT2 OVERVIEW

Connect 1 EDO51

Connect 2 EDO51

ONGOING

- Phase 2: Open-label MAD trial in patients
- Open in Canada: ongoing dosing and data collection in 10 mg/kg and 5 mg/kg LTE cohorts

Fast path to proof-of-concept: dystrophin expression at 13-16 weeks[1]

Temporarily Paused

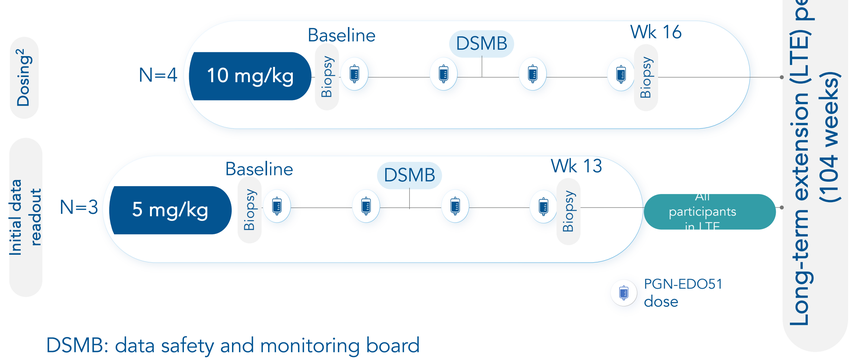
- Phase 2: Randomized, double-blind, placebo-controlled MAD trial in patients
- Temporarily paused in the UK[2]
- Clinical Hold in the US

Potential to support accelerated approval[3]: dystrophin expression at 28 weeks

1. Dystrophin expression measured at 13 weeks in Cohort 1 and at 16 weeks in Cohort 2
2. Decision to pause enrollment was made voluntarily by PepGen
3. Subject to acceptable benefit/risk profile and regulatory authority feedback

CONNECT1-EDO51 STUDY DESIGN

Open-label study in people with DMD amenable to exon 51 skipping therapy[1,2]



DSMB: data safety and monitoring board

1. PGN-EDO51 is administered as IV infusion every 4 weeks
2. Dosing remains ongoing in the 5 mg/kg and 10 mg/kg LTE groups without further escalation at this time; data collection remains ongoing.

CONNECT1-EDO51 Study, Eligibility , Objectives and Baseline Characteristics

KEY ELIGIBILITY CRITERIA

INCLUSION

- Males by birth, age ≥ 6 & ≤ 16 years of age at the time of consent/assent
- Body weight ≥18 kg; Body Mass Index (BMI) ≤32 kg/m2 at screening
- Diagnosis of DMD with exon 51 skippable mutation
- Performance of Upper Limb (PUL) 2.0 entry score of ≥ 4 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, COHORT 1 (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[1]

	n(%)
Any TEAEs, n(%)	3 (100)
Related to study drug	2 (66.7)
• Mild • Moderate • Severe	2 (66.7) 0 0
Any TEAEs of Special Interest (AESI)	1 (33.3)
Serious Adverse Events (AEs)	0
AEs leading to dose modification/ discontinuation/interruption	0
AEs leading to death	0

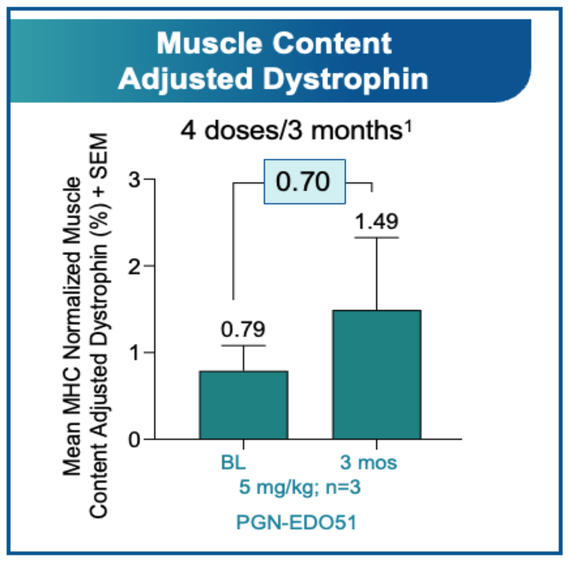
n= number of participants

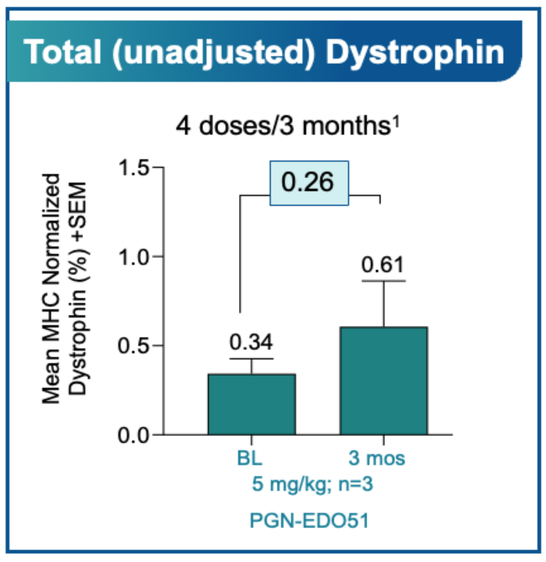
- All treatment emergent adverse events (TEAEs) were mild and resolved
- Treatment related TEAEs were mild (abdominal pain, flatulence, creatinine increased)
- AESI was increased creatinine that resolved without intervention
- No discontinuations, dose modifications or dose interruptions
  - –All participants 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

At 5 mg/kg, a total of 40 doses have been administered (12 doses in the MAD period+28 doses in the LTE period)[1]

1. Data as of Jan. 23, 2025

PGN-EDO51 PRODUCED DYSTROPHIN INCREASES OVER SHORT TREATMENT DURATION

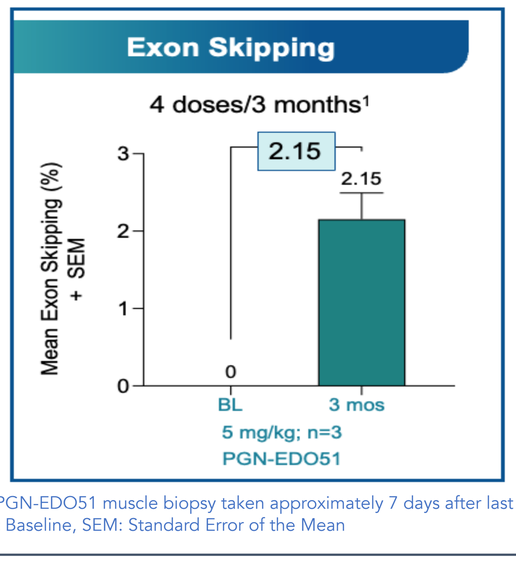




1. PGN-EDO51 muscle biopsy taken approximately 7 days after last dose

MHC: Myosin Heavy Chain, BL: Baseline, SEM: Standard Error of the Mean

PGN-EDO51 SHOWED HIGH MEAN LEVELS OF EXON SKIPPING



1. PGN-EDO51 muscle biopsy taken approximately 7 days after last dose

BL: Baseline, SEM: Standard Error of the Mean

CONCLUSIONS

- CONNECT1-EDO51 study has fully enrolled two cohorts at dose levels of 5 mg/kg and 10 mg/kg
- PGN-EDO51 emerging safety profile is favorable[1]
  - All treatment-related adverse events are mild[1,2]
  - No treatment-related serious adverse events[1]
- PGN-EDO51 was well tolerated at 5 mg/kg, currently dosing at 10 mg/kg
- PGN-EDO51 generated high mean levels of 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
- All patients dosed at 5 mg/kg demonstrated increased exon skipping and dystrophin production and have continued into the long-term extension study
- Potentially higher levels of dystrophin production are expected with higher doses of PGN-EDO51 over longer treatment periods, which will be assessed in the CONNECT2-EDO51 study

1. Data as of Jan. 23, 2025
2. Cohort 2 (10 mg/kg)
   - Mild hypomagnesemia occurred in 2 participants. The serum magnesium returned to normal levels after they received low-dose oral magnesium supplementation
   - Mild renal impairment (Glomerular Filtration Rate decreased) occurred in 1 participant, and the treatment was paused to investigate potential causes. The participant's lab value steadily improved toward their baseline value during this pause.

For details on PGN-EDO51 nonclinical data, you can visit poster P49

ACKNOWLEDGEMENTS

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

Disclosures: All PepGen employees hold PepGen equity