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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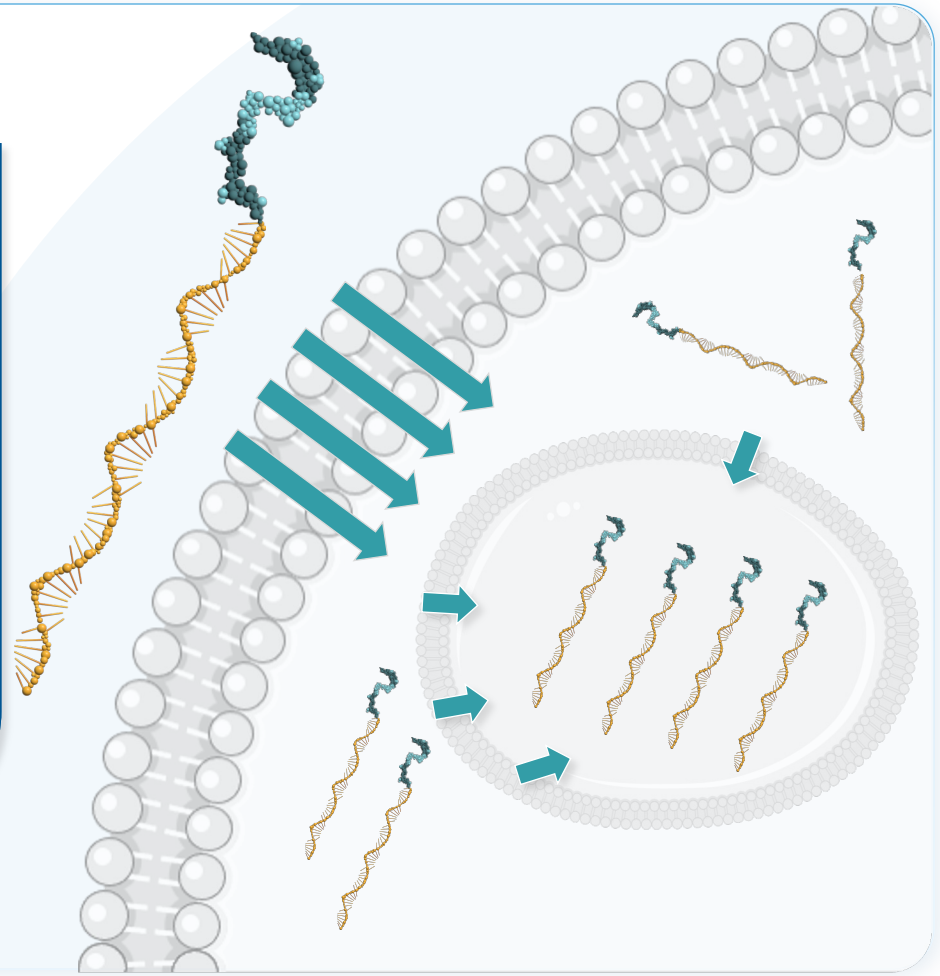
Disclosures

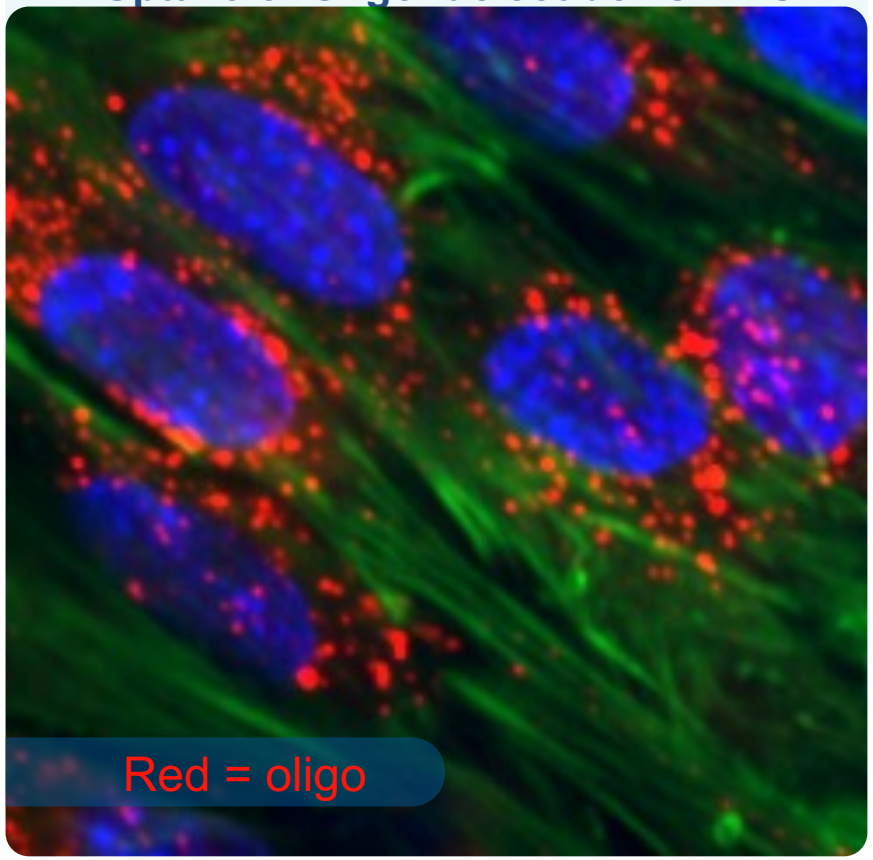
- Dr. Paul Streck is a full-time employee of PepGen and receives compensation, equity, and benefits from PepGen
- The study and the current analysis were sponsored by PepGen

PepGen's Enhanced Delivery Oligonucleotide (EDO) 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 vs PMO

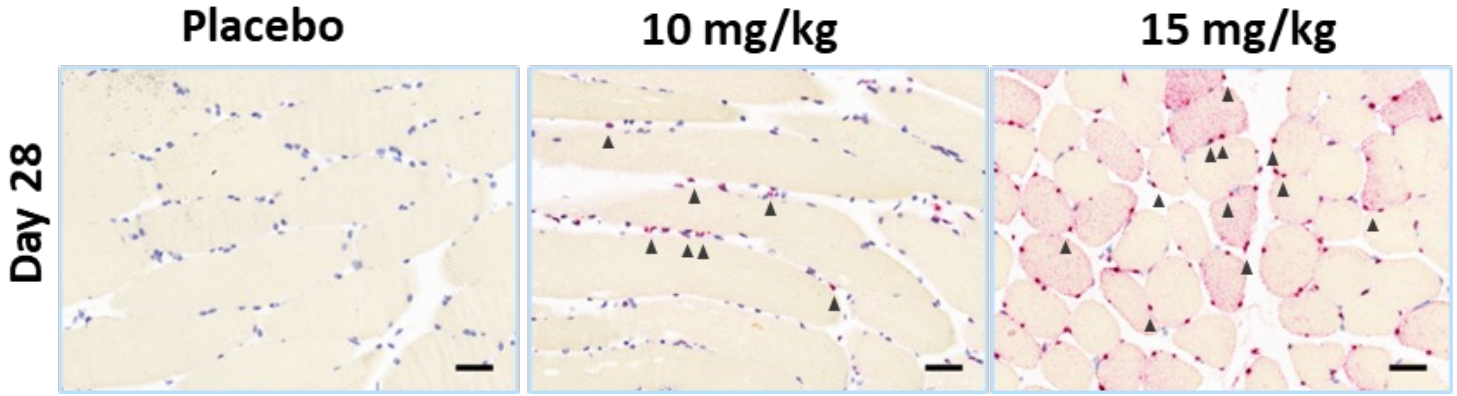


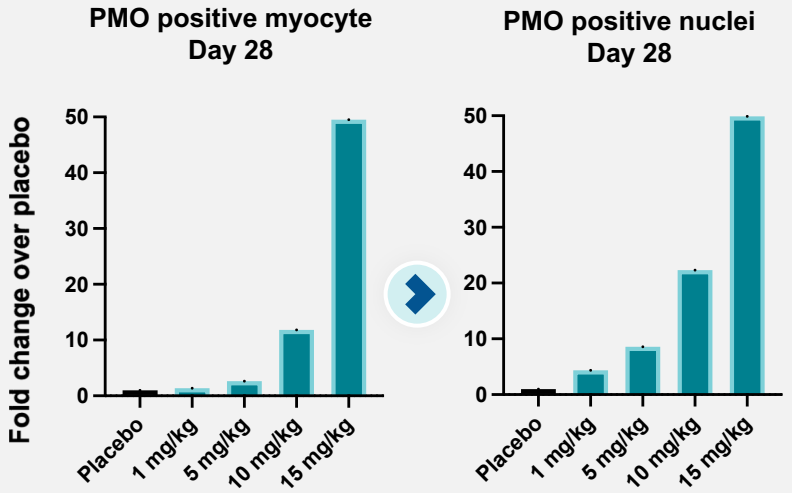
In vitro staining image is shown with 10μM conc. of EDO23. C2C12 mouse cells were differentiated for 4 days into myotubes and treated with fluorescently tagged compounds for 24h. PMO: phosphorodiamidate morpholino oligomer

EDO Peptides Enable Substantial Intracellular Uptake in Human Healthy Volunteer Muscle

Translation of uptake to human

- Study population: Healthy adult males (n=32; 8 per cohort, 3:1 PGN-EDO51:placebo)
- Dosing: Single dose, IV administration
- Bicep biopsies conducted on Day 10 and Day 28





Healthy volunteers were dosed with placebo or 1, 5, 10, 15 mg/kg PGN-EDO51 via iv infusion. Biceps samples were collected at day 10 and day 28, assessed for PGN-EDO51 levels in post hoc in situ hybridization analysis using a probe targeting the PMO sequence. Image analysis and quantification was done using Halo imaging software. Myocyte signal = nuclear signal + cytoplasmic signal. Scale = 50µm, Red – PMO, Blue-nucleus

PGN-EDO51 Development Path to Support Registration

Ongoing

Phase 2: Open-label MAD trial

Open in Canada; ongoing dosing and data collection in 10 mg/kg and 5 mg/kg LTE cohorts

Proof-of-concept: Dystrophin expression at 13-16 weeks[1]

Temporarily Paused[2]

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

Temporarily paused in UK[2]
Clinical hold in 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: Designed to Establish Proof-of-Concept and Inform CONNECT2 Clinical Trial Design

Connect 1
EDO51

CONNECT1 Study Overview

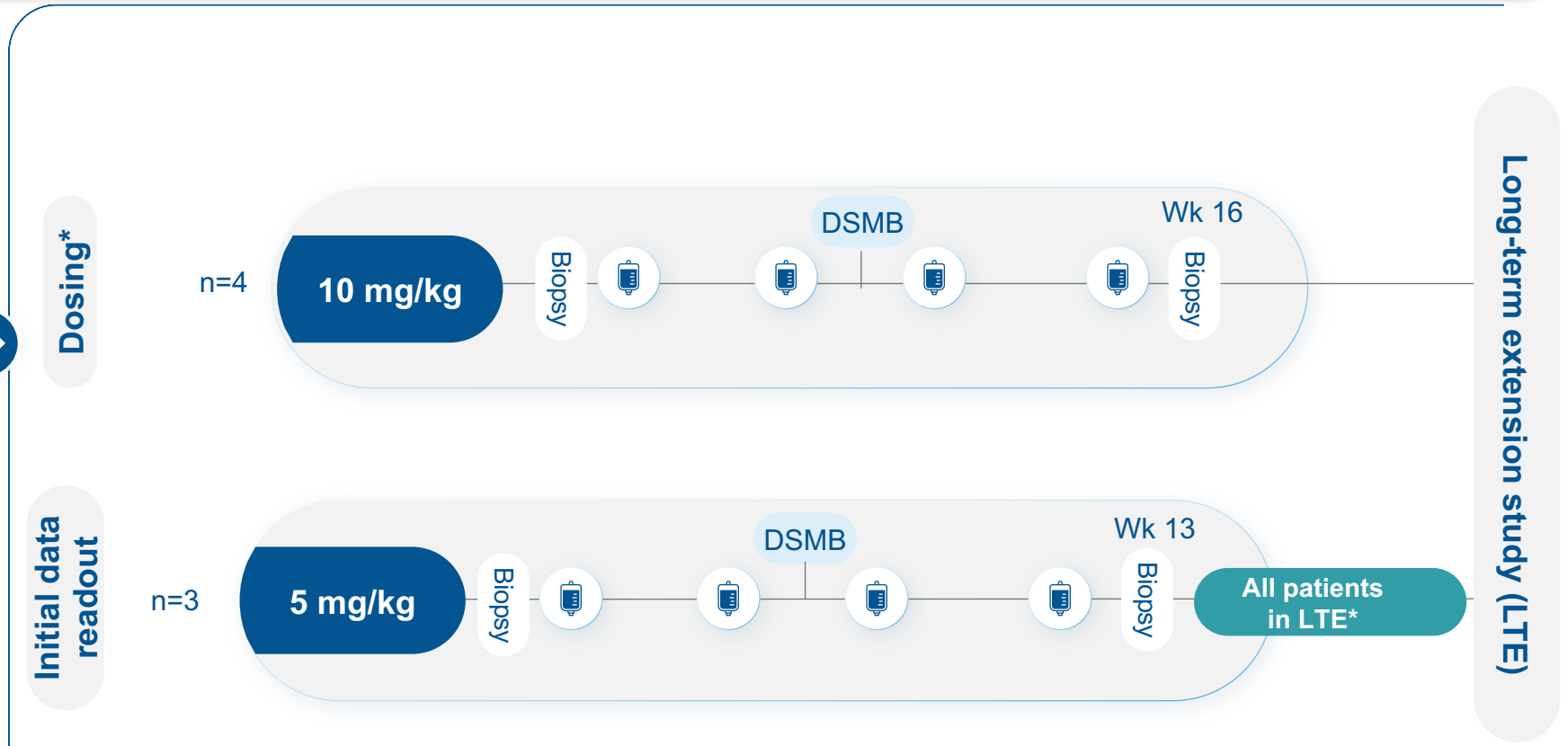
Open label, multiple ascending dose (MAD) clinical trial in Canada

DMD patients with exon 51 skippable mutation

Ages 6-16, ambulatory and non-ambulatory

Key endpoints: Safety and tolerability, dystrophin production, muscle tissue concentration of PGN-EDO51, exon skipping

Open Label Study in Patients with DMD Amenable to Exon 51 Skipping Therapy



*Dosing remains ongoing in the 5 mg/kg LTE and 10 mg/kg groups without further escalations at this time; data collection remains ongoing.
DSMB: data safety monitoring board

PGN-EDO51 dose every 4 weeks

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 5 mg/kg: Favorable Emerging Safety Profile[1]

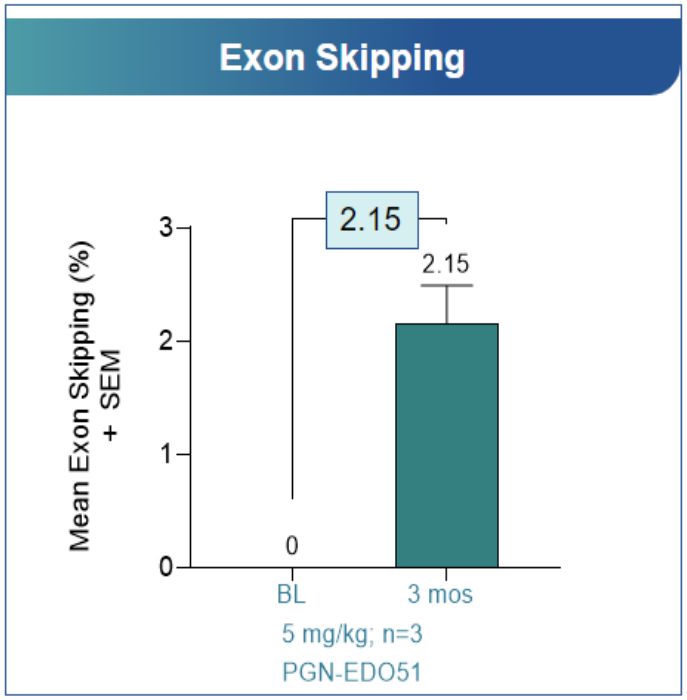
	n(%)*
Any TEAEs[3], n(%)	3 (100)
Related to study drug	2 (66.7)
• Mild • Moderate • Severe	2 (66.7) 0 0
Any TEAEs of Special Interest (AESI)	1 (33.3)
Serious Adverse Events (AEs)	0
AEs leading to dose modification/ discontinuation/interruption	0
AEs leading to death	0

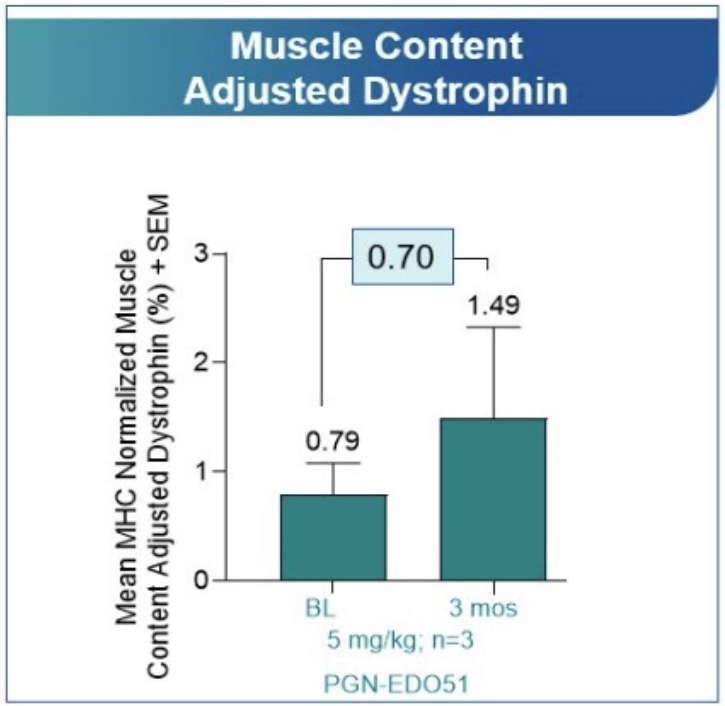
- All treatment emergent adverse events (TEAEs) were mild and resolved
- Related TEAEs were mild (abdominal pain, flatulence, creatinine increased)
- AESI was increased creatinine that resolved without intervention
- No discontinuations, dose modifications or dose interruptions
  - All participants rolled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

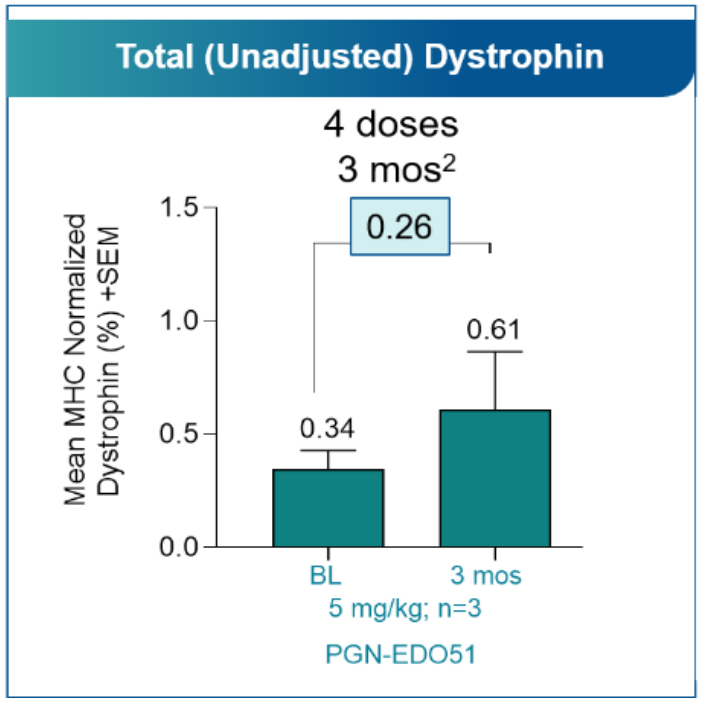
At 5 mg/kg, a total of 40 doses have been administered (12 doses in the MAD period+28 doses in the LTE period)[2]

1 & 2. Data as of January 23, 2025
3. TEAEs are defined as AEs that start after the first dose of study drug. AESIs are defined per protocol as events including hypomagnesemia, decrease in eGFR, increased serum creatinine levels, and hypersensitivity or allergic reaction.
* n=number of participants

PGN-EDO51 Produced High Levels of Mean Exon Skipping and Promising Dystrophin Increase over Short Treatment Duration and with Few Doses







4 doses over 3 months

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

Dosing Continues in Cohort 2 at 10 mg/kg[1]

- Observed favorable emerging safety profile
- At 10 mg/kg, a total of 17 doses have been administered
- All treatment-related adverse events have been mild
- No treatment-related serious adverse events
- Asymptomatic hypomagnesemia has been observed in 2 of the 4 total participants and has resolved with low-dose oral magnesium supplementation
  - Dosing pause due to low eGFR in 1 of the 2 participants which is resolving; the participant remains on study. Nuclear scan showed GFR is in the normal range
- No sustained elevation in kidney biomarkers
- No hypokalemia, anemia or thrombocytopenia

1. As per the data obtained through January 23, 2025
eGFR: estimated glomerular filtration rate

CONNECT1 Cohort 1 (5 mg/kg) Key Preliminary Takeaways

- Emerging safety profile is favorable[1]
- 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 encouraging levels of muscle adjusted dystrophin production (0.70%) and total dystrophin production (0.26%) after just 3 months and 4 doses at 5 mg/kg
- PGN-EDO51 produced high levels of mean exon 51 skipping (2.15%) after just 3 months and 4 doses at 5 mg/kg
- Initial results support that our EDO technology has the potential to deliver high levels of oligonucleotides to the nucleus

We believe potentially higher levels of dystrophin production are expected with higher doses of PGN-EDO51 over longer treatment periods

1. For the 5 mg/kg and 10 mg/kg cohorts, data as of January 23, 2025

Thank you!

All the study participants and their families

The clinical investigators and their teams

- Dr. Hugh McMillan, MD, MSc, FRCPC
  Children's Hospital of Eastern Ontario (CHEO)
- Dr. Hernan Gonorazky, MD, CSCN
  The Hospital for Sick Children (SickKids)
- Dr. Nicolas Chrestian, MD, FRCPC, CSCN
  CHU De Quebec-Universite Laval

The Duchenne patient communities

For more details, you can visit our posters

P49 Single- and Repeat-Dose Nonclinical Data for PGN-EDO51 Demonstrated Favorable Pharmacology and Safety Profiles for the Treatment of DMD

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