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# A Phase IIb Placebo-Controlled Study of the Exon-Skipping Drug Eteplirsen in Subjects with Duchenne Muscular Dystrophy

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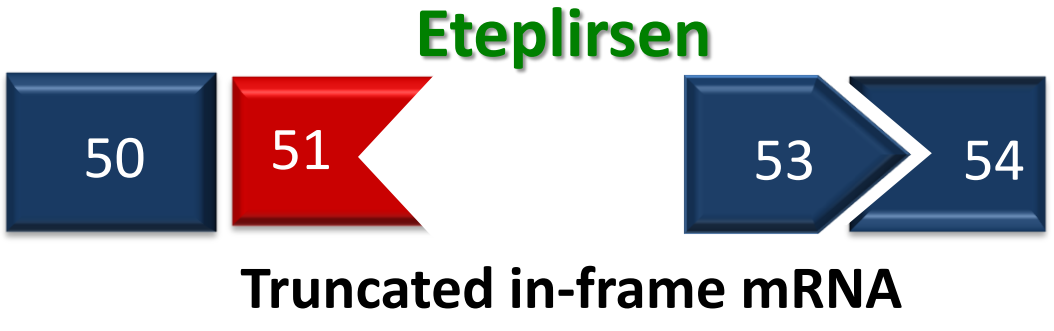
# Placebo-Controlled Exon Skipping Study of Eteplirsen in DMD

## Eteplirsen (AVI-4658)

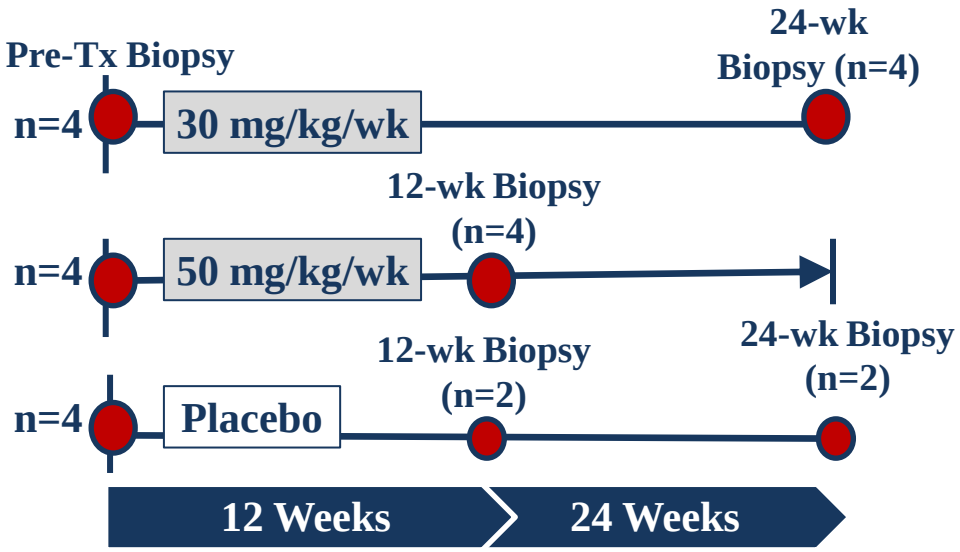
A phosphorodiamidate morpholino oligomer (PMO) validated to skip exon 51
Skipping exon 51 has the potential to restore the reading frame of the following mutations: 45-50, 47-50, 48-50, 49-50, 50, 52, 52-63




*DMD* gene shows an exon 52 deletion

## Study Design

- At NCH, double-blind, placebo-controlled, randomized, multiple dose, Weekly IV-dosing
- **Rationale:** To compare efficacy of duration of treatment vs dose
- **$1^0$ Outcome**
  - ✓ Dystrophin expression on muscle biopsy pre vs post-treatment.
  - ✓ Safety/tolerability



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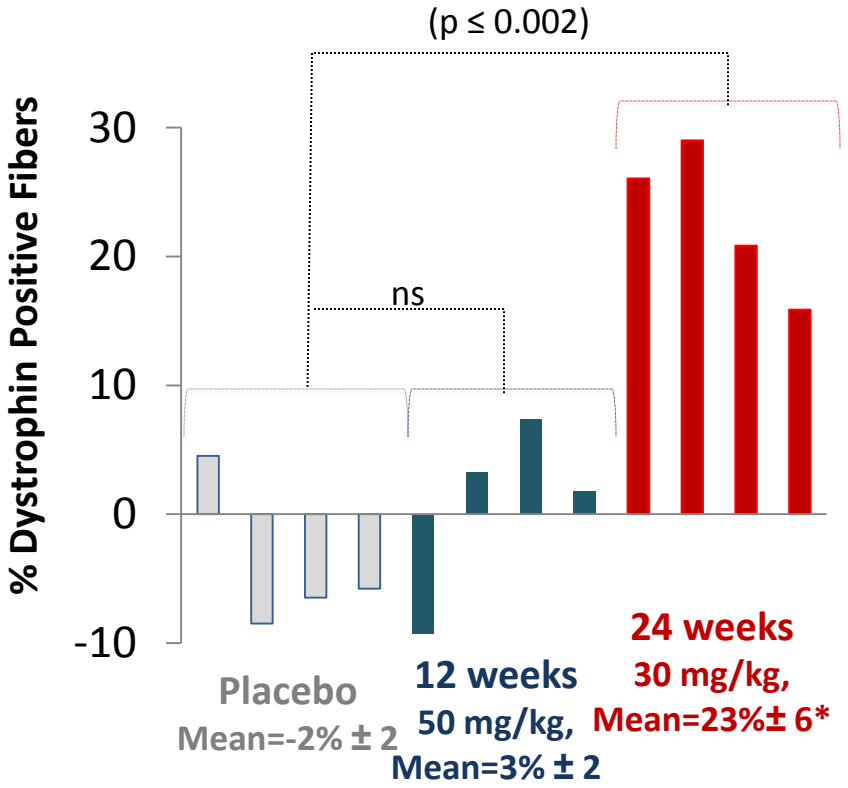
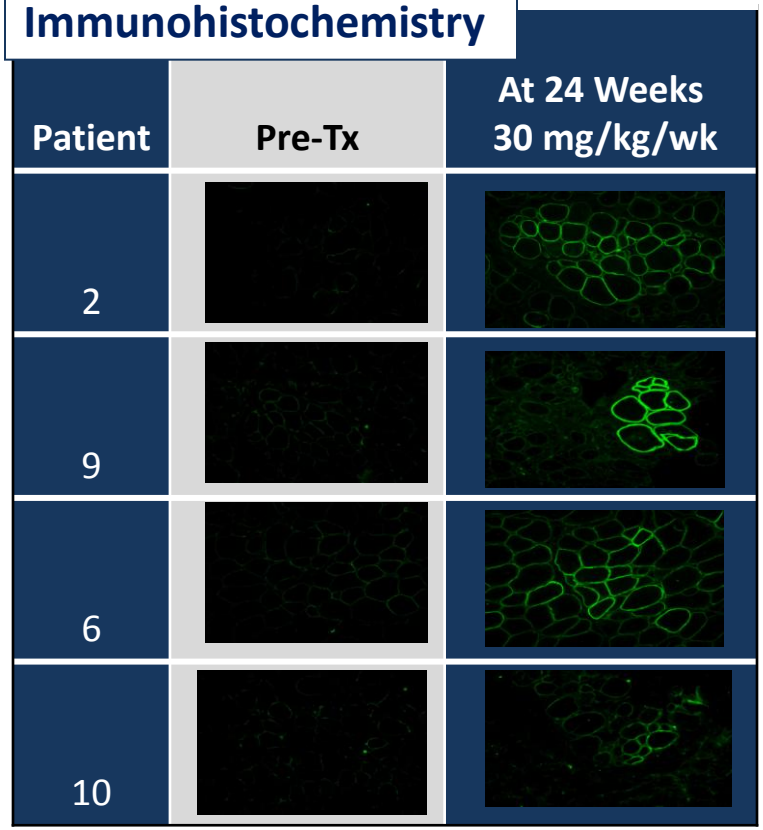
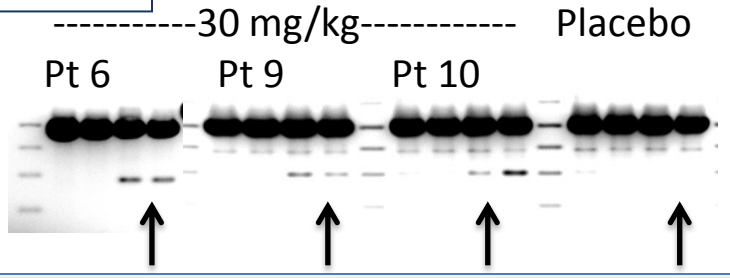
## % Dystrophin Positive Fibers Post-Treatment




## Immunohistochemistry




## RT-PCR




- **1⁰ Outcome**
  - ✓ Statistically significant increase in dystrophin production at 24 weeks with the low dose (30 mg/kg) eteplirsen relative to placebo.

# Placebo-Controlled Exon Skipping Study of Eteplirsen in DMD

## Conclusions

- Eteplirsen produced significant levels of dystrophin in DMD patients after 24 weeks of treatment (mean=23% of dystrophin-positive fibers).
- Eteplirsen proved safe at both dose levels (up to 50mg/kg/wk over 28 weeks) with no treatment-related adverse events.
  - Not a single dose missed in any study subject over the 28 week course of administration.
- Eteplirsen's favorable safety profile supports continuing treatment and may enable long-term chronic administration.
- Eteplirsen induced production of dystrophin at consistent levels; The range observed (between 15% to 30% dystrophin-positive fibers) is likely to produce a clinical benefit if maintained over time.

- Thanks to staff of NCH and cooperation of AVIBiopharma