

# Global Phase 3 PolarisDMD Trial for Edasalonexent, an Oral NF- $\kappa$ B Inhibitor in Boys with DMD

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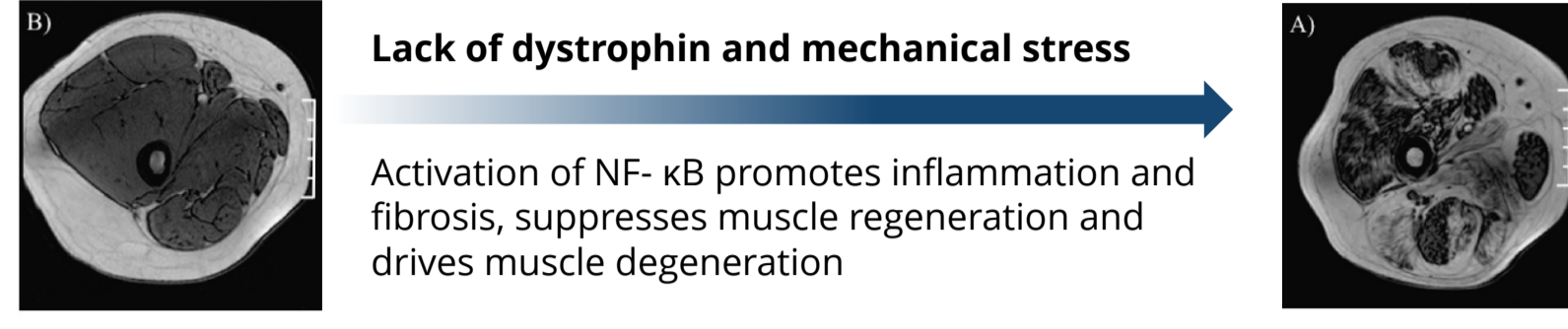
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## BACKGROUND

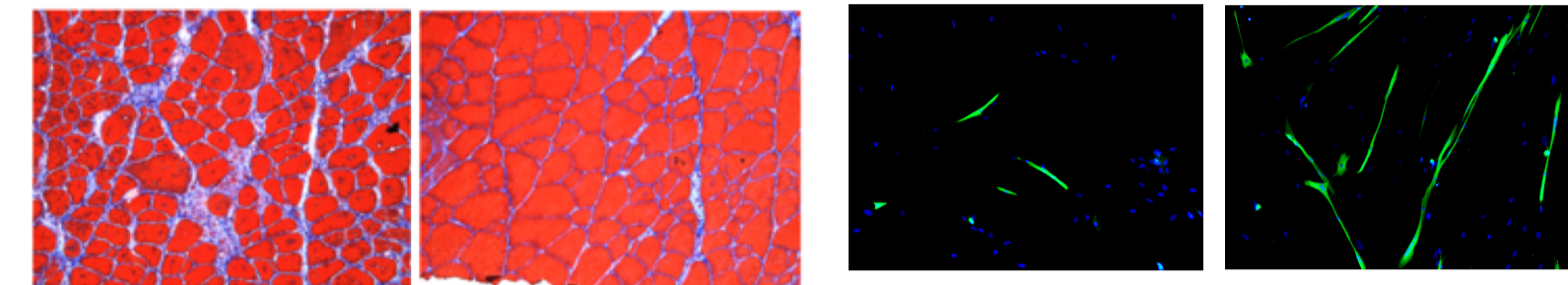
### Edasalonexent Inhibits NF- $\kappa$ B

- NF- $\kappa$ B pathway is the key link between loss of dystrophin and disease progression in DMD



(Akima et al., *Neuromuscular Disease*, 2012)

- Edasalonexent: NF- $\kappa$ B inhibition suppresses inflammation and fibrosis, and decreases muscle degeneration and enhances muscle regeneration



(Yin, et al., *Muscle Nerve* 2017)

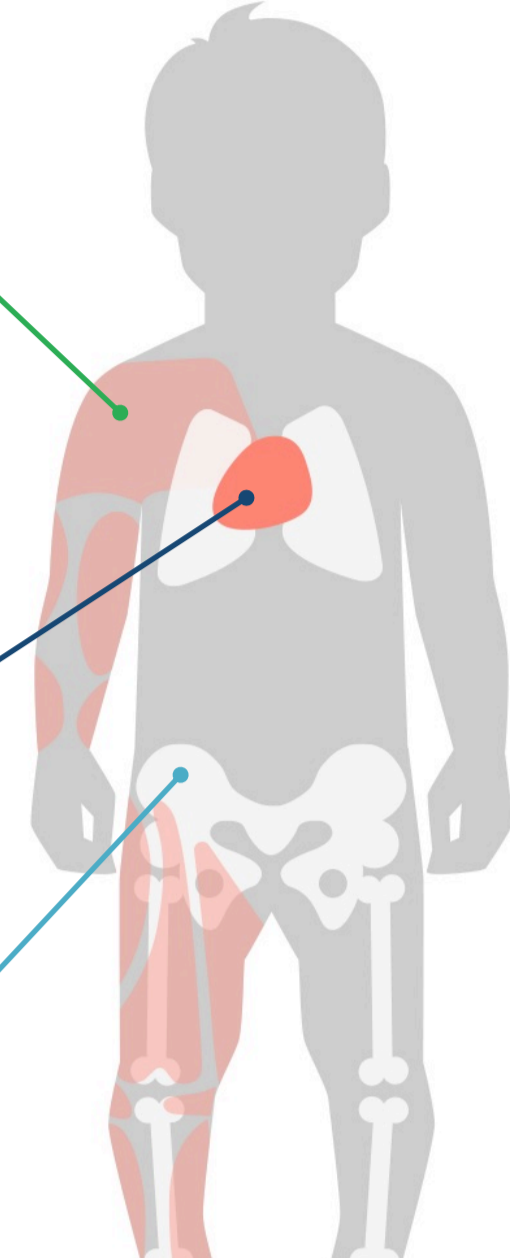
### NF- $\kappa$ B Inhibition Provides Potential for Broad Therapeutic Benefit in Duchenne Muscular Dystrophy

Activated NF- $\kappa$ B leads to disease progression in DMD

**Skeletal Muscle**  
Loss of ambulation, upper limb function, respiratory failure

**Heart**  
Cardiomyopathy

**Bone**  
Fractures



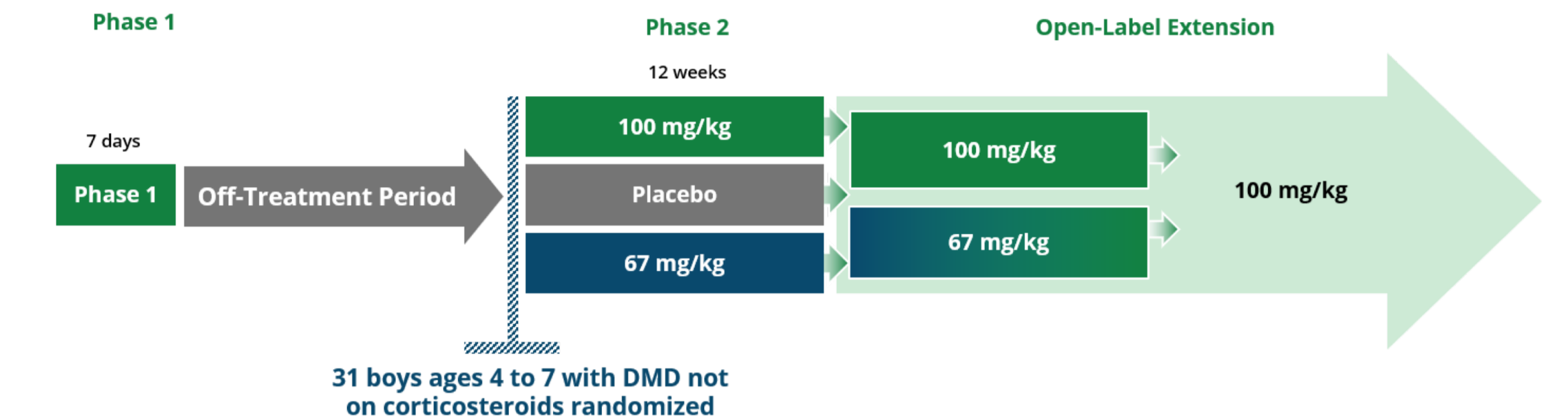
Vision for edasalonexent, an NF- $\kappa$ B inhibitor

✓ **Goal: Improve** skeletal muscle function

✓ **Goal: Preserve** cardiac function

✓ **Goal: Reduce** risk of fractures

### MoveDMD Trial Was Designed to Enable Phase 3

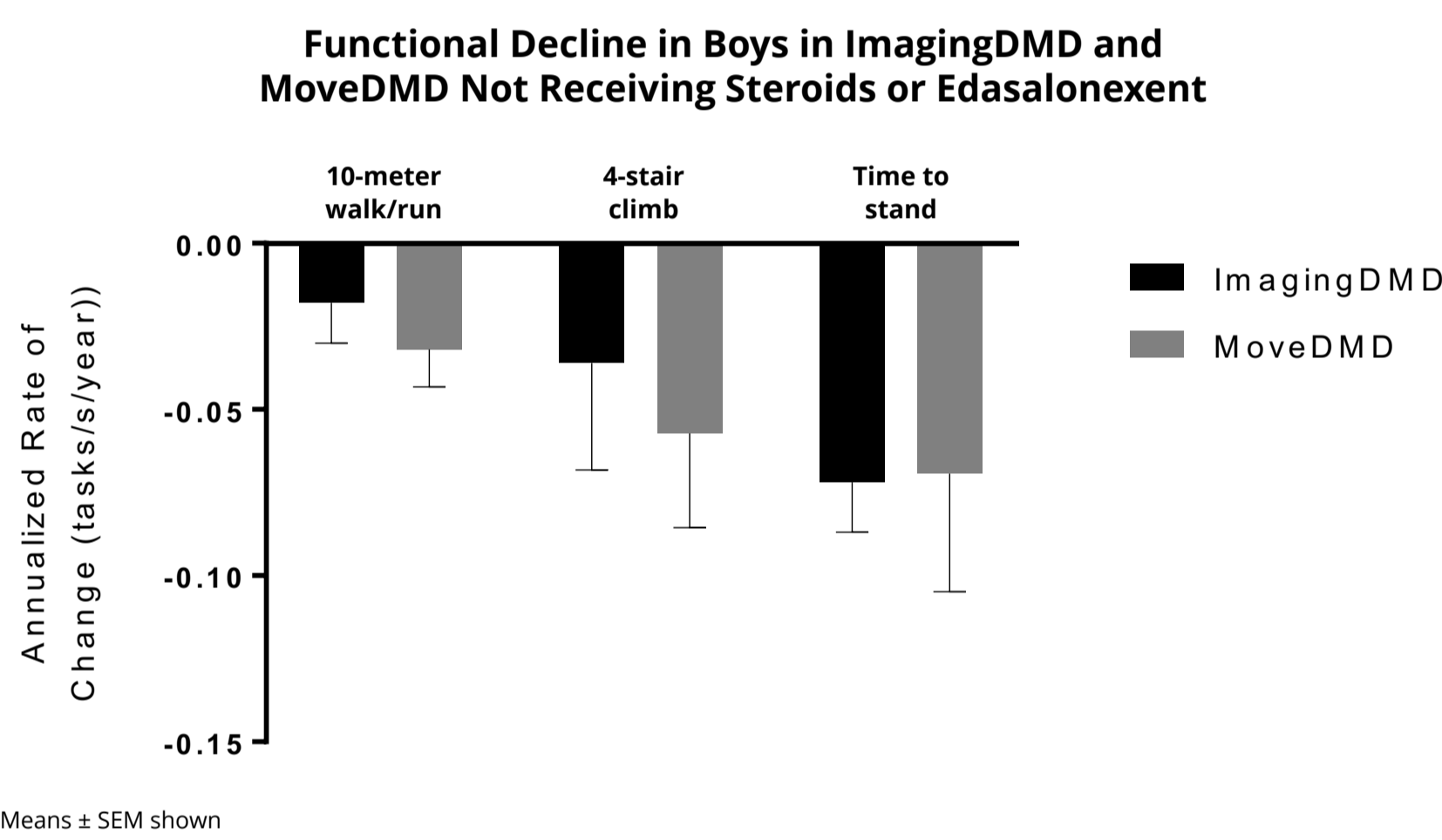


- Integrated multi-part trial design to evaluate efficacy, safety, tolerability**
  - Assessments included North Star Ambulatory Assessment, age-appropriate timed function tests, MRI
- Off-treatment control period measurements between Phase 1 and Phase 2**
  - Provides internal control for pre-specified MoveDMD analyses
  - Compared off-treatment control period disease progression with available natural history data
- Open-label extension enabled assessment of safety and efficacy following longer term treatment**

## NATURAL HISTORY DATA

### Boys in the MoveDMD Trial Were Declining in Function Prior to Treatment Similar to Natural History

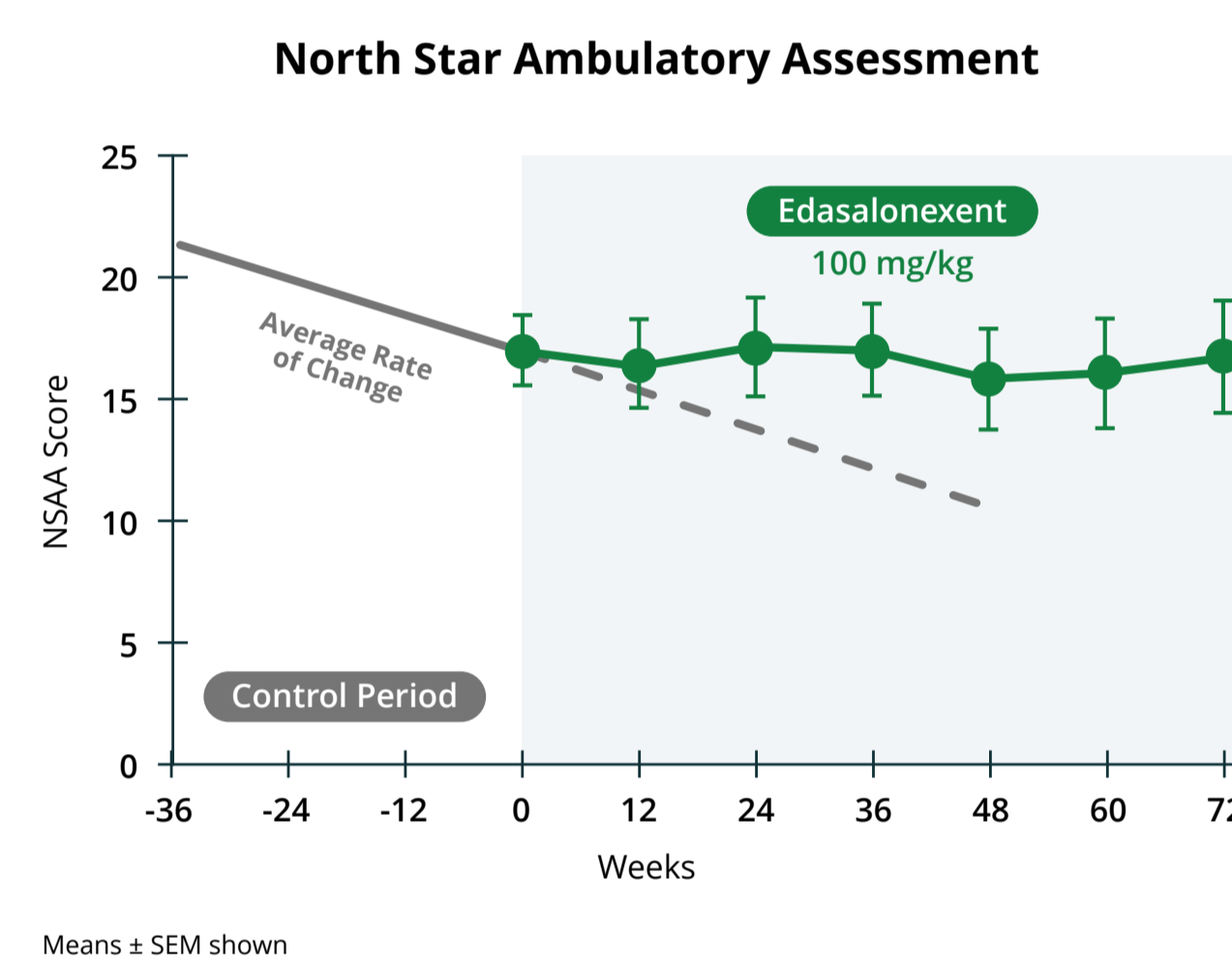
- The declines in function in the MoveDMD off-treatment period were similar to those in the observational ImagingDMD study in boys up to their 8<sup>th</sup> birthday who were not on steroids.



Means  $\pm$  SEM shown

## MoveDMD RESULTS

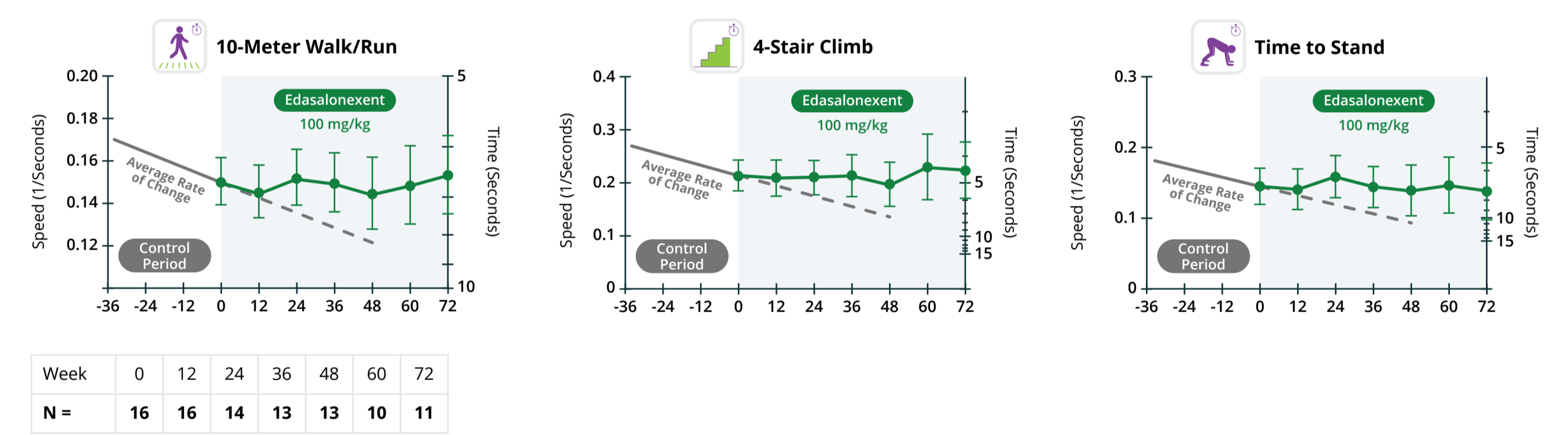
### North Star Ambulatory Assessment Score, a Measure of Overall Function in Young Boys, Stabilized with Edasalonexent Treatment Compared to Off-Treatment Control Period



Means  $\pm$  SEM shown

### Speed on All Timed Function Tests Stabilized with Edasalonexent Treatment, Consistent with Effect on NSAA

- Disease progression on edasalonexent improved compared with rate of change during off-treatment control period

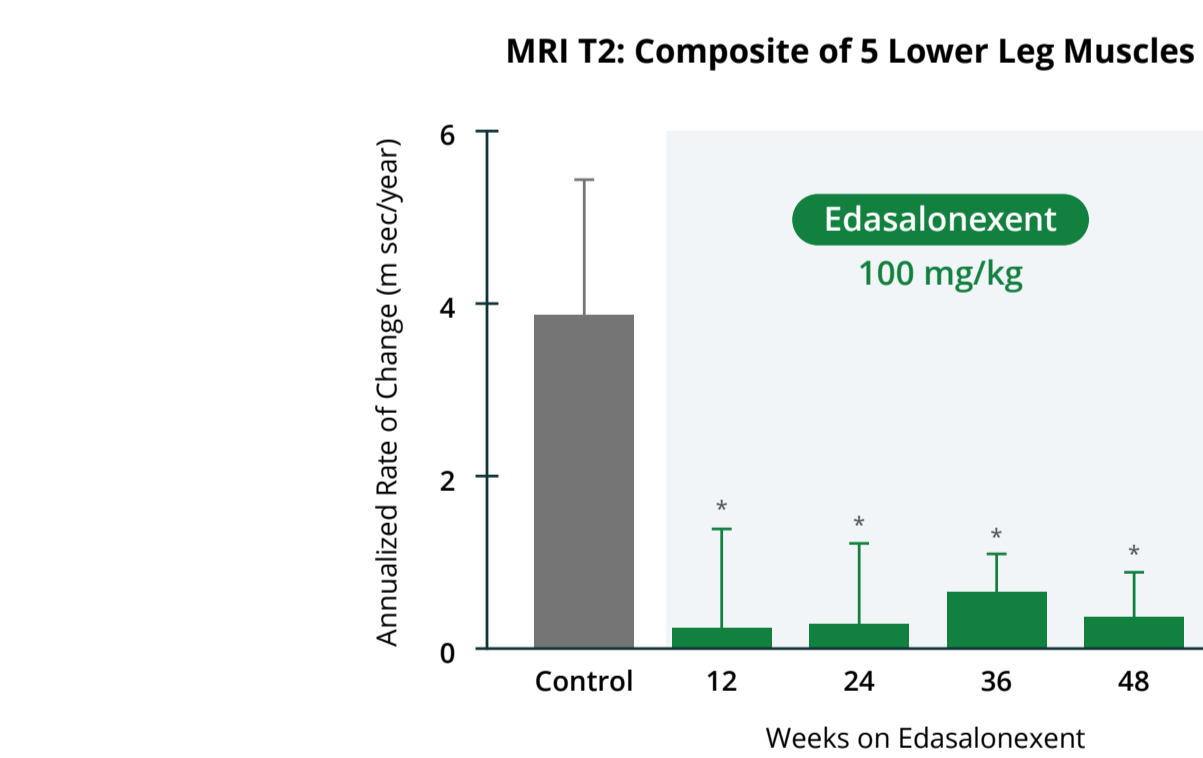


Means  $\pm$  SEM shown. Includes data of all boys initially started on 100 mg/kg dose (n=16)

## MoveDMD RESULTS

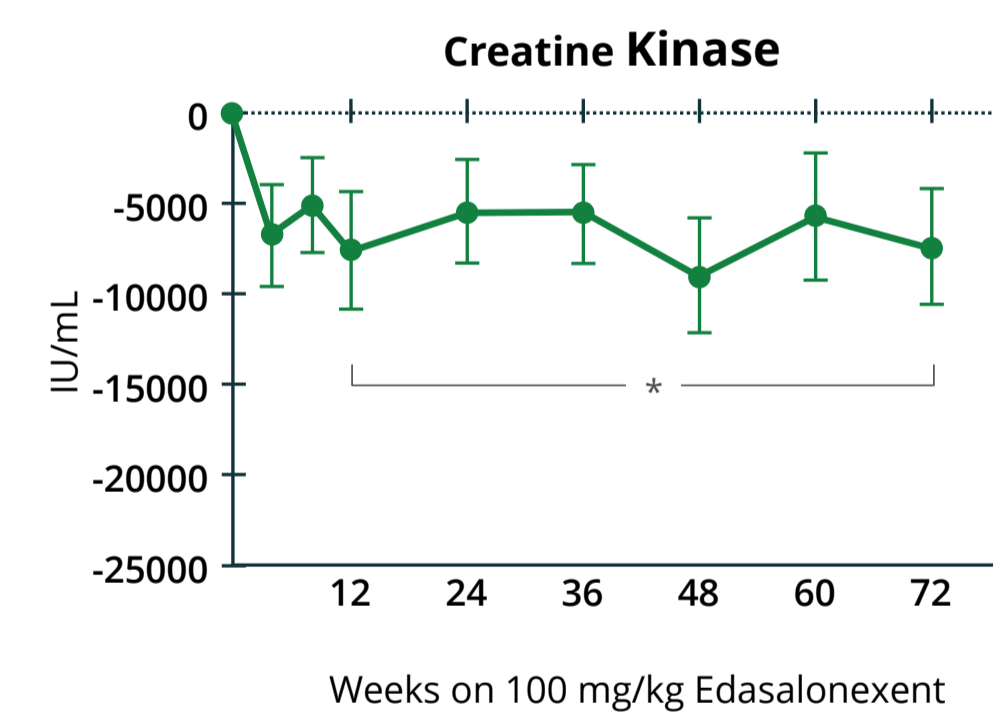
### Edasalonexent Significantly Improved Rate of Change of MRI T2

- On edasalonexent, the rate of change for the MRI T2 composite of the 5 lower leg muscles improved significantly compared to the rate of change during the off-treatment control period ( $p < 0.05$  for 12, 24, 36, and 48 weeks)
- Stabilization of MRI T2 is consistent with slowing of disease progression also observed in function assessments



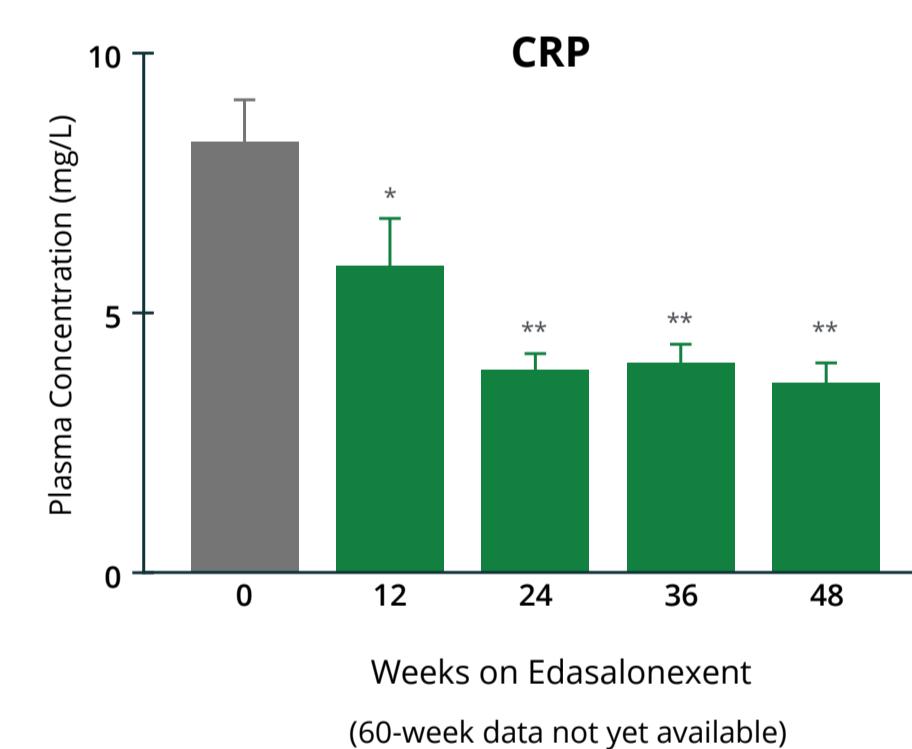
Means  $\pm$  SEM shown. \*  $p < 0.05$  for repeated measure mixed model comparison with off-treatment period

### Biomarkers Showed Significant Decrease with Edasalonexent Treatment



- All muscle enzymes (CK, ALT, AST and LDH) showed sustained decrease after 12 weeks ( $p < 0.05$ )
- Consistent positive impact on muscle supportive of an edasalonexent benefit

Means  $\pm$  SEM shown. \*  $p < 0.05$  for change from baseline after 12 weeks

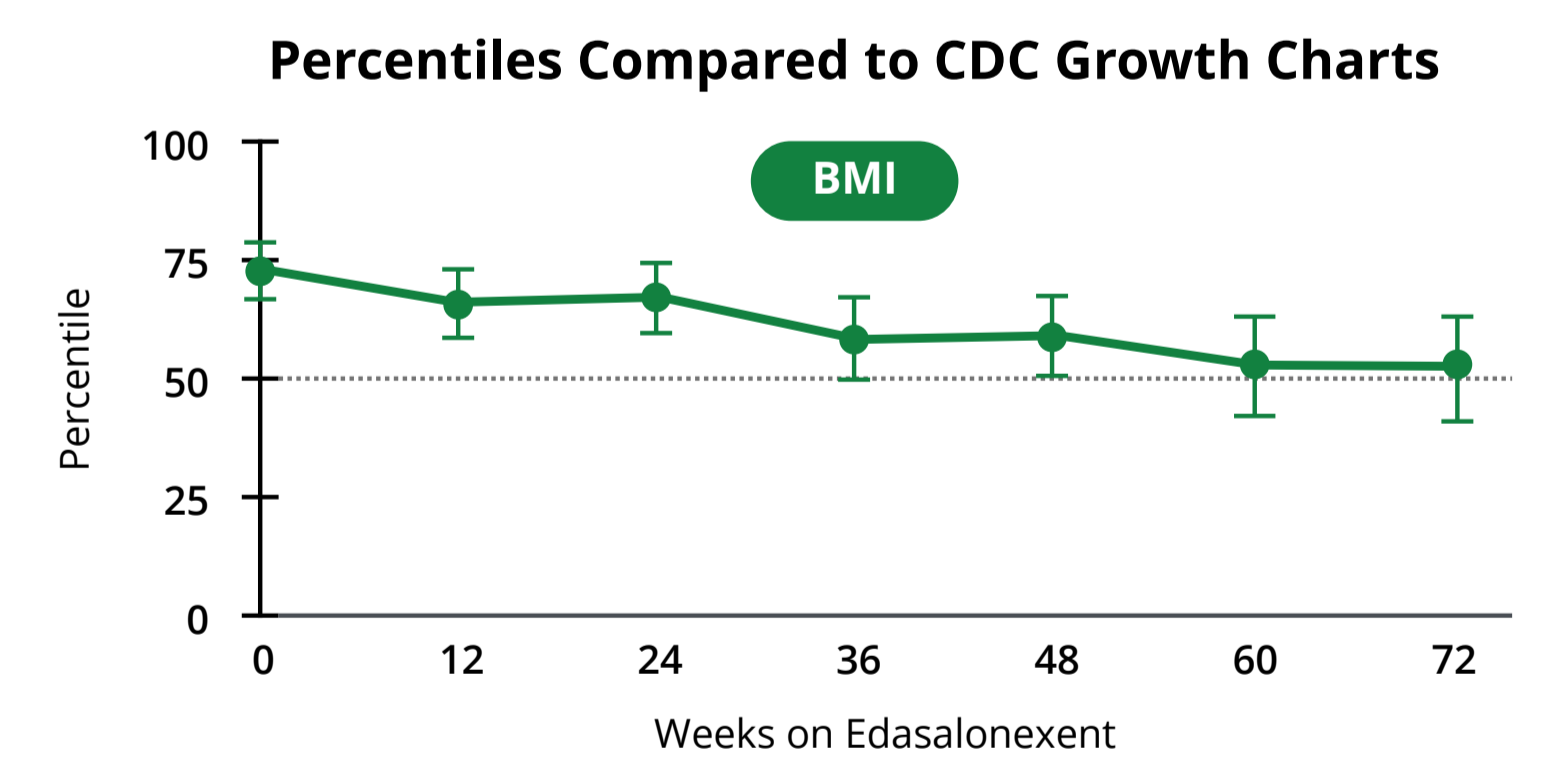


- C-reactive protein (CRP), a well-characterized blood test marker that provides a global assessment of inflammation is elevated in DMD
- CRP approximately 3-fold higher in boys affected by DMD compared to unaffected boys (Anderson, 2017)
- In MoveDMD, CRP significantly decreased from baseline throughout 48 weeks of 100 mg/kg edasalonexent

Means  $\pm$  SEM shown. \*  $p < 0.05$ , \*\*  $p < 0.001$  for comparison with pre-treatment baseline measurement. Anderson, et al. (2017). *Pediatr Cardiol* 38(8): 1606-1612.

### Safety: Growth Continues as Expected

- Well tolerated in 50+ years of patient exposure
  - Well tolerated, with majority of adverse events mild in nature and mostly gastrointestinal
- Growth: Age-appropriate increase in weight and height
  - Height increased an average of 2.1 inches/year, while weight increased by an average of 2.9 lbs/year, both in line with typical height and weight increases of unaffected boys

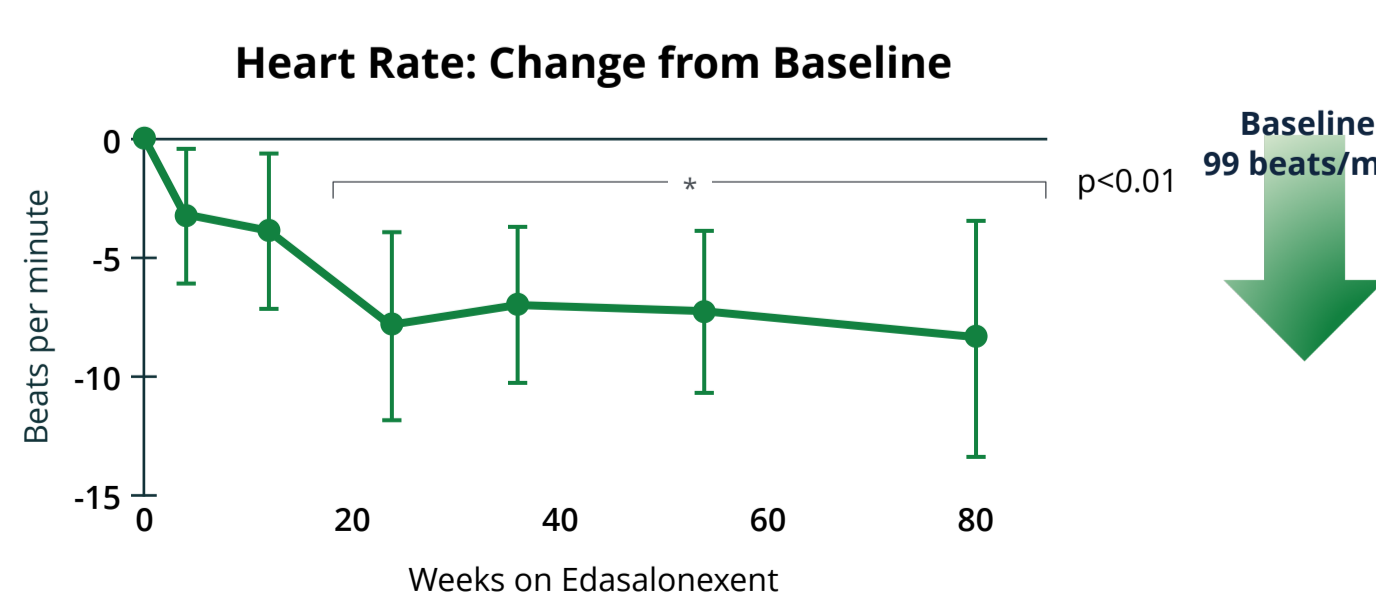


Means  $\pm$  SEM shown

## MoveDMD RESULTS

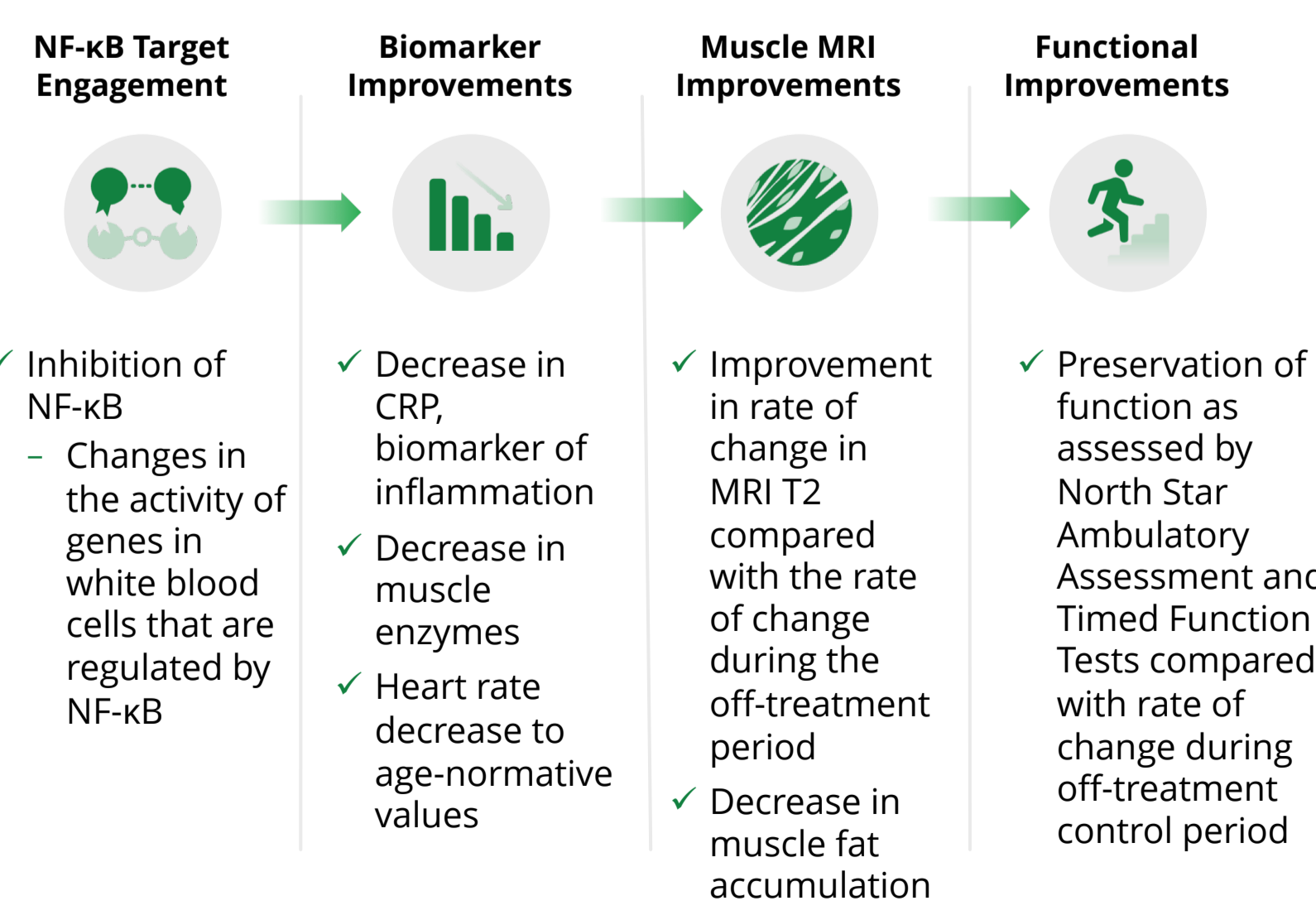
### Elevated Resting Heart Rate Characteristic of DMD Decreased to Age-Normative Values

- In DMD, heart rate does not decrease with age from 6-12 (Thomas, 2012)
- Age-normative value is ~92 beats per minute (Fleming, 2011)
- In MoveDMD, ECG heart rate decreased from baseline of 99 to 92 beats per minute
- Heart rate by physical examination showed similar trends
  - No significant changes in systolic or diastolic blood pressure



Means  $\pm$  SEM shown. Thomas, et al. *Pediatr Cardiol*. 2012 33(7):1175-9. Fleming, (2011). *The Lancet* 377(9770): 1011-1018.

### Edasalonexent: Translation from Biomarkers to Functional Improvements in Duchenne



- Inhibition of NF- $\kappa$ B
  - Changes in the activity of genes in white blood cells that are regulated by NF- $\kappa$ B

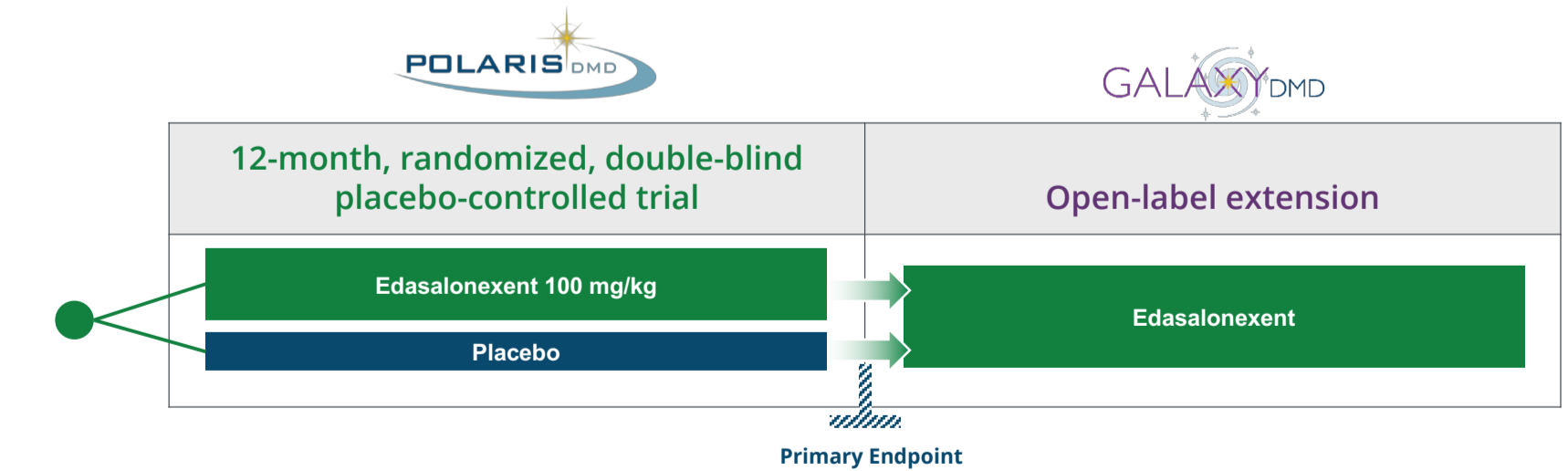
- Decrease in CRP, biomarker of inflammation
- Decrease in muscle enzymes
- Heart rate decrease to age-normative values

- Improvement in rate of change in MRI T2 compared with the rate of change during the off-treatment period
- Decrease in muscle fat accumulation

- Preservation of function as assessed by North Star Ambulatory Assessment and Timed Function Tests compared with rate of change during off-treatment control period

## PolarisDMD

### PolarisDMD: Global Phase 3 Registration Trial for Edasalonexent



- Study Population**
  - All mutations, age 4.0 to 8.0 (8<sup>th</sup> birthday), steroid naïve or off steroids for  $\geq 6$  months
- Visits / key assessments every 3 months**
  - Primary: Change in North Star Ambulatory Assessment
  - Key secondary: Age-appropriate timed function tests
  - Safety measures
  - Assessments of growth, cardiac, and bone health
  - No biopsy or 6 minute walk test
- Enrollment of approximately 125 boys, 2:1 randomization**
- After the 52 week placebo-controlled period, patients may elect to continue in the open-label study, GalaxyDMD**
- UK Locations: Bristol, London - Evelina, London - GOSH, Manchester**