Edasalonexent, an NF-κB Inhibitor, Slows Longer-Term Disease Progression on Multiple Functional and MRI Assessments Compared to Control Period in 4 to 7-Year Old Patients with Duchenne Muscular Dystrophy

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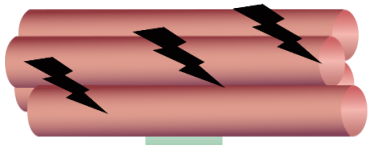
Disclosures

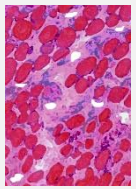
- The clinical trial was sponsored by Catabasis Pharmaceuticals, Inc. Richard Finkel, Krista Vandenborne, H. Lee Sweeney, Erika Finanger, Gihan Tennekoon, Perry Shieh, Rebecca Willcocks, Sean Forbes, William Triplett, and Sabrina Yum received research support from Catabasis
- Richard Finkel, H. Lee Sweeney, Erika Finanger, and Perry Shieh received honoraria from Catabasis
- Maria Mancini, James MacDougall, Angelika Fretzen, Pradeep Bista, Andrew Nichols, and Joanne Donovan are employees or consultants of Catabasis and hold stock in Catabasis
- Edasalonexent is an investigational agent that is not approved in any territory

Activation of NF-κB in Muscular Dystrophy is a Key Factor in Disease Progression in Skeletal and Cardiac Muscle

No Dystrophin + Mechanical Stress



Inflammation in Infancy



Inflammation

Cytokines

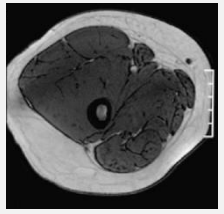
Fibrosis

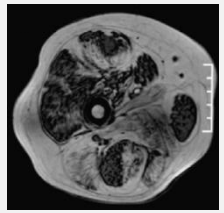
Degeneration

MuRF1/MAFbx

Control

DMD





Cross section of mid-thigh muscle in 12-14 YO boys

Activated NF-κB

Regeneration

Cyclin D1

Satellite Cell

Myoblasts

MyoD

Myotube

Dystrophin and Membrane Stability

MMP-9

miRNA

β-Dystroglycan

Dystrophin

Actin

NF-kB decreases dystrophin production, suggesting inhibition could increase dystrophin with dystrophin-targeted therapies

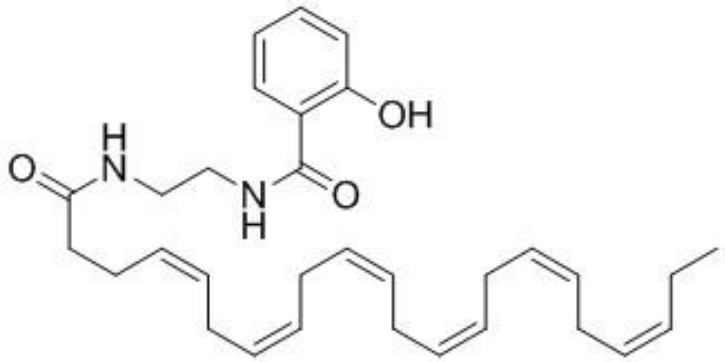
Disease Progression

Chen et al., *Neurology* 2005 65: 826
Fiorillo et al., *Physiol Genomics* 2018 50:735

Kumar et al., FASEB J 2003 17:386
Akima et al., *Neuromuscul Disord* 2012 22: 16

Edasalonexent Inhibits NF-κB, A Key Driver of Muscle Disease in DMD

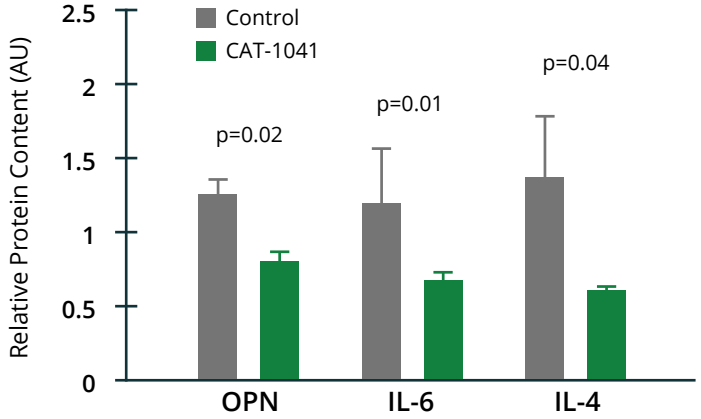
- **Edasalonexent is an orally-administered small molecule that is not a steroid**



- **Being developed for patients with DMD regardless of mutation, both as monotherapy and potentially to be combined with dystrophin-targeted therapies**

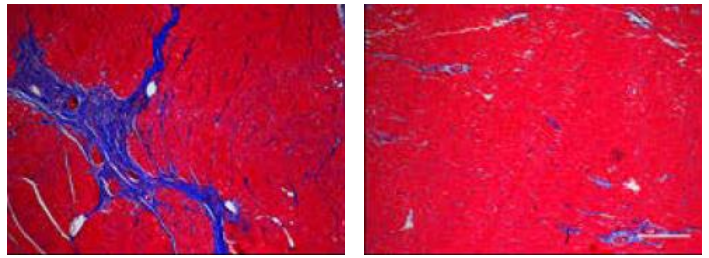
- **Inhibiting NF-κB slows disease progression in animal models of DMD**
  - Oral administration of edasalonexent or analog (CAT-1041) reduces muscle inflammation and improves function in mdx mice and GRMD dog

Reduced Inflammation in *mdx*



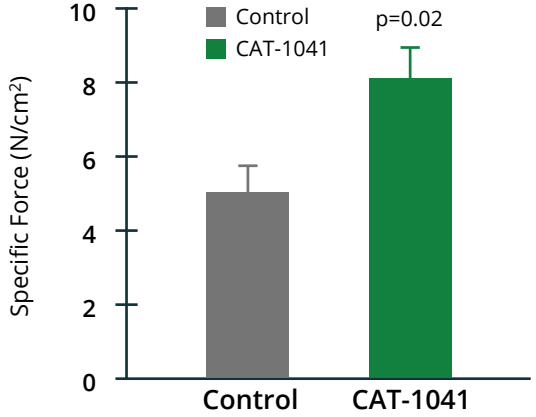
Decreased Cardiac Fibrosis

12 month-old GRMD



Masson's Trichrome Staining

Increased Diaphragm Specific Force in *mdx*



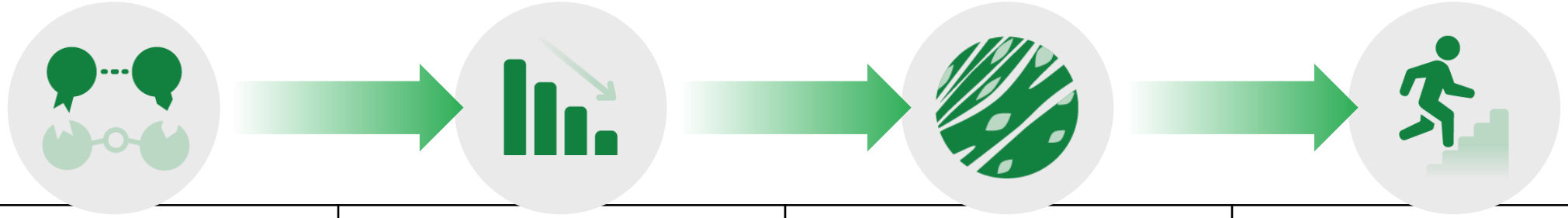
Means + SEM

Design of MoveDMD, a Phase 2 Trial with Open-Label Extension

- **Study Objectives**
  - Safety and PK in pediatric patients with DMD
  - Proof of concept using MRI to assess changes in muscle health
  - Long-term safety and effects on age-appropriate functional measures to enable design of Phase 3 study
- **Key Inclusion / Exclusion criteria**
  - Age 4 to up to 8th birthday not on corticosteroids for at least 24 weeks
  - Able to perform timed function tests and MRI
- **Design**
  - Phase 1: 1-week open label treatment to assess safety and PK, with initial assessments of function and MRI
  - Off-treatment period of ~6 months prior to Phase 2
  - Phase 2: 12-week placebo-controlled period
  - Open-label extension >72 weeks

- **Analysis Plan**
  - 12-week placebo control period
  - **Compare changes during pre-treatment control period with changes after initiation of edasalonexent**

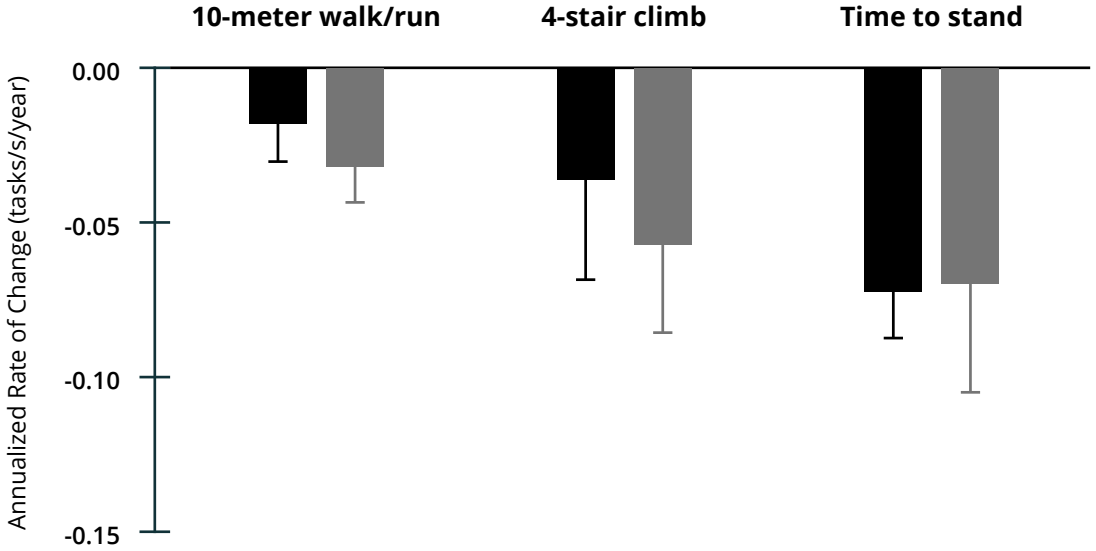
Range of Endpoints to Demonstrate Proof of Concept and Support Design of Phase 3



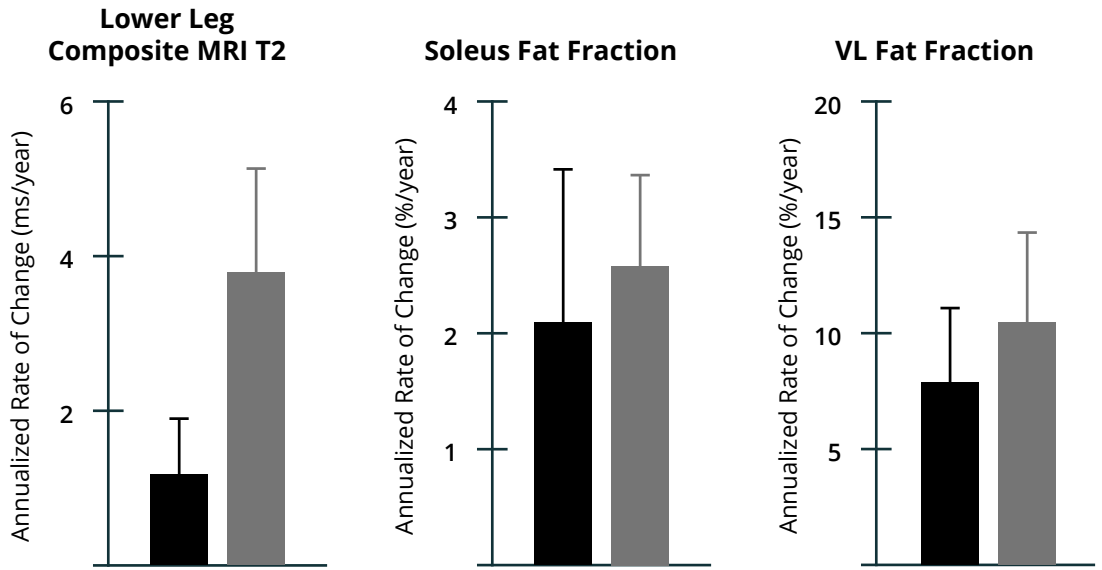
NF-κB Target Engagement	Biomarkers	Muscle MRI	Functional
▸ Inhibition of NF-κB targeted gene set in peripheral blood	▸ CRP, biomarker of inflammation ▸ Muscle enzymes	▸ MRI T2 of upper and lower leg ▸ MRS muscle fat	▸ North Star Ambulatory Assessment and Timed Function Tests

Steroid-Naïve Boys in Age Range 4 to 8th Birthday Are Declining in Function and Progressing on MRI

Functional Decline in Boys Not Receiving Steroids or Edasalonexent



MRI Shows Disease Progression



Natural History: ImagingDMD Prior to treatment: MoveDMD

- Declines in function in natural history study were similar to those observed in the MoveDMD trial off-treatment
- Decreases in function correlate with increases in composite lower leg MRI T2 as well as muscle fat fraction

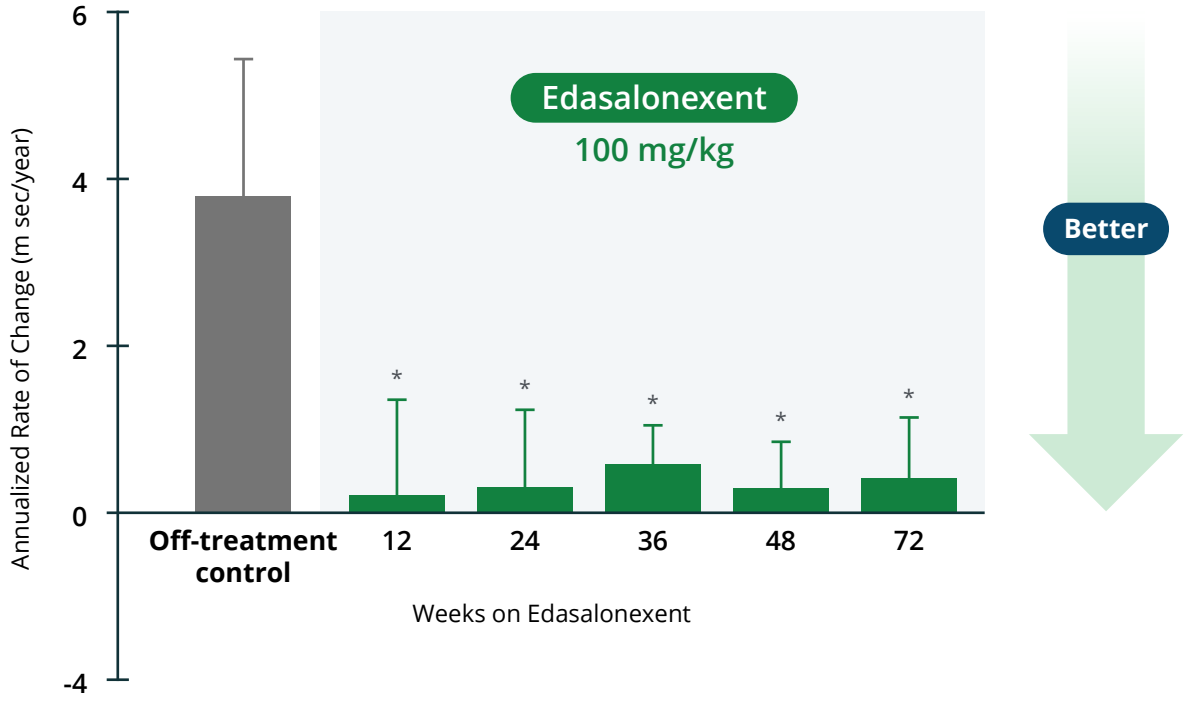
Means + SEM

Finkel et al., World Muscle Society, 2018; Vandenbourne et al., World Muscle Society, 2018

In Phase 2 MoveDMD Trial and Open-Label Extension:

Edasalonexent Improved Rate of Change of MRI T2 Compared to Off-Treatment Control Period

MRI T2: Composite of 5 Lower Leg Muscles

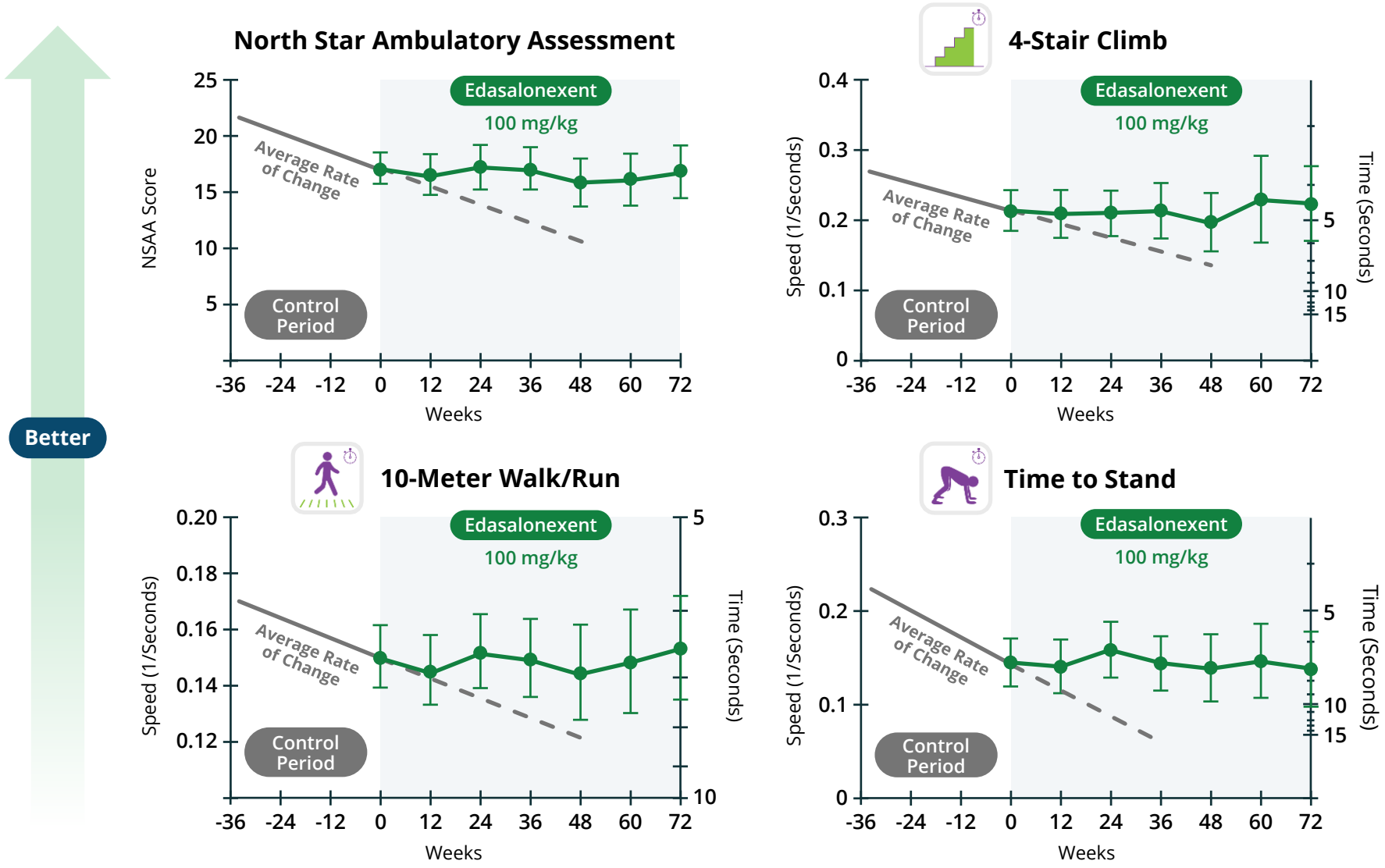


- Composite of 5 lower leg muscles MRI T2 used to encompass muscles at various stages of disease progression and minimize variability
- Following 72 weeks of edasalonexent, the rate of increase in the composite MRI T2 in the five lower leg muscles decreased as compared to the rate of increase during the off-treatment control period

Means + SEM; mixed model comparison with off-treatment period
* Week 12: p=0.002, n=16; Week 24: p=0.004, n=14; Week 36: p=0.032, n=13; Week 48: p=0.018, n=12; Week 72: p=0.052, n=9

In Phase 2 MoveDMD Trial and Open-Label Extension:

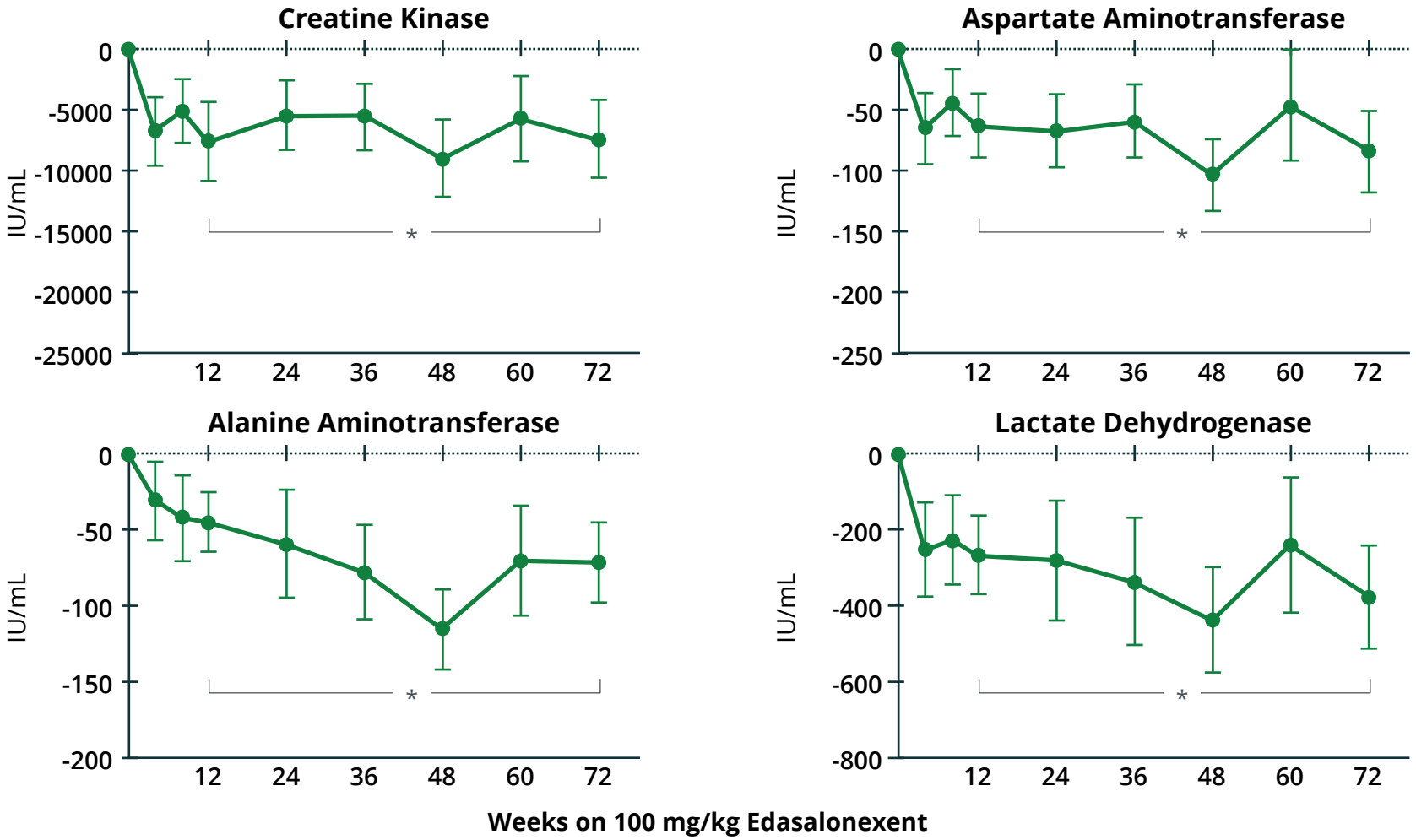
All Assessments of Function Stabilized on Edasalonexent Compared to Off-Treatment Control



Means ± SEM shown. Includes data of all boys initially started on 100 mg/kg dose (n=16) with 11 boys participating through 72 weeks.

In Phase 2 MoveDMD Trial and Open-Label Extension:

Muscle Enzymes Significantly Decreased on Edasalonexent, Supporting a Positive Drug Effect

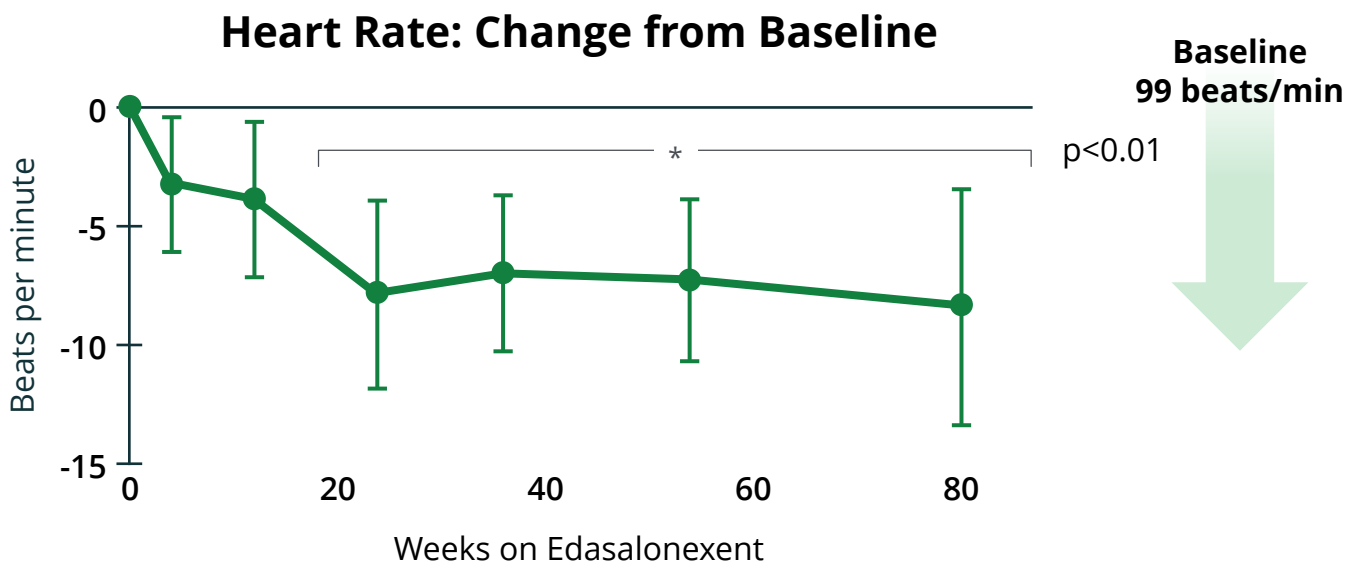


Plasma muscle enzymes are elevated 10 to 100 fold in DMD, indicative of leakage from damaged myocytes

Means ± SEM shown; * p<0.05 for mean change from baseline after 12 weeks

In Phase 2 MoveDMD Trial and Open-Label Extension:

Edasalonexent Showed Potential for Cardiac Benefits in DMD



- **Elevated resting heart rate is initial manifestation of cardiac disease in DMD**
  - Cardiac failure is a leading cause of mortality in DMD
  - Elevated heart rate triples the risk of cardiomyopathy several years later
- **Edasalonexent analog had positive effects on fibrosis in mdx and GRMD models**
  - Edasalonexent tissue levels in heart > skeletal muscle
- **In MoveDMD trial, mean resting heart rate significantly decreased, approaching age-normative heart rate ~92 beats per minute**

Thomas, et al. *Pediatr Cardiol.* 2012 33(7):1175-9.
Hammers, et al. *JCI Insight* 2016 1(21): e90341
Fleming, et al., *Lancet* 2011 377: 1011-18

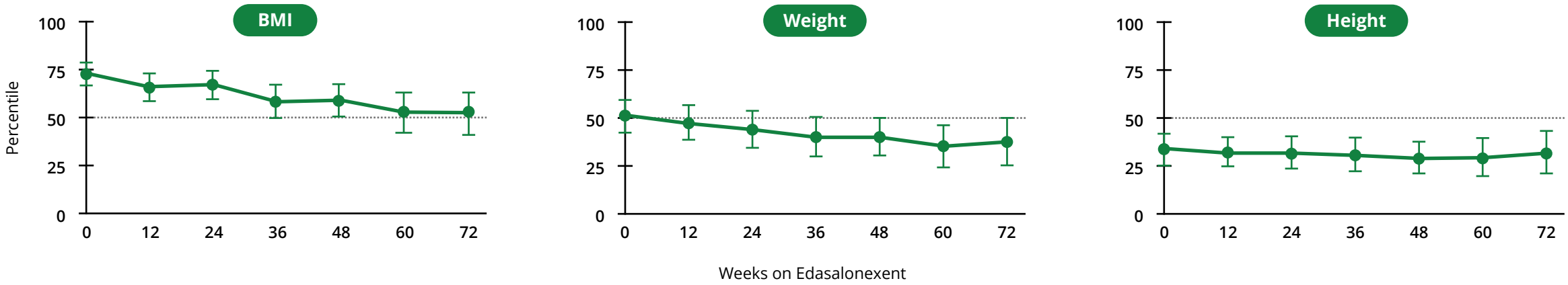
Means ± SEM shown;

In Phase 2 MoveDMD Trial and Open-Label Extension:

Safety: Growth Continues as Expected

- **50+ patient years of exposure**
- **Well tolerated, with majority of adverse events mild in nature**
  - Most common related adverse event was diarrhea, which did not require discontinuation
  - No adverse trends in chemistry, hematology, or measures of adrenal function (cortisol and ACTH)
- **Boys on edasalonexent grew similarly to unaffected boys**

Percentiles Compared to CDC Growth Charts

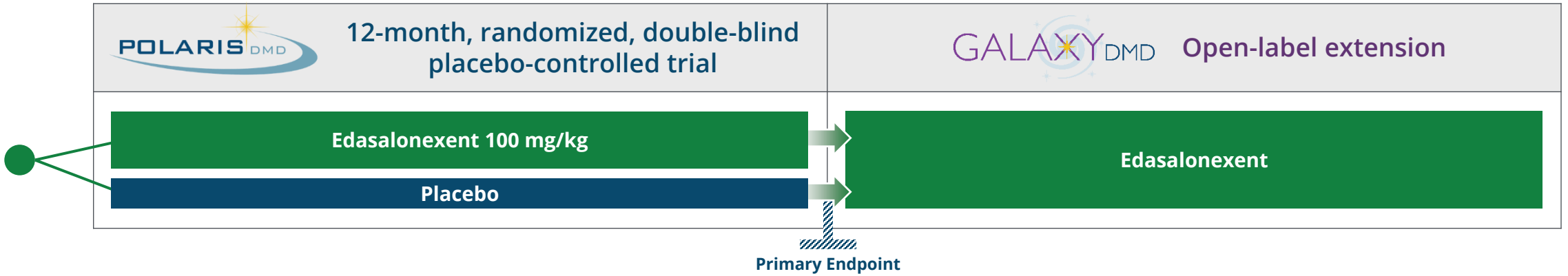


Means ± SEM shown

Conclusions from Phase 2 MoveDMD Trial and Open-Label Extension:

Substantially Slowed DMD Disease Progression on Edasalonexent

- **Edasalonexent, a oral NF-κB inhibitor, showed:**
  - Clinically meaningful slowing of disease progression on edasalonexent compared to off-treatment control period
    - North Star Ambulatory Assessment and all timed function tests stabilized
  - MRI measures supportive of positive edasalonexent treatment effects
    - Muscle MRI T2 rate of change improved with edasalonexent treatment versus off-treatment control period progression
  - No safety signal and well tolerated
- **Supportive of Phase 3 clinical trial that is currently ongoing**



  - Enrolling 4 to <8 year-old boys not on steroids for 6 months
  - Primary endpoint NSAA