



# Edasalonexent (CAT-1004)

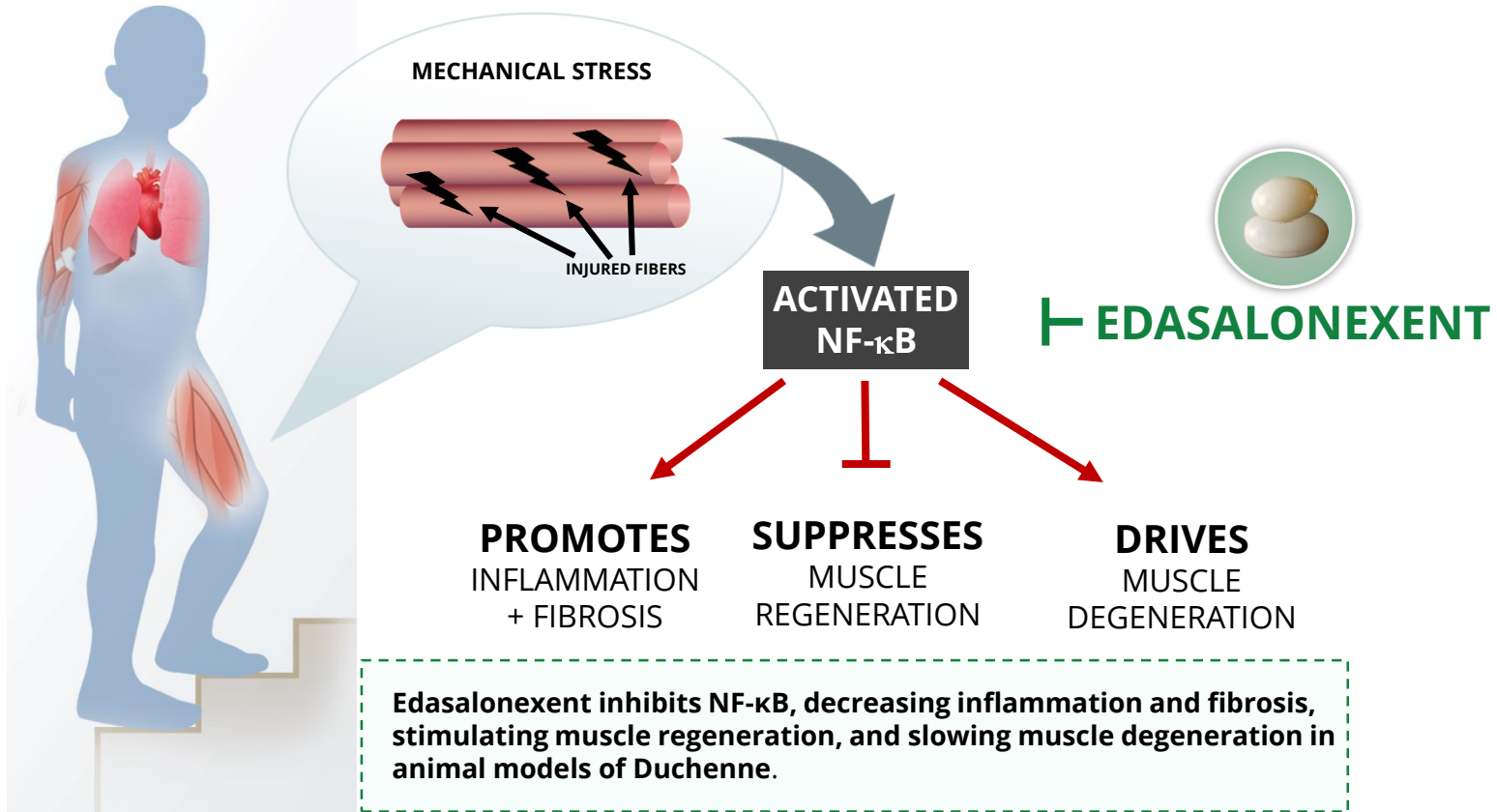
Oral small molecule designed to inhibit NF- $\kappa$ B for the treatment of Duchenne muscular dystrophy

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CMO, Catabasis Pharmaceuticals

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# Edasalonexent Inhibits NF- $\kappa$ B and Slows Muscle Degeneration and Stimulates Muscle Regeneration



# Edasalonexent: Translation from Target Engagement to Functional Improvements in Duchenne

## NF-κB Target Engagement



### Phase 1 Normal Healthy Volunteers

- ▶ Decrease in activated NF-κB
- ▶ Decrease in NF-κB gene expression

### MoveDMD Phase 1

- ▶ Decrease in NF-κB gene expression

## Biomarker Improvements



### MoveDMD Phase 2 / OLE

- ▶ Decrease in C-reactive protein
- ▶ Decrease in muscle enzymes

## Muscle Improvements



### MoveDMD Phase 2 / OLE

- ▶ Improvement in rate of change in MRI T2 compared to control
- ▶ Decrease in soleus and vastus lateralis fat accumulation compared to control

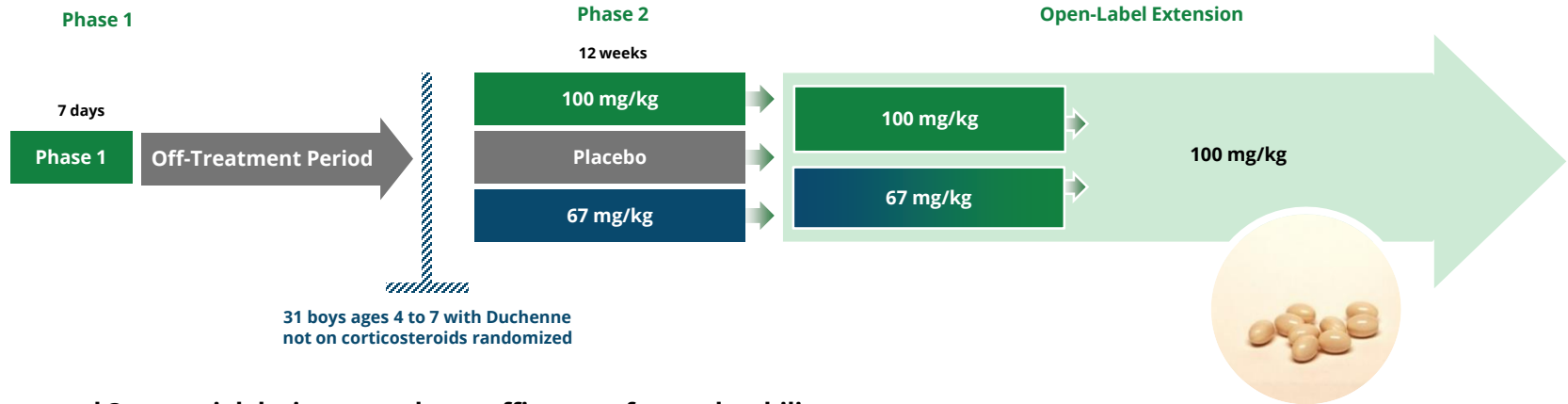
## Functional Improvements



### MoveDMD Phase 2 / OLE

- ▶ Slowing of decline in function as assessed by NSAA and Timed Function Tests compared to control

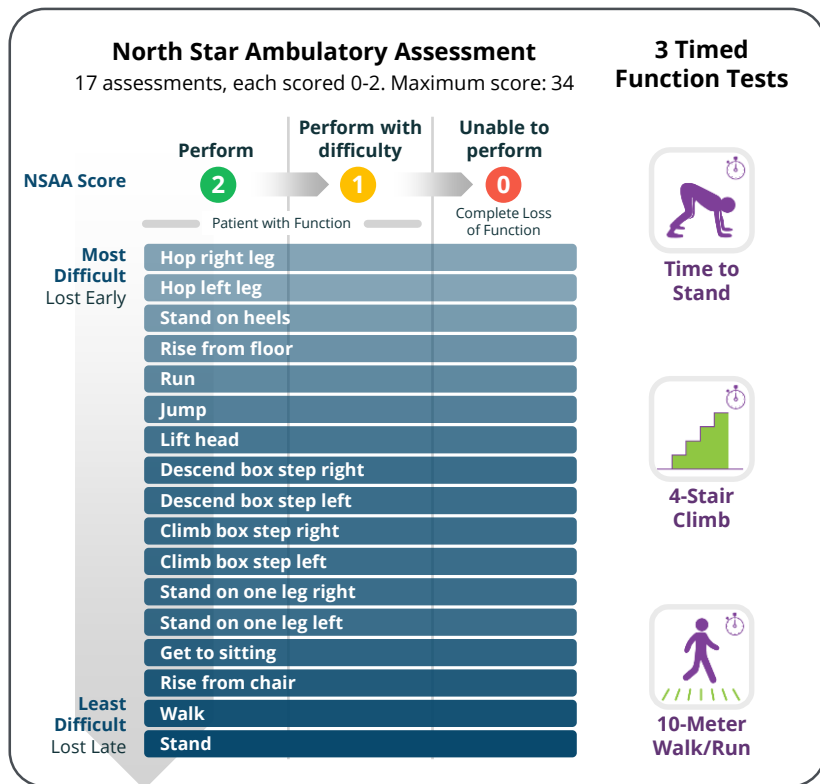
# MoveDMD Trial Design



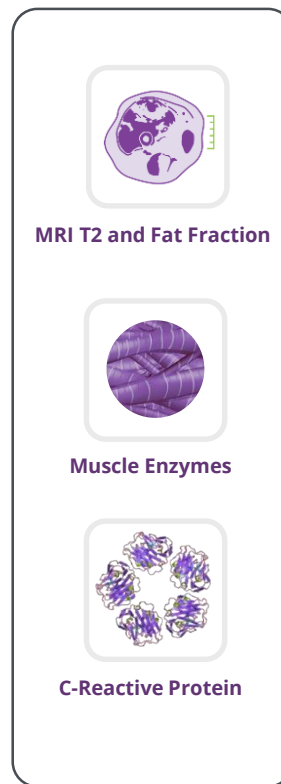
- ▶ **Integrated 3-part trial design to evaluate efficacy, safety, tolerability**
  - Assessments included North Star Ambulatory Assessment, age-appropriate timed function tests, MRI
- ▶ **Off-treatment control period measurements between Phase 1 and Phase 2**
  - Provided internal control for pre-specified MoveDMD analyses
  - To confirm consistency of patient off-treatment control period disease progression with available natural history data
- ▶ **Phase 2 showed favorable trends towards the slowing of disease progression after 12 weeks with no safety issues**
- ▶ **Open-label extension enabled assessment of safety and efficacy following longer term treatment**

# MoveDMD Trial Endpoints: Multiple Measures of Physical Function and Biomarkers

## Assessments of Physical Function\*

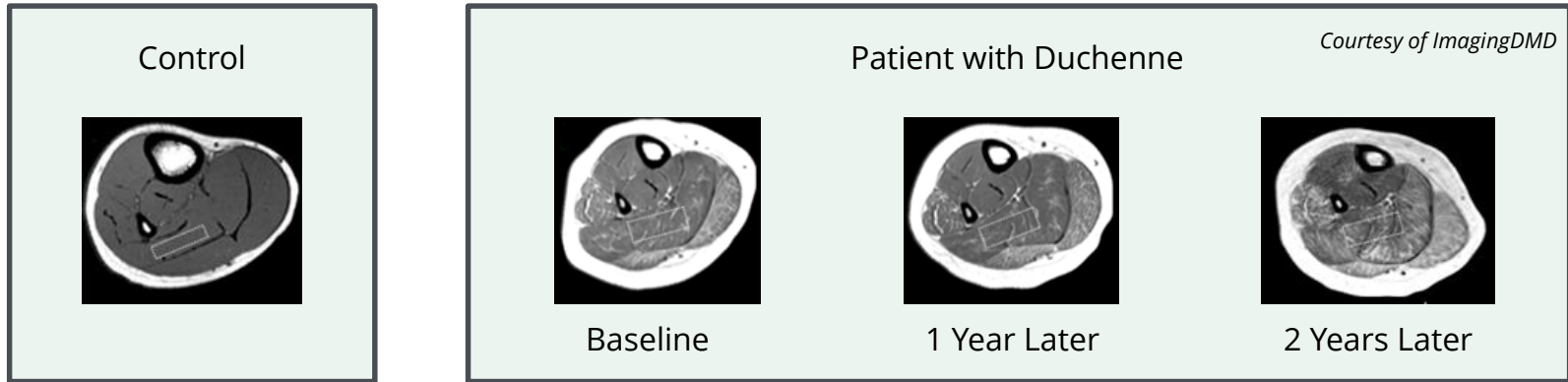


## Non-Effort Based Assessments\*



\*Assessed before initiation of active treatment and every 12 weeks during open-label extension

# MRI is a Non-Invasive Approach to Assess Disease Progression in Duchenne



- ▶ **MoveDMD incorporated both Magnetic Resonance Imaging (MRI) and Magnetic Resonance Spectroscopy (MRS)**
- ▶ **MRI T2 measures both inflammation and fat content**
  - MRI T2 is elevated from a young age and increases with age as fat increases
  - Changes in MRI T2 correlate with changes in function<sup>ϕ</sup> and loss of functional milestones
- ▶ **MRS Fat Fraction measures fat content**
  - Changes in MRS Fat Fraction correlate with changes in function<sup>ϕ</sup> and loss of functional milestones

# Changes in Fat Fraction on Edasalonexent Consistent with Slowing of Disease Progression

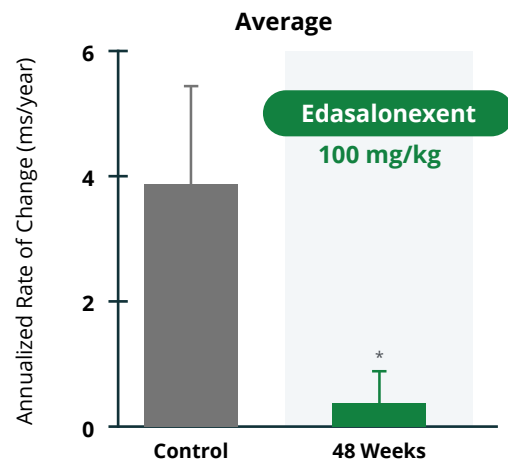
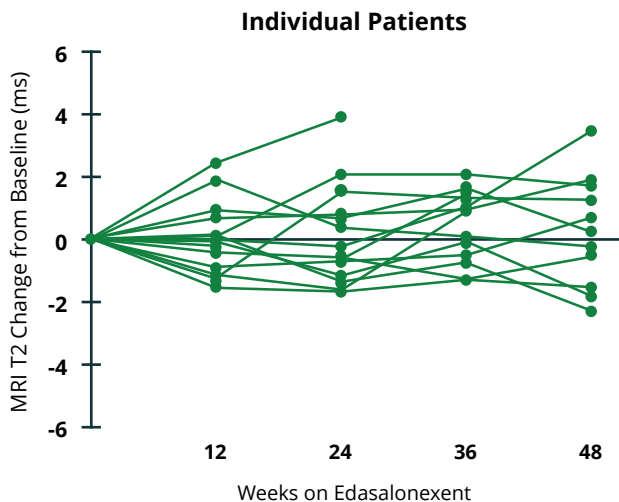
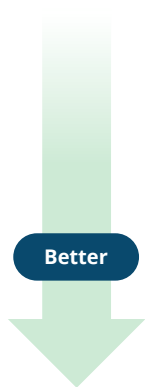
## MRS Fat Fraction Change from Baseline

Muscle	MoveDMD Off-Treatment Control Period Annualized Rate	MoveDMD 48 weeks on Edasalonexent	ImagingDMD Natural History Study* 1 Year Change
<b>Soleus (calf)</b>	2.6%	0.85%	3%
<b>Vastus lateralis (thigh)</b>	10.4%	5.9%	7%

- ▶ Rate of increase in Fat Fraction of the soleus and vastus lateralis was substantially decreased as compared to the off-treatment control period following 48 weeks of edasalonexent
- ▶ Increases in Fat Fraction correlate with declines in function and predict future loss of functional milestones\*
- ▶ In the ImagingDMD natural history study, boys were largely on steroids

# Edasalonexent Significantly Improved Rate of Change of MRI T2

## MRI T2: Composite of 5 Lower Leg Muscles



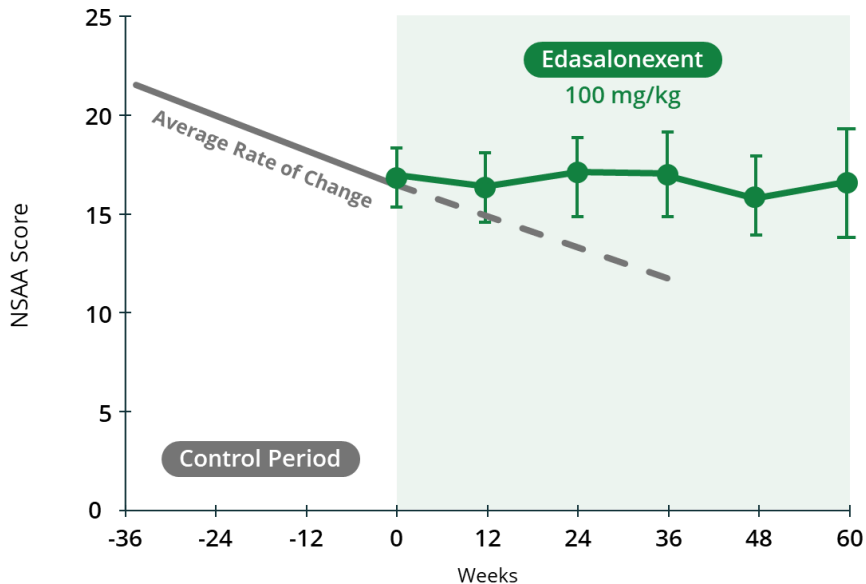
- ▶ On edasalonexent, the rate of change for the MRI T2 of lower leg muscles improved significantly compared to the rate of change during the off-treatment control period  $\phi$
- ▶ Stabilization of MRI T2 is consistent with slowing of disease progression also observed in functional assessments



# North Star Ambulatory Assessment Score Stabilized with Edasalonexent Treatment



## North Star Ambulatory Assessment



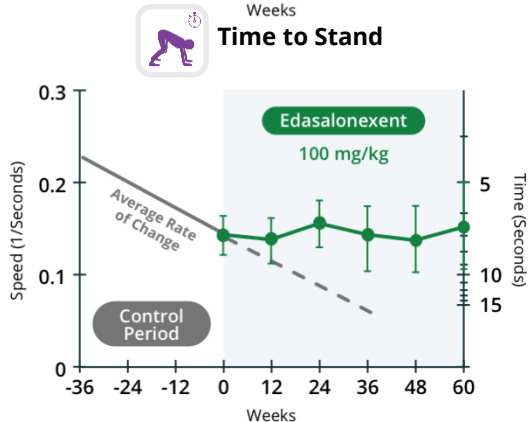
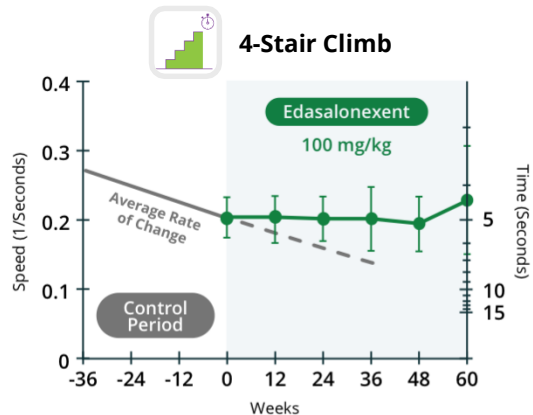
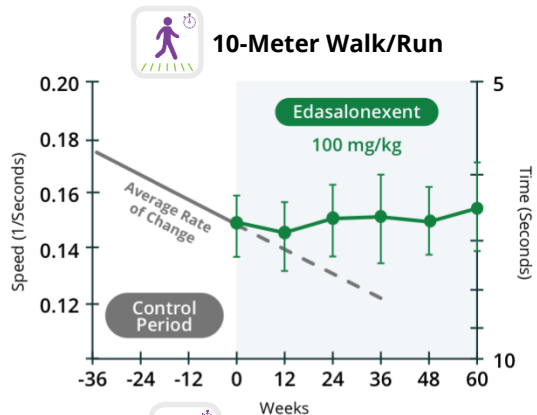
- ▶ Disease progression on edasalonexent improved compared with average rate of change during off-treatment control period

# All Timed Function Test Speeds Stabilized with Edasalonexent Treatment

## Pre-Specified Analyses



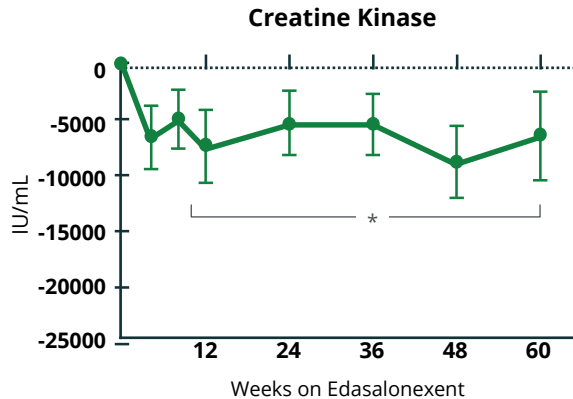
Better



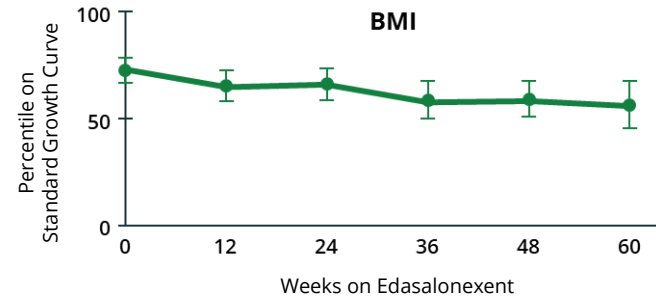
Means ± SEM shown

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

# Edasalonexent: Well Tolerated Without Safety Signals



\*  $p < 0.05$  for change from baseline after 12 weeks



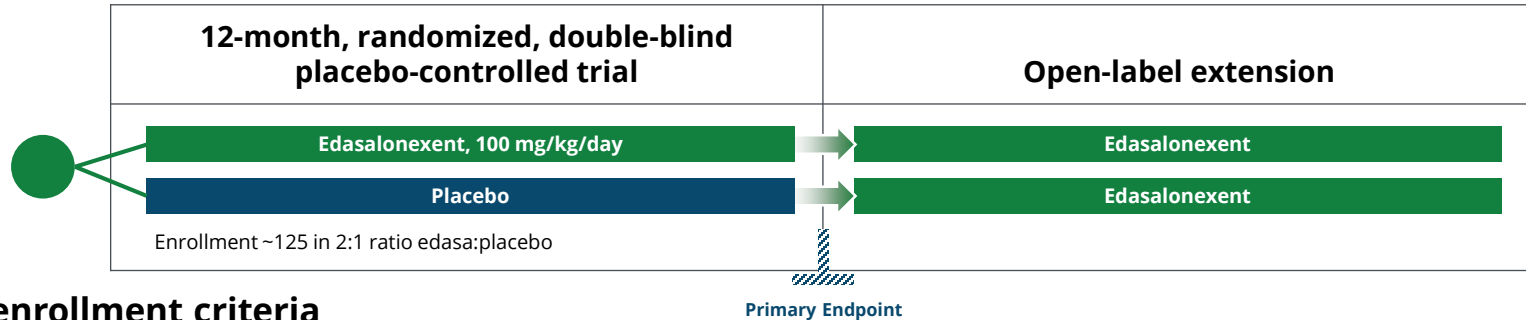
- ▶ No safety signals in MoveDMD trial to date
- ▶ Well tolerated, with majority of adverse events being mild in nature, mostly gastrointestinal
- ▶ No adverse trends in hematology, chemistry, renal or adrenal function, calcium and phosphate
- ▶ Growth: Age-appropriate increases in weight and height
- ▶ Heart rate decreased toward normal values at this age

## Summary: Edasalonexent Substantially Slowed Predicted Disease Progression in MoveDMD Study

- ▶ **Clinically meaningful slowing of disease progression on edasalonexent over more than 1 year compared to off-treatment control period**
  - North Star Ambulatory Assessment stabilized
  - All timed function tests stabilized (10-meter walk/run, 4-stair climb and time to stand)
- ▶ **MRI measures support positive edasalonexent treatment effects over 48 weeks**
  - Muscle MRI T2 significantly improved during edasalonexent treatment versus off-treatment control period progression
  - Increases in Fat Fraction decreased compared to the off-treatment control period and to that expected for natural history on corticosteroids
- ▶ **No safety signal and well tolerated over more than 1 year**
  - Height, weight and BMI growth patterns continued to be similar to unaffected boys
- ▶ **Supportive of Phase 3 clinical trial**

# Positive MoveDMD Data Support

## Phase 3 Registration Trial for Edasalonexent



### ▶ Key enrollment criteria

- Age 4 to 7<sup>th</sup> birthday
- Able to complete timed function tests
- Not on corticosteroids for at least 6 months
- Not on other investigational therapies for at least 1 month, can be on stable eteplirsen

### ▶ Visits / key assessments every 3 months

- North Star Ambulatory Assessment, Timed Function Tests, Muscle Strength
- Safety measures
- Assessments of growth, cardiac and bone health
- No biopsy or 6 minute walk test

### ▶ Expected Locations: US, Canada, Europe, Israel and Australia

# Edasalonexent: Potential to Slow Disease Progression for All Those Affected by Duchenne

- ▶ Investigational oral disease-modifying agent for all patients with Duchenne, regardless of mutation type
- ▶ Edasalonexent substantially slowed disease progression compared to control
- ▶ Preparing for Phase 3 clinical trial, POLARIS<sub>DMD</sub>
- ▶ Potential as monotherapy and also exploring potential to combine with dystrophin-targeted and other therapies



# Thank You

- ▶ **Patients and families**
- ▶ **Patient groups**
- ▶ **Nemours Children's Hospital**
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  - Pradeep Bista, PhD
  - Andrew Nichols, PhD
  - James MacDougall, PhD

- ▶ **For Questions email: [DMDTrials@catabasis.com](mailto:DMDTrials@catabasis.com)**



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