Baseline Characteristics of Patients Enrolled in PolarisDMD, a Phase 3 Trial of Edasalonexent for Duchenne Muscular Dystrophy

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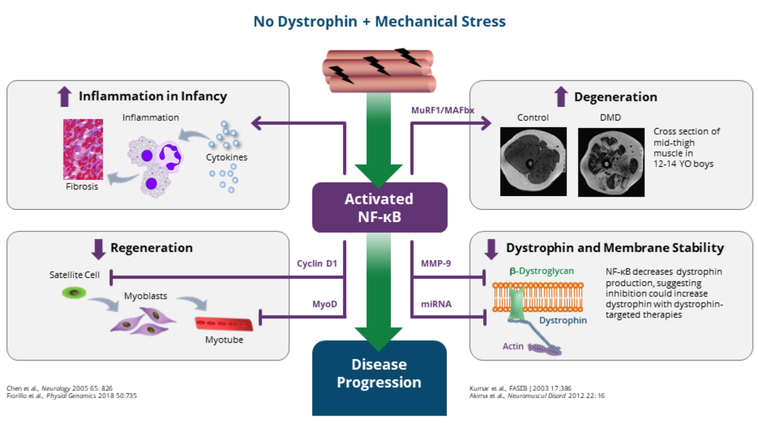
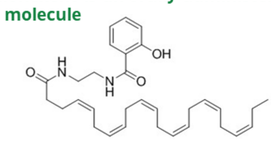
Background

Activation of NF-κB in Duchenne Muscular Dystrophy Is a Key Factor in Disease Progression

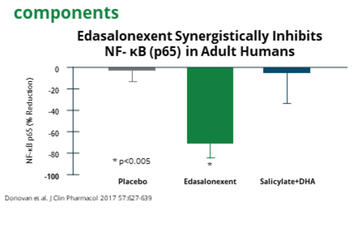


Edasalonexent Inhibits NF-κB, A Key Driver of Muscle Disease in DMD

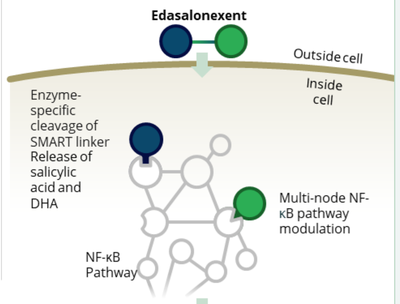
- Edasalonexent is an orally-administered small molecule



- Edasalonexent has a unique pharmacological profile that inhibits NF-κB better than its individual components



- Edasalonexent is a unique molecule delivering salicylic acid and the omega-3 docosahexaenoic acid (DHA) into cells by using SMART Linker Technology



Edasalonexent Clinical Development Program

- Edasalonexent is being developed as a foundational therapy for DMD for all patients, regardless of mutation.

MoveDMD

- The Phase 2 MoveDMD trial and open-label extension showed slowing of disease progression on MRI and functional measures and supported design of a pivotal Phase 3 trial, PolarisDMD, in a similar population.
- This Phase 2 trial was conducted at 5 sites in the US

PolarisDMD

- The Phase 3 trial is a one-year randomized, double-blind, placebo-controlled study to assess edasalonexent efficacy and safety and is fully enrolled.
- This Phase 3 trial is being conducted at 37 sites in 8 countries.

- The Phase 3 PolarisDMD trial is based on the MoveDMD trial, which showed improvements in MRI and functional measures compared to an off-treatment control period. The goal of this analysis was to compare baseline demographic and functional characteristics of the two trials.

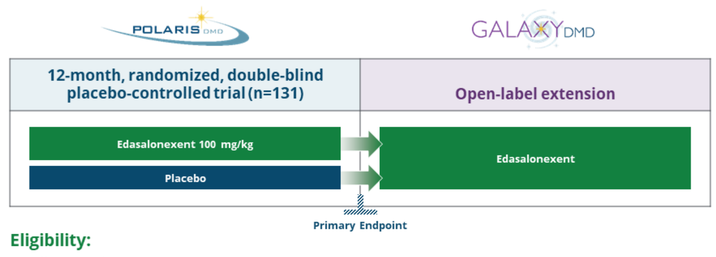
Study Design

MoveDMD®, a Phase 1/2 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

Design
- Study population
  - Age 4 to 7 (up to 8th birthday); off steroids for ≥6 months
  - Able to swallow placebo capsules at the Screening Visit
- **Phase 1:** 1-week open-label 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 of 67 mg/kg and 100 mg/kg doses of edasalonexent
- Open-label extension up to 150 weeks

Edasalonexent Phase 3 PolarisDMD Trial Designed for Global Registration



Eligibility:
- All mutations
- Age 4 to 7 (up to 8th birthday); off steroids for ≥6 months
- Able to swallow placebo capsules at the Screening Visit

Endpoints measured at Screening and Baseline, with Primary Endpoint at 52 Weeks:
- Primary: Change in North Star Ambulatory Assessment (NSAA)
- Key secondary: Velocity of age-appropriate timed function tests
- Additional assessments include growth, cardiac and bone measures

Entry Criteria of Phase 2 MoveDMD and Phase 3 PolarisDMD Trials Were Similar

MoveDMD

- Age 4 to 7 (up to 8th birthday)
- Not on corticosteroids for at least 6 months
- Diagnosis of DMD based on a clinical phenotype with increased serum CK and the presence of a mutation in the dystrophin gene known to be associated with a DMD phenotype
- Ability to walk independently
- No other prior or ongoing significant medical conditions
- No exposure to another investigational drug

PolarisDMD

- Age 4 to 7 (up to 8th birthday)
- Not on corticosteroids for at least 24 weeks
- Diagnosis of DMD based on a clinical phenotype with increased serum CK and the presence of a mutation in the dystrophin gene known to be associated with a DMD phenotype
- Ability to walk independently, perform the 4-stair climb and perform the stand from supine in ≤ 10 seconds
- No other prior or ongoing significant medical conditions
- No exposure to another investigational drug
- Stable eteplirsen allowed

Assessments

Functional Assessments and Additional Outcome Measures

Physical Function Outcomes

Primary Endpoint: North Star Ambulatory Assessment

Assessment measures

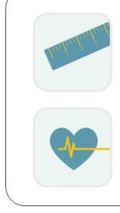
Hop right leg	Climb box step right
Hop left leg	Climb box step left
Stand on heels	Stand on one leg right
Rise from floor	Stand on one leg left
Run	Get to sitting
Jump	Rise from chair
Lift head	Walk
Descend box step right	Stand
Descend box step left	

How measures are scored

2 Can perform | 1 Can perform with difficulty | 0 Unable to perform

3 Timed Function Tests

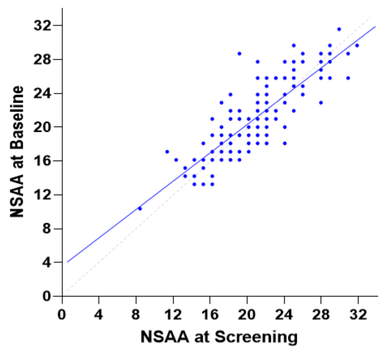
Additional Outcomes Include:



- Functional measures assessed at screening and baseline, which were within 4 weeks apart
- Clinical assessors were trained and certified prior to screening visits

Results

NSAA Reproducible Between Screening and Baseline Visits in Young Boys in PolarisDMD



- Paired valid screening and baseline values show consistency
- Lines of identity and best fit shown with Pearson correlation coefficient = 0.84
- No systematic differences for high vs. low screening NSAA score
- Between Screening and Baseline there was a mean increase of 0.3 points, which did not depend on age

Reproducibility of Additional Functional Measures Between Screening and Baseline

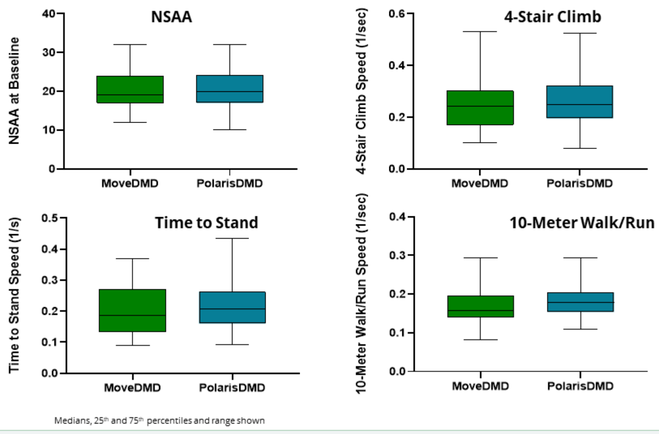
- The NSAA and timed function tests were highly reproducible in the Phase 3 PolarisDMD study population
- NSAA was more reproducible than the timed function tests in this population

	Pearson Correlation Coefficient
North Star Ambulatory Assessment (NSAA) score	0.84
10-Meter Walk/Run speed (1/s)	0.82
4-Stair Climb speed (1/s)	0.81
Time to Stand speed (1/s)	0.79

Results

Distribution of Functional Measures at Baseline Was Similar in MoveDMD and PolarisDMD Trials

- Age, baseline NSAA, and speeds of timed function tests (time to stand, 4-stair climb, and 10-meter walk/run) were similar in both studies (mean differences NS, and differences between distributions tested by Kolmogorov-Smirnov test NS)



Medians, 25th and 75th percentiles and range shown

Phase 3 PolarisDMD and Phase 2 MoveDMD Trials Have Similar Baseline Characteristics

- Analysis shows that Phase 3 trial enrolled the expected patient population
  - Comparison of baseline age and function (NSAA, time to stand, 4-stair climb, and 10-meter walk/run) were similar in both trials; there were no significant differences in baseline characteristics between the two trials*

	MoveDMD (n=23)	PolarisDMD (n=131)
Age (years)	6.0 ± 1.1	5.7 ± 1.0
% never previously on steroids	100%	98%
Baseline CK	19842	18964
Heart Rate	99	102
NSAA score	20.1 ± 5.5	20.8 ± 4.7
10-Meter Walk/Run velocity (1/s)	0.168 ± 0.045	0.181 ± 0.037
4-Stair Climb velocity (1/s)	0.254 ± 0.110	0.265 ± 0.097
Time to Stand velocity (1/s)	0.193 ± 0.080	0.212 ± 0.070

Means ± standard deviation shown
*Kolmogorov-Smirnov test used to assess for population distribution differences

Conclusion

Conclusions

- With expansion from a US only trial to a global trial in 8 countries, both the Phase 2 MoveDMD and the Phase 3 PolarisDMD trial enrolled a similar population, without significant differences in baseline age or functional measures.
- NSAA and timed function tests were highly reproducible in repeat measures at Screening and Baseline in boys as young as 4.
- As expected with the entry criteria, mean time to stand velocity was numerically faster in the Phase 3 trial. Distribution of baseline NSAA and timed function tests were less variable in the Phase 3 trial than in the Phase 2 trial.
- These findings support the design of the Phase 3 PolarisDMD trial in young boys regardless of mutation. Results are expected in Q4 2020.

Acknowledgements

- Patients and families
- Patient groups
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- MoveDMD Phase 2 Site staff
- Catabasis team
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