Edasalonexent, an Oral NF-κB Inhibitor, in Development for Treatment of Duchenne Muscular Dystrophy: the Phase 3 PolarisDMD Study Design

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BACKGROUND: NF-κB is Central to DMD Disease Pathogenesis

Role of NF-κB mediated muscle damage in DMD

- In DMD, NF-κB is activated in early infancy as seen by nuclear NF-κB and upregulation of NF-κB regulated genes in muscle biopsies (Chen, et al., Neurology, 2005)
- NF-κB promotes muscle inflammation and fibrosis in DMD (Acharyya, et al., JCI, 2007)
- NF-κB drives muscle degeneration and suppresses muscle regeneration (Acharyya, et al., JCI, 2007)

Inhibiting NF-κB in DMD for functional benefit

- Genetic disruption of NF-κB in mdx mice (p65 haploinsufficient, or deletion of IKKε in muscle) improves muscle health

NF-κB also regulates

- cardiac muscle pathology in DMD (Peterson, et al., 2018)
- miRNAs that affect dystrophin levels in muscle (Kuribara, et al., 2015)

STUDY DESIGN: Rationale for Patient Population

- We are enrolling 125 4-7 year old boys (up to 8th birthday) in a 2:1 ratio because we believe early intervention offers potential to have greatest benefits and is important to developing a new standard of care starting treatment shortly after diagnosis.
- In the US almost 40% of diagnosed boys in this age range are currently not on steroids (data from The Duchenne Registry, Coven et al., WMS 2017)
- Boys with DMD in this age group who are not on steroids are experiencing declines in timed function tests and NSAA
- In the 23 boys in MoveDMD who had an off-treatment period and in 9 steroid naive boys in the ImagingDMD natural history study, average annualized decreases in the TFI’s are shown:

STUDY DESIGN: Developing a New Foundational Therapy

Objective: A registration study to comprehensively define the benefit/risk profile for edasalonexent that has the potential to lead to a new standard of care

Inclusion criteria

- Diagnosis of DMD based on a clinical phenotype and genetic confirmation
- Male sex by birth
- Age ≥4.0 to ≤8.0 years
- Able to perform stand from supine without assistance in ≤10 seconds, as well as the 10mWR and 4-stair climb

Exclusion criteria

- Use of corticosteroids within 24 weeks
- Use of an investigational drug, idebenone, or dystrophin-focused therapy within 4 weeks or a period of 5 half-lives prior to Day 1. Patients who have received at least 24 weeks of a stable dose of eteplirsen prior to Day 1, and expected to continue treatment, will be eligible.
- Recent use of the following within 4 weeks prior to Day 1: immunosuppressive therapy, warfarin, phenytoin, human growth hormone
- Hemoglobin <10.5 g/dL or GGT > ULN
- Other prior or ongoing medical conditions that could impair the assessment of study results

Expected PolarisDMD Clinical Trial Sites

Sites also anticipated in Canada, Europe, Israel and Australia