CAT-1004, an Oral Agent Targeting Activated NF-κB in Development as a Disease-Modifying Treatment for Treatment for Duchenne Muscular Dystrophy: Design of MoveDMD, a Phase 1 / 2 Trial

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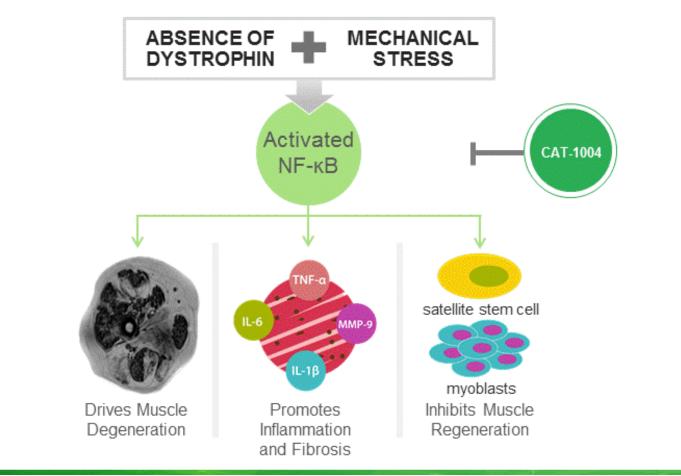
Background

CAT-1004 Modulates the NF-kB Pathway and Has Potential to be Disease-Modifying in DMD

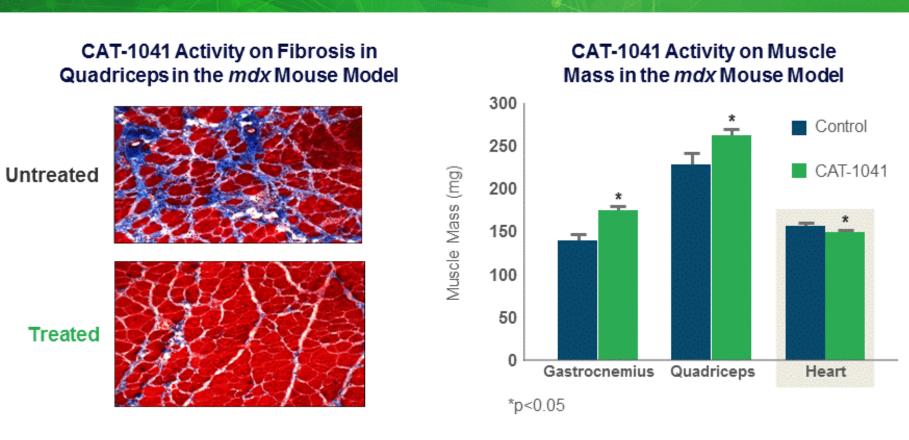
Why CAT-1004?

In DMD, lack of dystrophin and mechanical stress activate NF-κB in muscles, leading to muscle degeneration, inflammation, fibrosis and inhibition of muscle regeneration and ultimately loss of function

Steroids suppress NF-KB inflammation but have significant side effects



CAT-1004 Analog (CAT-1041) Demonstrated Significant Improvements in Muscle Fibrosis and Muscle Mass



Central Role of NF-KB: Lack of Dystrophin is Necessary but Not Sufficient for DMD Disease Progression

Control

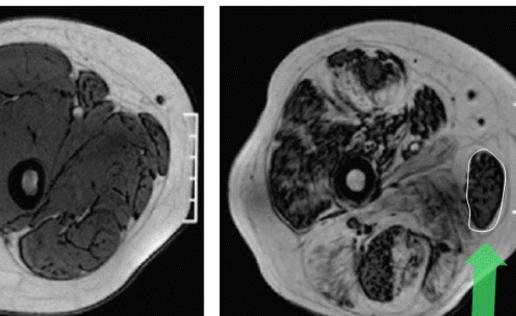
 Mechanical stress activates NF-κB in mouse diaphragm muscle

Muscles with no dystrophin but less mechanical stress are relatively protected from

MRI shows replacement of muscle with fat and fibrosis

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

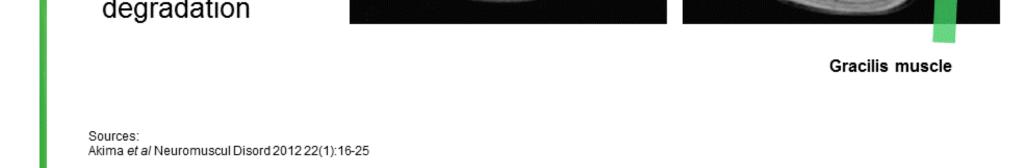
DMD



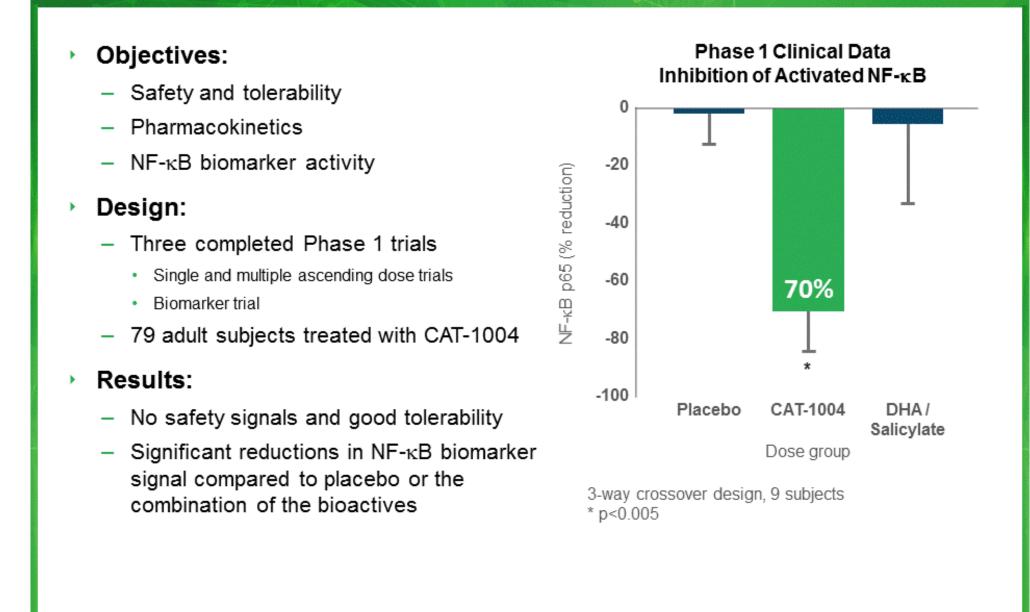


6-month mdx mouse study conducted by Prof. Lee Sweeney

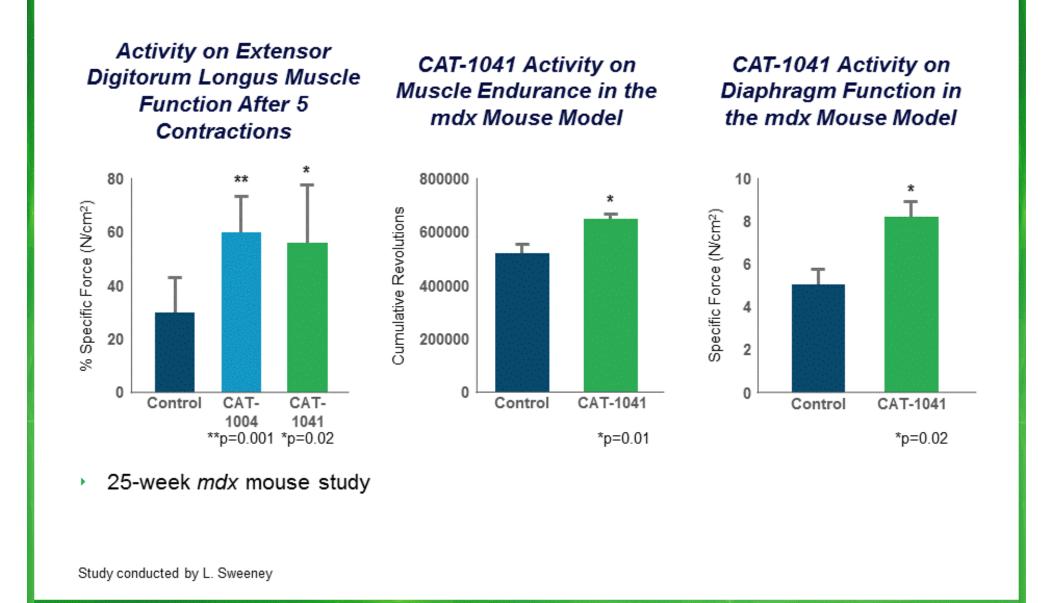
Study conducted at University of Pennsylvania *mdx* mice treated for 25 weeks



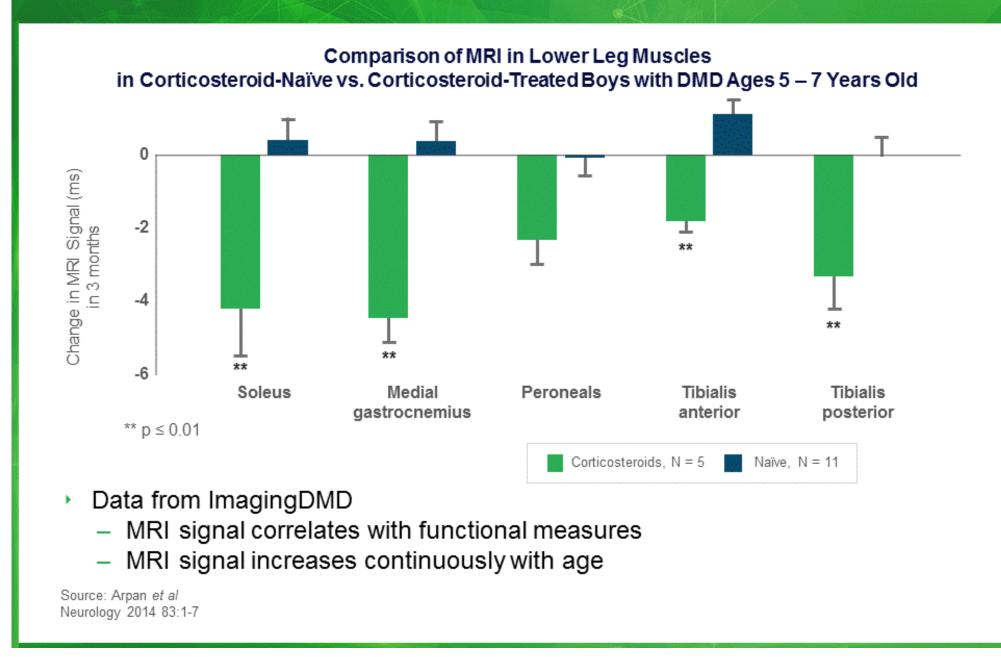
Completed Phase 1 Trials: Significant Reduction in Activated NF-κB Observed with CAT-1004



CAT-1004 Analog (CAT-1041) Demonstrated Significant Improvements in Muscle Function, Running Wheel Activity and Diaphragm Function



Significant MRI Changes Observed at 12 Weeks with Corticosteroids



MoveDMD Study Design

Study Population

Initial approach is to assess safety, pharmacokinetics and MRI as a biomarker of inflammation in young boys not on steroids

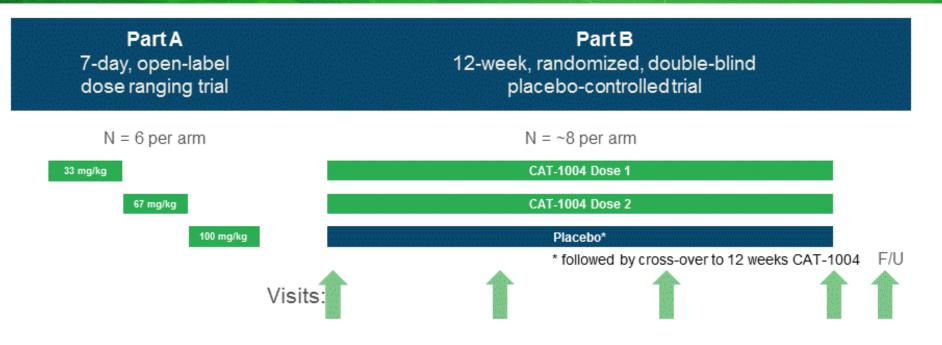
Inclusion Criteria

- 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
- Ambulatory
- Age ≥4 years and <8 years</p>
- Adequate immunization for varicella and influenza

Exclusion Criteria

- Use of corticosteroids within prior 6 months to treatment initiation or planning to initiate steroid therapy within the next 6 months
- Abnormal GGT, creatinine, hemoglobin <10.5 g/dL
- Ongoing immunosuppressive therapy

CAT-1004 The MoveDMD Trial



Safety: Monitored by investigators and Sponsor and overseen by Data Safety and Monitoring Committee

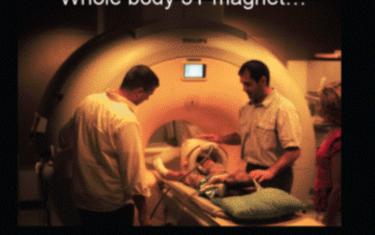
Key Endpoints:

- Changes in Magnetic Resonance Imaging (MRI) of muscles at 12 weeks
- Changes in appropriate Timed Function Tests at 12 weeks
- 10 meter walk/run, 4 step climb, time to stand
- Assess safety, tolerability and pharmacokinetics

What can MRI Show?

Whole body 3T magnet...

Magnetic Resonance Imaging (MRI) allows investigators to understand more about natural history of DMD, to assess muscle health, and to assess potential effects of investigational drugs on muscle without need for biopsy



- No radiation exposure or injections
- MRI shows that different areas of the same muscle can be affected differently, so the whole muscle can be looked at instead of a small biopsy sample
- The same muscles with inflammation go on to develop fibrosis and replacement of muscle tissue by fat



Move

DMD

MoveDMD will include MRI to understand the effects of CAT-1004 in boys with DMD

Endpoints: Assessments of Disease

- MRI assessments:
 - T2 as measure of muscle damage
 - Prior to initial 1-week safety study
 - At baseline and endpoint of 12-week CAT-1004 vs PBO
- Functional assessments



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CAT-1004 Modulates the NF-κB Pathway and Has Potential to be Disease-Modifying in DMD

- Oral agent with potential efficacy across age groups and mutations
 - Potential to regenerate muscle
 - Positive effects on skeletal, respiratory and cardiac muscle shown in pre-clinical models

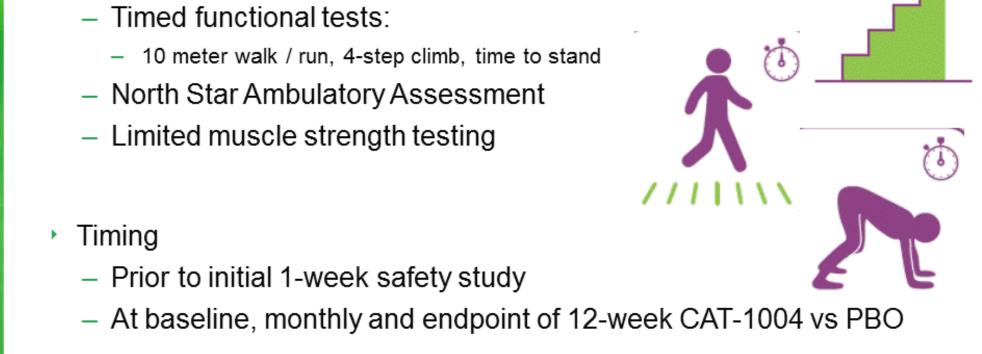
Enrollment in Part A of MoveDMD is Ongoing

 University of Florida, Gainesville, Florida

Thank you for support!

- Dr. Krista Vandenborne
- Dr. Peter Kang
- Dr. S. Subramony
- Dr. J. Sladky

Parent Project



 Safety profile to enable early intervention
 Potentially effective as monotherapy and as complement to dystrophin / utrophin-targetted treatments

 Granted Orphan, Fast Track and Rare Pediatric Disease Designations by FDA and Orphan Medicinal Product Designation by EMA Oregon Health Science University, Portland, Oregon

 Dr. Erika Finanger

Dr. Barry Russman

 Children's Hospital of Philadelphia, Pennsylvania

Dr. Gihan Tennekoon

Dr. Sabrina Yum



