At Santhera, we’re studying a potential new treatment to preserve respiratory function in DMD.
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The following presentation is for educational purposes. It features information about:

- The role of mitochondria in Duchenne muscular dystrophy (DMD)
- The importance of respiratory health in DMD
- Santhera’s role in studying potential treatment options
- Santhera clinical trials currently enrolling
Meet Santhera

US headquarters in Burlington, MA, with global headquarters in Pratteln, Switzerland

Working in DMD since 2008

3 completed studies and 1 ongoing study in DMD; majority of clinical trial patients were no longer able to walk

Idebenone approved for Leber’s hereditary optic neuropathy (LHON) in Europe

All products considered as investigational in the U.S.

OUR PIPELINE

idebenone in DMD (Duchenne muscular dystrophy) Phase 3

vamorolone in DMD (exclusive option to license) Phase 2b ReveraGen

omigapil in CMD (congenital muscular dystrophy) Phase 1

POL6014 in CF (cystic fibrosis) Phase 1b/2a
Respiratory Dysfunction in DMD
In DMD, Respiratory Muscles Weaken in the Same Way as Leg and Heart Muscles

Over time, respiratory muscles lose strength and put people with DMD at risk:

- Muscles supporting the lungs continue to weaken
- Lungs can’t move air in and out as well
- Small changes in health or infections can become serious quickly
Protect respiratory health—be mindful of small changes in health, routinely test, and manage symptoms

**GOOD CARE**
- Find the right care team of experts that includes a neurologist
- See pulmonologist every year if walking
- Twice yearly pulmonary visits if using wheelchair full-time

**BE AWARE**
- When no long able to walk, watch for early signs that respiratory muscles are weakening:
  - Headaches
  - Restless sleep
  - Shallow breathing at night
  - Trouble concentrating
  - Difficulty staying awake
  - Unexpected weight loss
- Protect against infections
  - Clear airways on a regular basis
  - Breath stacking
  - Get flu and pneumococcal vaccines
  - Watch colds carefully
  - Use cough assist and non-invasive ventilation as prescribed
Visit TakeabreathDMD.com

Important web-based information about DMD respiratory health including:

- Ways to help manage lung function and well-being for all ages
- How to address respiratory complications
- Sign up for monthly newsletters
Respiratory Health and Mitochondrial Dysfunction
Mitochondrial Dysfunction Occurs in DMD

Lack of dystrophin contributes to mitochondrial dysfunction

- Mitochondria supply energy to cells to perform important functions
- Powerhouses of cell
- Muscle cells need a lot of energy and have large number of mitochondria

- Unhealthy mitochondria are associated with muscle cell death which can lead to muscle weakness
- Mitochondrial activation and protection are important treatment strategies

Healthy mitochondria

Unhealthy mitochondria
Clinical Trials of Idebenone in DMD
DELOS: Phase 3 clinical trial in patients with DMD ages 10 and older not on steroids (completed)

Objective: To study how effective idebenone is compared to no treatment (placebo) on respiratory function in patients with DMD not on steroids

Study details

64 males with DMD

92% of patients were no longer walking

17 centers around the world

52 weeks

Idebenone or placebo
Results: Idebenone in DMD Clinical Trials (DELOS)

DELOS primary end point
- Peak expiratory flow* percent predicted (PEF%p)
- Change in respiratory function from week 1 to week 52

DELOS results
- Trial met its primary endpoint
- 3.05% decline for idebenone group
- 9.01% decline in placebo group

* PEAK EXPIRATORY FLOW (PEF)
A measure of the peak or maximum flow of air when a person breathes out as hard as he can

66% reduction in loss of respiratory function
(p=0.044)
Objective: To study how effective idebenone is compared to placebo in delaying the loss of respiratory function in patients with DMD who are on steroids.

**Study details**

266 males with DMD

10 years of age and older who are using steroids

64 centers around the world (20 in the US)

78 weeks

Idebenone or placebo
Patients included in the study:

- Any dystrophin mutation type
- FVC
  - Total amount of air forcibly blown out after one big breath
  - Normalized to population of same age, race, gender and height
- On any steroid regimen of prednisone or deflazacort
- 12 months Corticosteroids use for at least 12 months prior to trial without any dosage changes in last 6 months

35-80%
SIDEROS DMD Clinical Trial Sites

Visit www.Siderosdmd.com for an in-depth trial overview

ClinicalTrials.gov identifier: NCT#02814019

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Welcome to BreatheDMD.com

BreatheDMD is an expanded access program that may allow eligible patients with DMD to gain access to idebenone.

Contact your treating physician or visit www.breathedmd.com for more information.

Participants must:*  
• Be diagnosed with DMD  
• Not be eligible for SIDEROS trial participation  
• Be 8 years or older  
• Have PEF or FVC of 25-80%p  
• Have the ability to swallow pills  
• Visit a participating center

*additional criteria and restrictions may apply
Santhera is a proud partner of the DMD community.
Thank you for joining us today.

At Santhera, we believe information and support can be empowering.
Vamorolone Drug Development Program
Enrolling Phase 2b

- 120 boys
- 4-7 years old
- Never used steroids
- Daily dosing by mouth at home
- 24 weeks randomized: 50% vamorolone, 25% prednisone, 25% placebo
- 24 weeks: all participants on 1 of 2 doses of vamorolone (2 or 6mg/kg)
- Visits approximately monthly
- Expanded access post-trial is available
- ReveraGen covers most travel costs

www.clinicaltrials.gov  NCT03439670
Patients excluded from the study:

- Daytime ventilator assistance
- Part of any other ongoing therapeutic trial
- Any experimental drug within 90 days prior to start of SIDEROS participation
SIDEROS – US Clinical Trial Sites

Dr. Bradley Troxler
University of Alabama
Birmingham, Alabama

Dr. James Woodward
Phoenix Children’s Hospital
Phoenix, Arizona

Dr. Cori Daines
Banner–University Medical Center
Tucson, Arizona

Dr. David Michelson
Loma Linda University Medical Center
Loma Linda, California

Dr. Leigh Maria Ramos-Platt
Children’s Hospital of Los Angeles
Los Angeles, California

Dr. Perry Shieh
David Geffen School of Medicine at UCLA
Los Angeles, California

Dr. Craig McDonald
UC Davis Department of Physical Medicine and Rehabilitation
Sacramento, California

Dr. Marisa Couluris
Shriners Hospitals for Children
Tampa, Florida

Dr. Han Phan
Center for Integrative Rare Disease Research
Atlanta, Georgia

Dr. Kathy Mathews
University of Iowa
Iowa City, Iowa

Dr. Jeffrey Statland
University of Kansas Medical Center
Kansas City, Kansas

Dr. Thomas Crawford
Johns Hopkins University Hospital
Baltimore, Maryland

Dr. Basil Darras
Boston Children’s Hospital
Boston, Massachusetts

Dr. Carla Grosmann
Gillette Children’s Specialty Healthcare
St Paul, Minnesota

Dr. Emma Ciafaloni
University of Rochester
Rochester, New York

Dr. Benjamin Brooks
Carolinas HealthCare System
Charlotte, North Carolina

Dr. Cuixia Tian
Cincinnati Children’s Hospital Medical Center
Cincinnati, Ohio

Dr. Andre Prochoroff
MetroHealth Medical Center
Cleveland, Ohio

Dr. Oscar Henry Mayer
Children’s Hospital of Philadelphia
Philadelphia, Pennsylvania

Dr. Warren Marks
Cook Children’s Medical Center
Fort Worth, Texas