At Santhera, we’re studying a potential new treatment to preserve respiratory function in DMD.

Teresa Chu, Ph.D.
Regional Medical Director
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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
How to Protect Respiratory Health: Good Care and Be Aware

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
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
Idebenone in DMD Clinical Trials (DELOS)

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

66% reduction in loss of respiratory function (p=0.044)

*PEAK EXPIRATORY FLOW (PEF)
A measure of the peak or maximum flow of air when a person breathes out as hard as he can
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
- 35-80% FVC
- On any steroid regimen of prednisone or deflazacort
- 12 months

What is FVC?

- Total amount of air forcibly blown out after one big breath
- Normalized to population of same age, race, gender and height

Corticosteroids use for at least 12 months prior to trial without any dosage changes in last 6 months
SIDEROS DMD Clinical Trial Sites

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

ClinicalTrials.gov identifier: NCT#02814019

Jodi Wolff, PhD
Jodi.wolff@santhera.com
Sideros@santhera.com
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%
- 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.
APPENDIX
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
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<tr>
<th>Dr. Bradley Troxler</th>
<th>University of Alabama</th>
<th>Birmingham, Alabama</th>
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<tr>
<td>Dr. James Woodward</td>
<td>Phoenix Children’s Hospital</td>
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<td>Dr. Cori Daines</td>
<td>Banner–University Medical Center</td>
<td>Tucson, Arizona</td>
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<tr>
<td>Dr. David Michelson</td>
<td>Loma Linda University Medical Center</td>
<td>Loma Linda, California</td>
</tr>
<tr>
<td>Dr. Leigh Maria Ramos-Platt</td>
<td>Childrens Hospital of Los Angeles</td>
<td>Los Angeles, California</td>
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<tr>
<td>Dr. Perry Shieh</td>
<td>David Geffen School of Medicine at UCLA</td>
<td>Los Angeles, California</td>
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<tr>
<td>Dr. Craig McDonald</td>
<td>UC Davis Department of Physical Medicine and Rehabilitation</td>
<td>Sacramento, California</td>
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<tr>
<td>Dr. Marisa Couluris</td>
<td>Shriners Hospitals for Children</td>
<td>Tampa, Florida</td>
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<tr>
<td>Dr. Han Phan</td>
<td>Center for Integrative Rare Disease Research</td>
<td>Atlanta, Georgia</td>
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<tr>
<td>Dr. Kathy Mathews</td>
<td>University of Iowa</td>
<td>Iowa City, Iowa</td>
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<tr>
<td>Dr. Jeffrey Statland</td>
<td>University of Kansas Medical Center</td>
<td>Kansas City, Kansas</td>
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<tr>
<td>Dr. Thomas Crawford</td>
<td>Johns Hopkins University Hospital</td>
<td>Baltimore, Maryland</td>
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<td>Dr. Basil Darras</td>
<td>Boston Children’s Hospital</td>
<td>Boston, Massachusetts</td>
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<tr>
<td>Dr. Carla Grosmann</td>
<td>Gillette Children’s Specialty Healthcare</td>
<td>St Paul, Minnesota</td>
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<tr>
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<td>University of Rochester</td>
<td>Rochester, New York</td>
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<tr>
<td>Dr. Benjamin Brooks</td>
<td>Carolinas HealthCare System</td>
<td>Charlotte, North Carolina</td>
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<tr>
<td>Dr. Cuixia Tian</td>
<td>Cincinnati Children's Hospital Medical Center</td>
<td>Cincinnati, Ohio</td>
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<tr>
<td>Dr. Andre Prochoroff</td>
<td>MetroHealth Medical Center</td>
<td>Cleveland, Ohio</td>
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<tr>
<td>Dr. Oscar Henry Mayer</td>
<td>Children’s Hospital of Philadelphia</td>
<td>Philadelphia, Pennsylvania</td>
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<tr>
<td>Dr. Warren Marks</td>
<td>Cook Children’s Medical Center</td>
<td>Fort Worth, Texas</td>
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