

Focused

on the Respiratory Health of Boys and Men With Duchenne Muscular Dystrophy (DMD)

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



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Regional Medical Director
April, 2019

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Educational Purposes



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

This presentation is intended for educational and/or informational purposes only, and should not be used in place of a discussion with a health care professional. All decisions regarding patient care must be handled by a health care professional, and be made based on the unique needs of each patient.

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

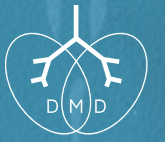
**POL6014
in CF**
(cystic
fibrosis)

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 longer 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





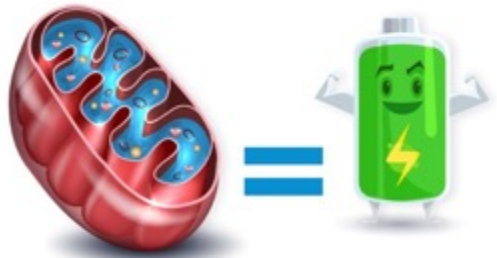
Respiratory Health and Mitochondrial Dysfunction

Mitochondrial Dysfunction Occurs in DMD



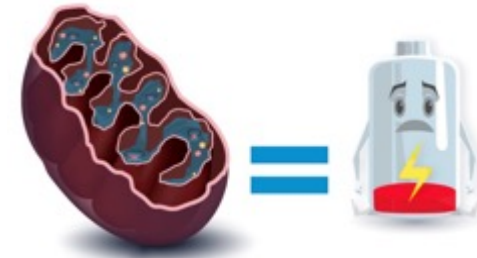
Lack of dystrophin contributes to mitochondrial dysfunction

- 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



Healthy
mitochondria

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



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

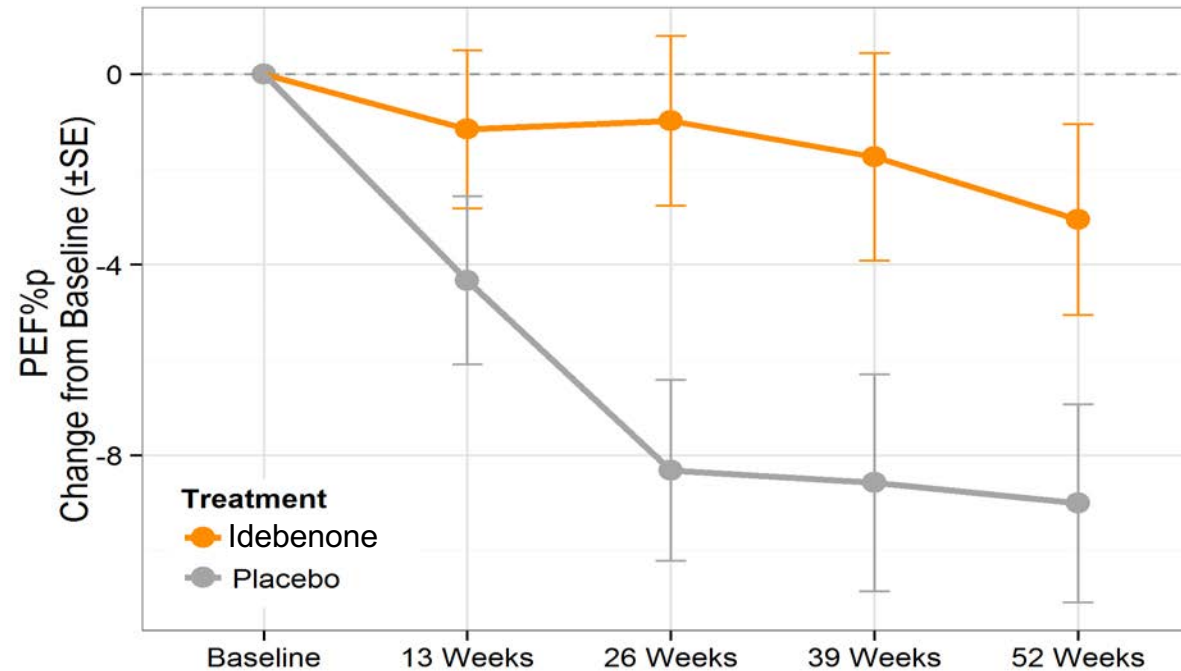
- Peak expiratory flow* percent predicted (PEF%p)
- Change in respiratory function from week 1 to week 52

DELOS results

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

* PEAK EXPIRATORY FLOW (PEF)

A measure of the peak or maximum flow of air when a person breathes out as hard as he can

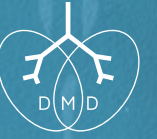


66%

reduction
in loss of
respiratory
function

(p=0.044)

Idebenone in DMD Clinical Trials (SIDEROS)



SIDEROS: Phase 3 trial in patients with DMD on steroids (ongoing)

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**

Idebenone in DMD Clinical Trials (SIDEROS)



Patients included in the study:



Any
dystrophin
mutation type

35-80%

FVC

What is FVC?

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

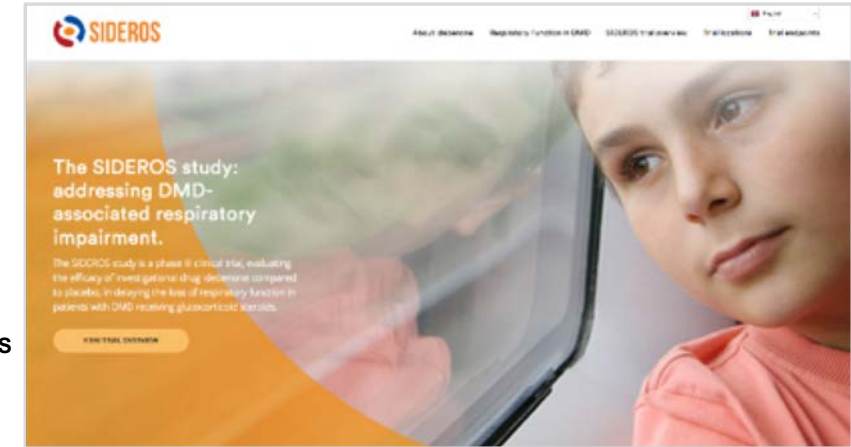
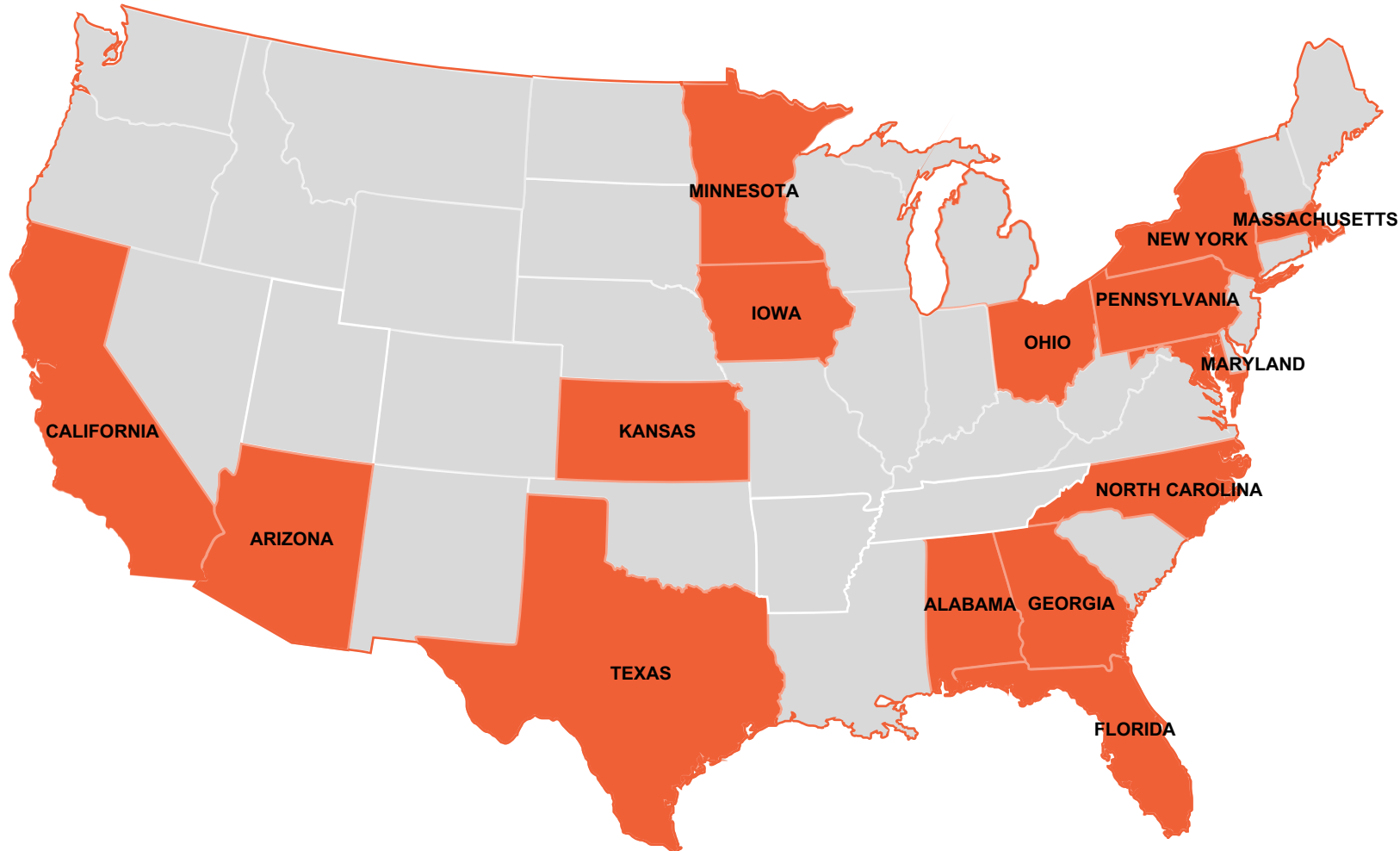
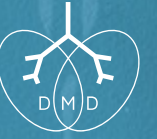


On any steroid
regimen of
prednisone or
deflazacort

12 months

Corticosteroids use for at
least 12 months prior to trial
without any dosage changes in
last 6 months

SIDEROS DMD Clinical Trial Sites



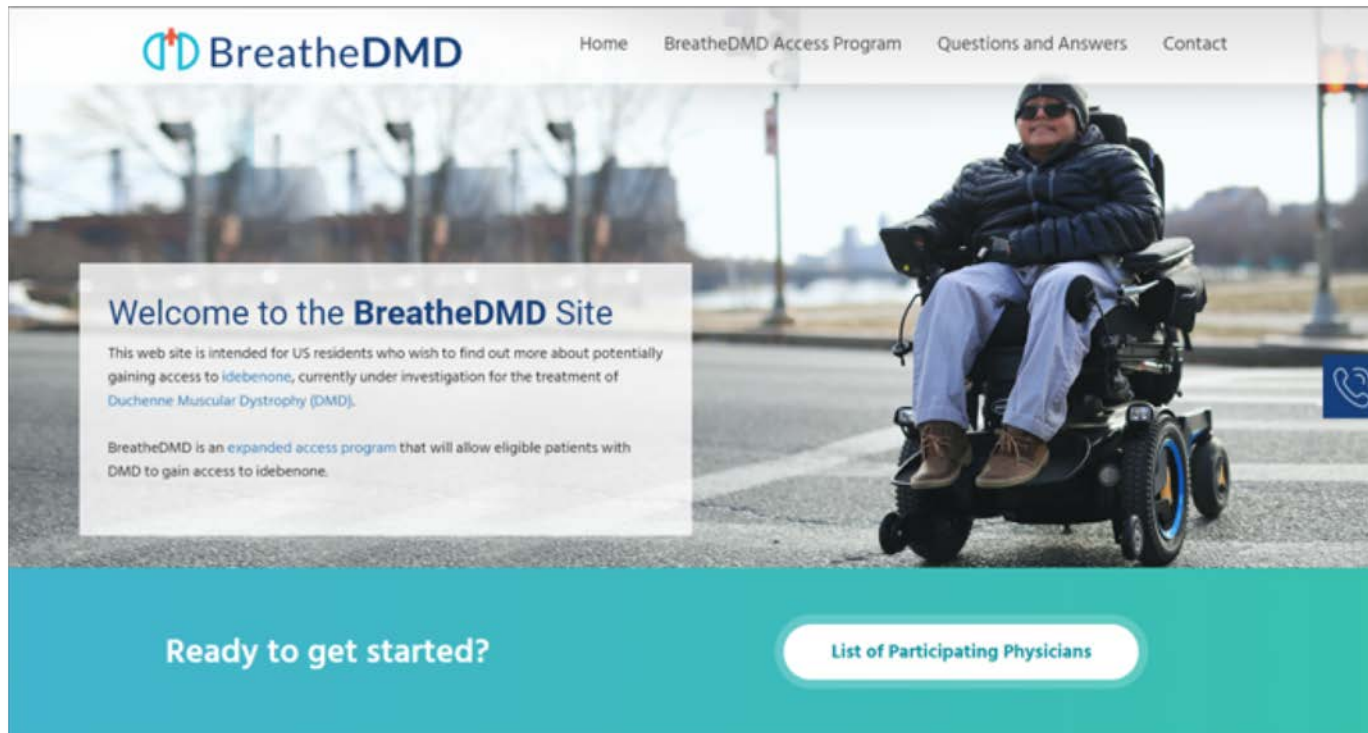
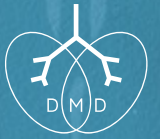
Visit www.Siderosdmd.com
for an in-depth trial overview

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.

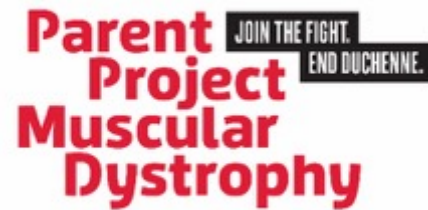
Contact your treating physician or visit www.breathedmd.com for more information.

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.



APPENDIX

Idebenone in DMD Clinical Trials (SIDEROS)



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
Childrens 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 Cialfoni
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