

# Challenges in Drug Development for Muscle Disease: A Stakeholders' Meeting

August 4-5, 2005  
Hyatt Regency Bethesda



**MDA**<sup>®</sup>

People Help MDA...Because MDA Helps People

**The Muscular Dystrophy Association Presents:**

**“Challenges in Drug Development for Muscle  
Disease: A Stakeholders’ Meeting”**

August 4-5, 2005

Hyatt Regency Bethesda  
One Bethesda Metro Center  
Bethesda, MD 20814

Co-Chairs:

**Jerry Mendell, M.D., Columbus Children’s Research Institute**  
**R. Rodney Howell, M.D., University of Miami**

**Planning Committee:**

Wilson Bryan, MD, Food and Drug Administration (ad hoc)  
Diana Escolar, MD, Children’s National Medical Center  
Fang Wang, Wyeth Pharmaceuticals  
Julaine Florence, PT, DPT, Washington University  
Sharon Hesterlee, PhD, Muscular Dystrophy Association  
R. Rodney Howell, MD, University of Miami  
Jerry Mendell, MD, Columbus Children’s Research Institute  
Richard T. Moxley III, MD, University of Rochester Medical Center  
John Porter, PhD, National Institute of Neurological Disorders and Stroke (ad hoc)  
Julie Anne Smith, Genzyme General

All meeting sessions will be held in the **Cabinet Judiciary** meeting room.

## **THURSDAY, AUGUST 4**

- 8:00am –8:30am**      **CONTINENTAL BREAKFAST—Diplomat Ambassador Room**
- 8:30am –8:35am**      **Welcome on Behalf of MDA and Announcements**  
R. Rodney Howell, University of Miami, and MDA Board Member and Scientific Advisory Committee Chair
- 8:35am – 8:40am**      **The Charge: Main Meeting Goals**  
Jerry Mendell, Children’s Research Institute

### **Introduction to Drug Development**

- 8:40am – 8:45am**      **Introduction by Moderator**  
Langdon Miller, PTC Therapeutics
- 8:45am – 9:15am**      **From “Proof-of-Principle” Trials Through Phase III: The Process**  
Wilson Bryan, FDA
- 9:15am – 9:45am**      **FDA Perspective: General Philosophy of Drug Development With a Particular Focus on Muscle Disease**  
Marc Walton, FDA
- 9:45am – 10:15am**      **Industry Perspective: Needs for Drug Development**  
**A. Philosophy of Drug Development from Industry Perspective**  
Edward Kaye, Genzyme  
**B. Needs of Industry for Drug Development for Muscle Disease**  
Cristina Csimma, Wyeth
- 10:15am – 10:30am**      **COFFEE BREAK**

### **Taking Stock of Natural History Data in Muscle Disease: Good, Bad and Missing:**

- 10:30am –11:00am**      **Introduction to Natural History Data in Clinical Trial Design**  
Moderator, Wilson Bryan, FDA
- 11:00am – 11:30am**      **Natural History of Pompe Disease**  
Priya Kishnani, Duke University
- 11:30am – 12:00pm**      **Natural History of Duchenne Muscular Dystrophy**  
Phillip Miller, Washington University
- 12:00pm – 1:00pm**      **BUFFET LUNCH—Concourse Terrace**
- 1:00pm – 2:00pm**      **Round Table Review: Natural History of Myotonic Dystrophy, FSHD, LGMD**  
Richard Moxley, University of Rochester; John Kissel, Ohio State University; and Kate Bushby, University of Newcastle
- 2:00pm – 3:00pm**      **Break-Out Groups on Natural History:**
- **Pompe Disease:** Led by Priya Kishnani, Duke University
  - **Duchenne Muscular Dystrophy:** Led by Craig McDonald, UC Davis
  - **Limb-girdle MD:** Led by Katie Bushby, University of Newcastle
  - **Myotonic Dystrophy:** Led by Richard Moxley, University of Rochester
  - **FSH Dystrophy:** Led by John Kissel, Ohio State University

- 3:00pm – 3:15pm**      **COFFEE BREAK**
- 3:15pm – 3:55pm**      **Group Discussion on Natural History**
- Challenges in Translational Research**
- 3:55pm – 4:05pm**      **Introduction to Challenges in Translational Research**  
Moderator, Sharon Hesterlee, MDA
- 4:05pm – 4:25pm**      **NIH on Funding Clinical Trials**  
Scott Janis, NIH Clinical Trials Group
- 4:25pm – 4:40pm**      **FDA Office of Orphan Products Development Grant Program**  
\*Sarah Linde-Feucht, FDA
- 4:40pm – 5:00pm**      **Industry Perspective on Translational Research**  
Frank Walsh, Wyeth Pharmaceutical
- 5:00pm – 5:30pm**      **Case Studies and Round Table Discussion**  
Jerry Mendell, Columbus Children’s Research Institute: DMD gene therapy;  
Barry Byrne, University of Florida: Pompe gene therapy; and Katie Bushby,  
University of Newcastle: Exon-skipping for DMD
- 6:00pm –**              **DINNER—Diplomat Ambassador Room**

## **FRIDAY, AUGUST 5**

- 8:00am – 8:30am**      **BREAKFAST—Diplomat Ambassador Room**

### **Clinically Significant Endpoints for Muscle Disease Trials**

- 8:30am – 8:45am**      **Introduction to Clinically Meaningful Endpoints for Muscle Disease**  
Moderators, Jane Scott, FDA and Marc Walton, FDA
- 8:45am – 9:15am**      **Muscle Strength Testing**  
Diana Escolar, Children’s National Medical Center
- 9:15am – 9:45am**      **Functional Assessments**  
Craig McDonald, UC Davis
- 9:45am – 10:15am**      **Patient Reported Outcomes**  
Ted Abresch, UC Davis
- 10:15am – 10:30am**      **COFFEE BREAK**
- 10:30am – 11:00am**      **Pulmonary and Cardiac Assessments**  
Hugh Allen, Columbus Children’s Hospital and Jonathan Finder, University of Pittsburgh
- 11:00am – 11:30am**      **Surrogate Markers: Enzyme Levels, Muscle Histology and Gene Expression**  
Steve Moore, University of Iowa
- 11:30am – 12:00pm**      **Muscle Imaging**  
Glenn Walter, University of Florida
- 12:00pm – 1:00pm**      **BUFFET LUNCH—Concourse Terrace**
- 1:00pm – 1:15pm**      **Safety Endpoints**  
Langdon Miller, PTC Therapeutics

- 1:15pm – 2:15pm Breakout Groups**
- **Muscle Strength Testing:** Led by Diana Escolar, Children's National Medical Center
  - **Functional Testing:** Led by Kathy Mathews, University of Iowa
  - **Patient Assessed Outcomes:** Led by Ted Abresch, UC Davis
  - **Pulmonary and Cardiac Endpoints:** Led by Jonathan Finder, University of Pittsburgh
  - **Surrogate Markers:** Led by Steve Moore, University of Iowa
  - **Muscle Imaging:** Led by Glenn Walter, University of Florida
- 2:15pm – 3:00pm Group Discussion on Endpoints**  
Moderators, Jane Scott, FDA and Marc Walton, FDA

## Summary and Wrap-Up

- 3:00pm – 3:20pm Lessons Learned and the Way Forward**  
Jerry Mendell, Columbus Children's Research Institute
- 3:20pm – 3:50pm Final Round Table Discussion with Moderators from All Main Sessions**
- 3:50pm – 4:00pm Conclusions**  
R. Rodney Howell, University of Miami

## Speakers, Moderators and Group Leaders

**Ted Abresch, MS**, University of California Davis, Physical Medicine and Rehabilitation  
**Hugh Allen, MD**, Columbus Children's Hospital, Heart Center  
**Wilson Bryan, MD**, Food and Drug Administration, Center for Drug Evaluation and Research  
**Kate Bushby, MD**, University of Newcastle Upon Tyne, Institute of Human Genetics  
**Christina Csimma, RPh, MHP**, Wyeth Pharmaceutical, Translational Research  
**Diana Escolar, MD**, Children's National Medical Center, CINRG  
**Jonathan Finder, MD**, University of Pittsburgh, Division of Pediatric Pulmonology  
**Sharon Hesterlee, PhD**, Muscular Dystrophy Association, Translational Research Program  
**R. Rodney Howell, MD**, University of Miami, Pediatrics  
**Scott Janis, PhD**, National Institutes of Health, National Institute of Neurological Disorders and Stroke  
**Edward M. Kaye, MD**, Genzyme General, Clinical Research  
**Priya Kishnani, MD**, Duke University Medical Center, Pediatrics: Medical Genetics  
**John T. Kissel, MD**, Ohio State University College of Medicine, Neurology  
**Sarah Linde-Feucht, MD**, Food and Drug Administration, Office of Orphan Products Development  
**Katherine Mathews, MD**, University of Iowa, Pediatrics  
**Jerry Mendell, MD**, Columbus Children's Research Institute, Neurology  
**Langdon Miller, MD**, PTC Therapeutics, Medical Officer  
**Phillip Miller, AB**, Washington University, Biostatistics  
**Steven A. Moore, MD, PhD**, University of Iowa, Pathology  
**Richard T. Moxley, III, MD**, University of Rochester Medical Center, Neurology  
**Jane Scott, PhD**, Food and Drug Administration, Study Endpoints and Label Development Team  
**Frank Walsh, PhD**, Wyeth Pharmaceutical, Discovery Research Worldwide  
**Glenn A. Walter, PhD**, University of Florida, Physiology and Functional Genomics  
**Marc Walton, MD, PhD**, Food and Drug Administration, Center for Drug Evaluation and Research

MDA gratefully acknowledges the following for their support

**Genzyme General**  
**Wyeth Pharmaceutical**

Pfizer

PTC Therapeutics

Amicus Therapeutics

CepTor Corporation

## MDA's Purpose and Programs

The Muscular Dystrophy Association fights neuromuscular diseases through an unparalleled worldwide research effort, a nationwide program of medical services and far-reaching professional and public health education. Individual MDA research grants to investigators in the United States and abroad number some 400. Through MDA's services program, comprehensive medical services are furnished to children and adults with neuromuscular diseases and some 240 MDA hospital-affiliated clinics and through the Association's chapter. The following diseases are included in MDA's program:

### Muscular Dystrophies

Myotonic dystrophy (Steinert's Disease)  
Duchenne (pseudohypertrophic) muscular dystrophy  
Becker muscular dystrophy  
Limb-girdle muscular dystrophy  
Facioscapulohumeral (Landouzy-Dejerine) muscular dystrophy  
Congenital muscular dystrophy  
Distal muscular dystrophy  
Emery-Dreifuss muscular dystrophy

### Motor Neuron Diseases

Amyotrophic lateral sclerosis (ALS)  
Infantile progressive spinal muscular atrophy  
(Type 1, Werdnig-Hoffman disease)  
Intermediate spinal muscular atrophy  
(Type 2)  
Juvenile spinal muscular atrophy  
(Type 3, Kugelberg-Welander disease)  
Adult spinal muscular atrophy  
(Aran-Duchenne type)  
Spinal bulbar muscular atrophy  
(Kennedy's disease)

### Inflammatory Myopathies

Polymyositis  
Dermatomyositis  
Inclusion-body myositis

### Diseases of Neuromuscular Junction

Myasthenia gravis  
Lambert-Eaton (myasthenic) syndrome  
Congenital myasthenic syndromes

### Diseases of Peripheral Nerve

Peroneal muscular atrophy  
(Charcot-Marie-Tooth disease)  
Friedreich's ataxia  
Dejerine-Sottas disease

### Metabolic Diseases of Muscle

Phosphorylase deficiency  
(McArdle's disease)  
Acid Maltase Deficiency  
(Pompe's disease)  
Phosphofructokinase deficiency  
(Tarui's disease)  
Debrancher enzyme deficiency  
(Cori's or Forbe's disease)  
Mitochondrial Myopathy  
Carnitine Deficiency  
Carnitine palmityl transferase deficiency  
Phosphoglycerate kinase deficiency  
Phosphoglycerate mutase deficiency  
Lactate dehydrogenase deficiency  
Myoadenylate deaminase deficiency

### Myopathies Due to Endocrine Abnormalities

Hyperthyroid myopathy  
Hypothyroid myopathy

### Other Myopathies

Myotonia congenita  
Paramyotonia congenita  
Central core disease  
Nemaline myopathy  
Myotubular myopathy  
Periodic paralysis



## Muscular Dystrophy Association

Jerry Lewis, National Chairman  
Lois West, Chairman of the Board  
Robert Ross, President & CEO

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