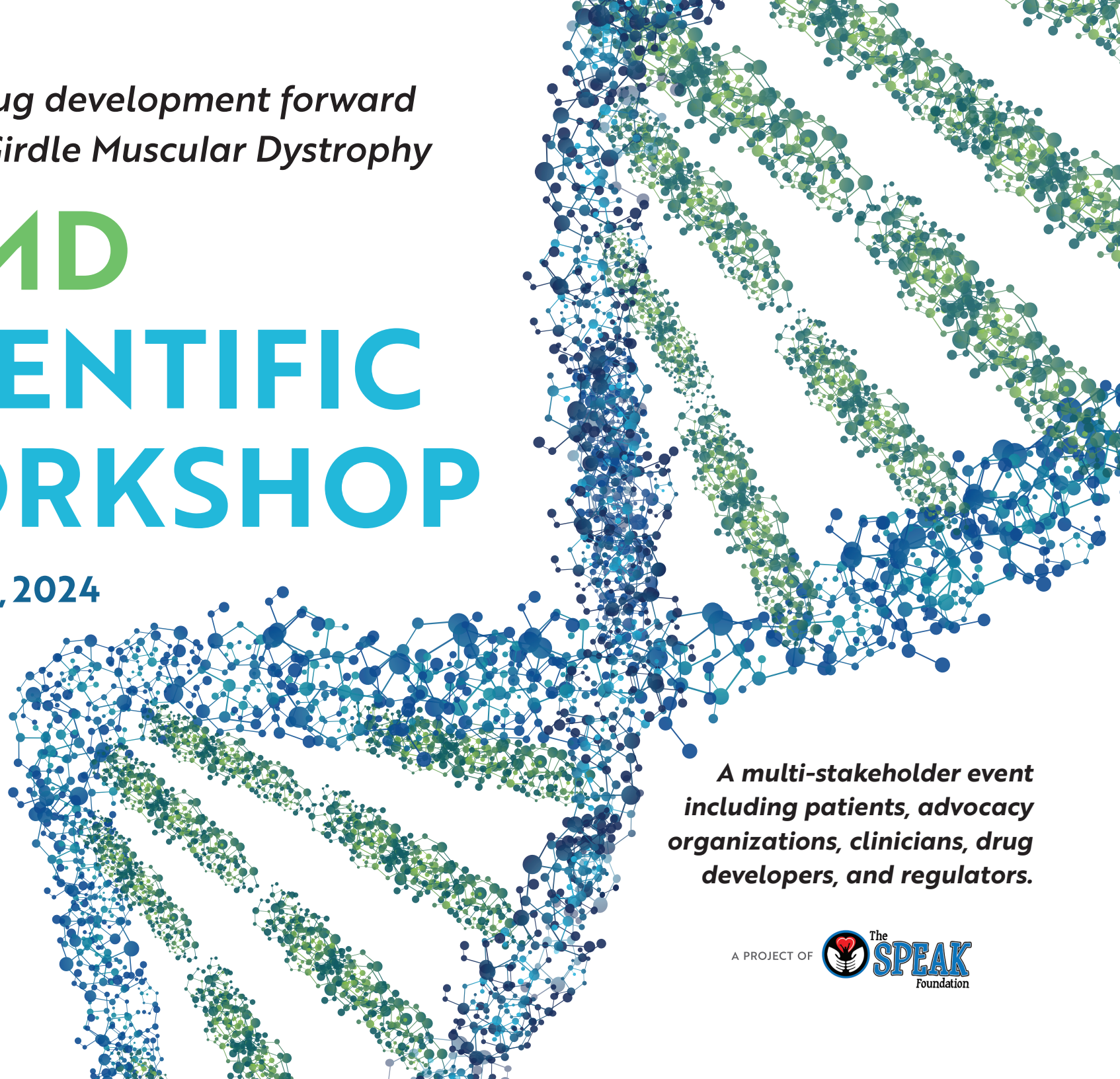
Moving drug development forward for Limb-Girdle Muscular Dystrophy

LGMD SCIENTIFIC WORKSHOP

February 8, 2024



A multi-stakeholder event including patients, advocacy organizations, clinicians, drug developers, and regulators.

A PROJECT OF The SPEAK Foundation

WORKSHOP AGENDA

TIME	TOPIC	SPEAKERS
8:30 – 8:40 AM	**Welcome and Opening Remarks**	Kathryn Bryant Knudson, CEO, The Speak Foundation
8:40 – 8:45 AM	**Workshop Run of Show**	Keith Flanagan
LGMD Pathophysiology		
8:45 – 9:05 AM	**KEYNOTE ADDRESS**	Jerry Mendell, MD
9:05 – 10:00 AM	**LGMD Subtype Overview Presentation:** **LGMD 2C/R5 | LGMD 2D/R3 | LGMD 2E/R4** **LGMD 2I/R9** **LGMD 2A/R1 | LGMD 2B/R2**	 Peter Kang, MD Kathy Mathews, MD Matthew Wicklund, MD
10:00 – 10:25 AM	**Presentation:** **LGMD Natural History Landscape**	 Nicholas Johnson, MD
MORNING BREAK		
Patient Focused Drug Development		
10:40 – 11:00 AM	**Presentation:** **Patient Focused Drug Development in LGMD**	 Jennifer Levy, PhD
11:00 – 11:30 AM	**Presentations:** **Introduction Video** **Patient Video** **Patient and Caregiver:** **Experiences and Treatment Preferences**	 *Early Impact on Children and Families Living with LGMD* Donavon Decker (LGMD 2D/R3) Kathryn Bryant Knudson | *Moderator* Patrick Moeschen (LGMD 2E/R4) Kelly Brazzo (LGMD 2I/R9) Brooklyn Garza (LGMD 2A/R1) Rachel DeConti (LGMD 2C/R5, LGMD 2D/R3, LGMD 2E/R4) Joshua Thayer (LGMD 2B/R2)
LUNCH BREAK		

WORKSHOP AGENDA

(Continued)

TIME	TOPIC	SPEAKERS
Clinical Endpoints, Accelerated Approval, and Clinical Trial Design		
12:20 – 1:10 PM	**Fireside Chat:** **Accelerated Approval Pathway, Surrogate Endpoints, and Clinical Trial Design for LGMD**	Annie Kennedy | *Moderator* Peter Marks, MD, PhD Peter Stein, MD
1:10 – 1:40 PM	**Presentation:** **Innovative Clinical Trial Design for LGMD**	James Signorovitch, PhD
1:40 – 2:00 PM	**Presentation:** **Clinical Endpoint Considerations**	Lindsay Alfano, PT, DPT
2:00 – 2:30 PM	**Presentations:** **Surrogate Endpoints in LGMD:** **Subtype Case Studies**	Douglas Sproule, MD Louise Rodino-Klapac, PhD
AFTERNOON BREAK		
2:45 – 4:15 PM	**Roundtable:** **LGMD Endpoints and Clinical Trial Design**	Keith Flanagan | *Moderator* Kathryn Bryant Knudson, Patient Advocate Michelle Campbell, PhD Joanne Donovan, MD, PhD Anh Nguyen, MD Sophie Olivier, MD Louise Rodino-Klapac, PhD Laura Rufibach, PhD James Signorovitch, PhD Douglas Sproule, MD Nicole Verdun, MD Matthew Wicklund, MD
4:15 – 4:30 PM	**Fireside Chat:** **Key Take-Aways and Next Steps**	Keith Flanagan | *Moderator* Kathryn Bryant Knudson, Patient Advocate Peter Marks, MD, PhD Peter Stein, MD

WORKSHOP SPEAKERS

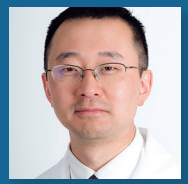
Lindsay Alfano, PT, DPT
Principal Investigator, Assistant Professor
The Abigail Wexner Research Institute
at Nationwide Children's Hospital
Center for Gene Therapy

Michelle Campbell, PhD
Associate Director,
Stakeholder Engagement and Clinical Outcomes,
Office of Neuroscience
United States Food and Drug
Administration (FDA)

Joanne Donovan, PhD, MD
Chief Medical Officer
Edgewise Therapeutics

Keith Flanagan
Consultant
Flanagan Strategies, LLC

Nicholas Johnson, MD
Associate Professor, Division Chief of Neuromuscular,
and Vice Chair of Research, Department of Neurology
Virginia Commonwealth University
Head, GRASP LGMD Consortium



Peter Kang, MD
Professor and Vice Chair of Research
Department of Neurology
University of Minnesota Medical School

Annie Kennedy
Chief of Policy, Advocacy, and Patient Engagement
EveryLife Foundation for Rare Diseases

Kathryn Bryant Knudson
Founder and CEO
The Speak Foundation

Jennifer Levy, PhD
Scientific Director
Coalition to Cure Calpain 3 (C3)

Peter Marks, MD, PhD
Director of the Center for Biologics
Evaluation and Research (CBER)
United States Food and Drug
Administration (FDA)

Katherine Mathews, MD
Professor of Pediatrics — General Neurology
University of Iowa Health Care,
Carver College of Medicine

WORKSHOP SPEAKERS

(Continued)

Jerry R. Mendell, MD
Former Attending Neurologist
Nationwide Children's Hospital
Senior Advisor, Medical Affairs
Sarepta Therapeutics

Anh Nguyen, MD
Vice President, Therapeutic Sector Leader
AskBio Therapeutics

Sophie Olivier, MD
Chief Medical Officer
Atamyo Therapeutics

Louise Rodino-Klapac, PhD
Executive Vice President, Head of R&D,
Chief Scientific Officer
Sarepta Therapeutics

Laura Rufibach, PhD
Co-President
Jain Foundation

James Signorovitch, PhD
Managing Principal
Analysis Group

Douglas Sproule, MD
Chief Medical Officer
ML Bio Solutions

Peter Stein, MD
Director of CDER's Office of New Drugs (OND)
United States Food and Drug
Administration (FDA)

Nicole Verdun, MD
Director,
Office of Therapeutic Products (OTP)
CBER, U.S. FDA

Matthew Wicklund, MD
Professor of Neurology
University of Texas San Antonio

PATIENT PANEL

Kelly Brazzo
(Mom & Caregiver of Sammy)
Subtype: LGMD 2I/R9 (Dystroglycanopathy)
Age of Onset: Age 2

Key Struggles: Sammy was diagnosed with heterozygous LGMD 2I/R9 at the age of two. Since that time, she has had a significant decline in her mobility resulting in frequent falls and an inability to rise from the chair or the floor. She has suffered from contractures requiring surgery for a heel cord lengthening procedure followed by serial casting as well as a complete spinal fusion.

Why this Event is Important: It is imperative that we continue to share the story of the LGMD patient experience to help accelerate drug development. We are grateful to have so many experts in this area coming together to expedite an approved therapy for this ultra rare, progressive and life-limiting disease.

Rachel DeConti
(Mom & Caregiver of Jacob)
Subtype: LGMD 2D/R3 (Sarcoglycanopathy)
Age of Onset: Age 5

Key Struggles: Jacob was diagnosed with LGMD 2D/R3 during the summer of 2021 when he suffered a case of Rhabdomyolysis. Since this diagnosis, he has had additional cases of Rhabdo when he overexerts himself, is in cold water for an extended time, and doesn't hydrate enough during physical activity. At now 7-years-old, he doesn't fully understand why he is slower than his peers at gym/recess, or why he can't play team sports with all of his friends. He also experiences trips/falls and we are constantly worried of impactful injuries.

Why this Event is Important: This event is so important for our entire LGMD community. It helps key stakeholders — drug researchers, developers and regulators — better understand what LGMD patients face daily with disease progression. Despite how far we have come over the years with various disease treatments, there is still not an approved treatment for LGMD. To us, this gathering brings us one step closer to helping expedite treatments for patients who critically need them, including my son. I am so appreciative of the collaboration and partnership this event represents.

PATIENT PANEL
(Continued)

Brooklyn Garza
Subtype: LGMD 2A/R1 (Calpainopathy)
Age of Onset: Age 9

Key Struggles: Weakness in arms — struggles to lift, get up, get dressed, bathe, carry things — even a backpack at school, reach above shoulders. Weakness in legs — walking long distances, climbing stairs, falling, lifting legs, bending down, can't run.

Why this Event is Important: To share my experiences living with Limb-Girdle Muscular Dystrophy in order to promote accelerated treatment and a cure for this disease. My goal is to further research and provide as much data as I can to help this go faster.

Patrick Moeschen
Subtype: LGMD 2E/R4 (Sarcoglycanopathy)
Age of Onset: Age 11

Key Struggles: The relentless progression of the condition renders it impossible to not worry about how bad things are going to get. As time ticks by, our bodies are slowly killing us. As adults, our risk/benefit scale differs from other patient groups.

Why this Event is Important: Safe, but accelerated access to trials and treatments must be at the forefront to provide hope. The FDA must think outside the box when presented with drug/genetic proposals about all types of muscular dystrophy.

Joshua Thayer
Subtype: LGMD 2B/R2 (Dysferlinopathy)
Age of Onset: Age 18

Key Struggles: I am no longer able to stand up or walk at all. I rely on a power wheelchair and conversion ramp van for mobility, and I require assistance to transfer, bathe, dress, prepare meals and perform most other activities of daily living.

Why this Event is Important: I applaud the FDA, clinicians, research doctors and drug sponsors for increasingly turning to patients for our input on clinical trial design, and I am encouraged to see our involvement extended to events like this one. My primary requests are for the stakeholders to accept what we tell you are clinically meaningful improvements, to apply surrogate endpoints for accelerated approval of LGMD drugs, and to develop and validate novel clinical outcome measurements that are appropriate to the LGMD community at all levels of progression.