Vol 4 / Issue 1

LGMD News

Uniting the Limb-Girdle Muscular Dystrophy Community

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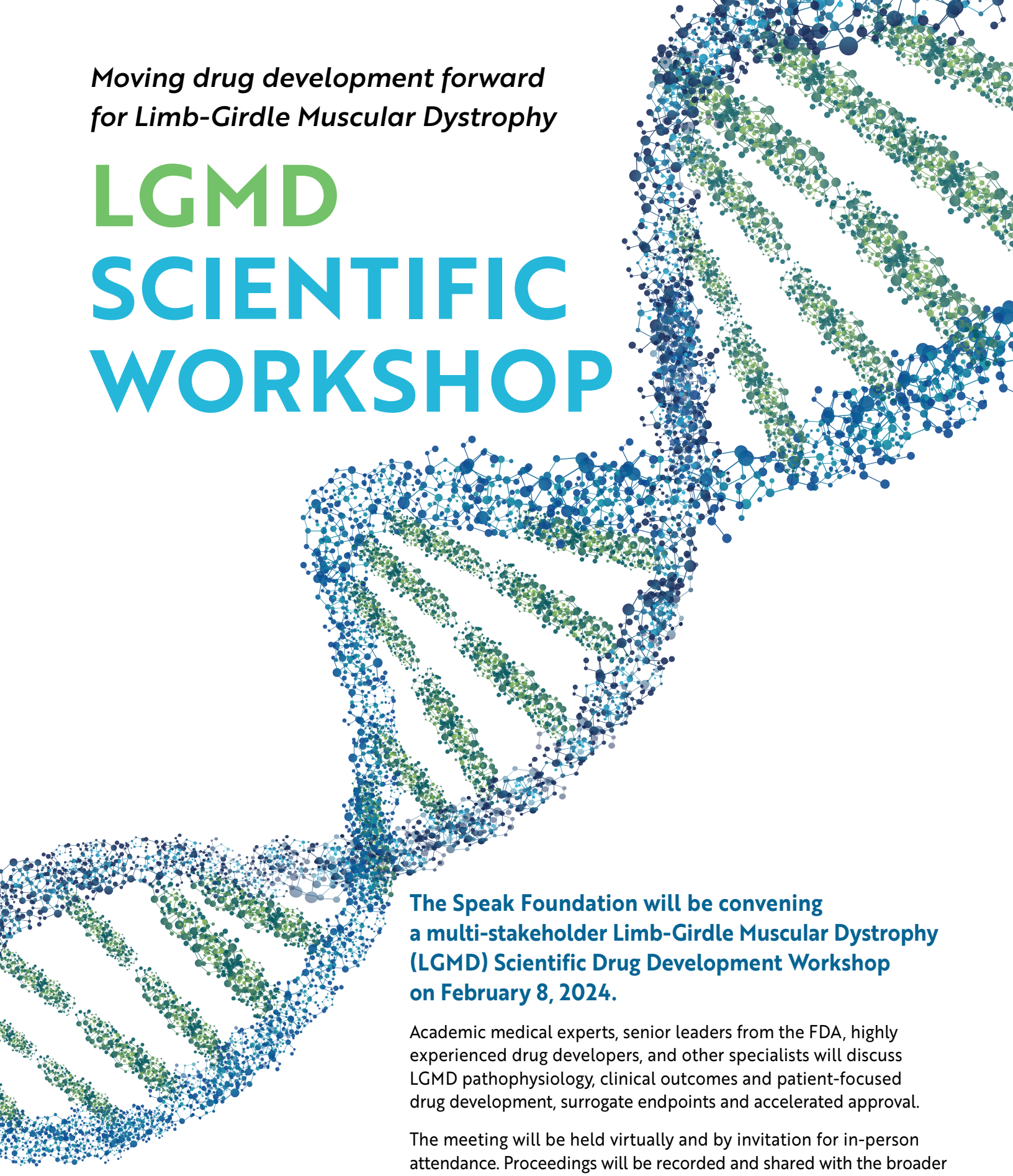
LGMD Awards of Excellence

Recognizing Those Who are Leading the Way with Excellence in Their Field or Category of Service

Moving drug development forward for Limb-Girdle Muscular Dystrophy

LGMD SCIENTIFIC WORKSHOP



The Speak Foundation will be convening a multi-stakeholder Limb-Girdle Muscular Dystrophy (LGMD) Scientific Drug Development Workshop on February 8, 2024.

Academic medical experts, senior leaders from the FDA, highly experienced drug developers, and other specialists will discuss LGMD pathophysiology, clinical outcomes and patient-focused drug development, surrogate endpoints and accelerated approval.

The meeting will be held virtually and by invitation for in-person attendance. Proceedings will be recorded and shared with the broader patient and scientific communities through The Speak Foundation.

Stay tuned for more details!

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Thank you for your support!

The Speak Foundation

Uniting the entire LGMD community to make a difference together in future treatments for this rare disease.

The origin of The Speak Foundation's name comes from Proverbs 31:8. It is: "Speak up for those who have no voice." Living with a rare disease means many of us wait years to have a voice in areas that impact our daily lives personally. The Speak Foundation helps our voices to be heard.

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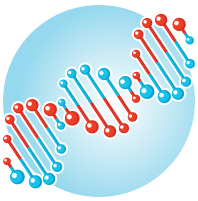

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Looking Forward: *LGMD News* and LGMD Advocacy

You have responded with overwhelming support of our efforts. In the next two years, our goal will be to grow our subscribers and registry.

Connect with Us

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Dear LGMD Community,

When we started *LGMD News* magazine, our goal was to ensure our patient community would always have a trusted, reliable resource for the latest medical and scientific advancements for LGMDs. You have responded with overwhelming support of our efforts. In the next two years, our goal will be to grow our subscribers and registry. As we see more drug developers enter our space, it is critical that we continue to communicate with the LGMD patient community.

In this issue, we are announcing winners for our Awards of Excellence, chosen by our patient community. We want to thank each of these companies and individuals for making a difference in the lives of those living with LGMD. As part of our Excellence in Care series, the Speak Foundation will begin a Health Equity Travel Program for individuals living in the USA to receive care at Centers of Excellence for LGMD. Further details will be provided in our next issue.

We are also excited to share that on February 8, 2024, we will hold the first LGMD Scientific Workshop. Scientific leaders in the LGMD community along with leaders in industry, the FDA, and invited patient delegates will convene for a one-day workshop to discuss the status of drug development. The goal of this event is to increase awareness of the science of LGMDs and to further drug development. The event will then be posted to the Speak Foundation's YouTube channel for playback, and we will announce when it is available for viewing.

Lastly, we thank all our volunteers and attendees who participated in the recent International LGMD Conference in Washington, D.C. We had great collaboration with an excellent team of volunteers. We could not do what we do without you!

Thank you! ▪

Kat Bryant Knudson

Kathryn Bryant Knudson
Editor In Chief
Founder & CEO, The Speak Foundation

Our Mission

The Speak Foundation was based on the principle of "Speak up for those who have no voice." *Speak up for those who cannot speak for themselves.* —Proverbs 31:8

LGMD News is a program of the Speak Foundation. In order to help individuals and families living with limb-girdle muscular dystrophy receive critical and life-saving information, the Speak Foundation began publishing this resource in 2021.

International Consortium of LGMD Organizations

United States

The Speak Foundation
Uniting the entire LGMD community
TheSpeakFoundation.com

Beyond Labels & Limitations
Funding research for LGMD R1/2A and educating on its disease course
BeyondLabelsLimitations.com

Breathe with MD
Educating and raising awareness about breathing muscle weakness in neuromuscular disease
BreatheWithMD.org

CamronsCure
Funding research for LGMD R19/2S
CamronsCure.com

Coalition to Cure Calpain 3
Funding research for LGMD R1/2A
CureCalpain3.org

Cure LGMD2i
Funding research for LGMD R9/2i
CureLGMD2i.org

Kurt + Peter Foundation
Funding research for LGMD R5/2C
KurtPeterFoundation.org

LGMD Awareness Foundation
Raising awareness of and advocating for the LGMD community
LGMD-Info.org

LGMD-1D DNAJB6 Foundation
Representing LGMD D1/1D and DNAJB6 subgroup
LGMD1D.org

LGMD2D Foundation
Funding research for LGMD R3/2D and educating patients and physicians
LGMD2D.org

LGMD2i Research Fund
Funding research for LGMD R9/2i and educating the patient community
LGMD2iFund.org

LGMD2L Foundation
Representing the LGMD R12/2L Anoctamin5-related community
LGMD2L-Foundation.org

Team Titin
Strengthening the titin community: LGMD R10/2J
TitinMyopathy.com

The Jain Foundation
Funding research for LGMD R2/2B and educating the patient community
Jain-Foundation.org

Argentina

ADM Argentina Muscular Dystrophy LGMD Group
Funding research for neuromuscular diseases
ADM.org.ar

Australia

Daniel Ferguson LGMD2A Foundation
Funding research for LGMD R1/2A and educating the patient community
DFFoundation.com.au

France

"GI LGMD"/LGMD Patient Group of AFM-Telethon
Focusing on all subtypes of LGMD, supporting research and educating the patient community
LGMD.AFM-Telethon.fr

Italy

Conquistando Escalones Association
Funding research for LGMD D2/1F
ConquistandoEscalones.org

"GFB ONLUS"/ Family Group of Beta-Sarcoglycanopathy
Representing the LGMD R5/2C Gamma Sarcoglycan-related, LGMD R3/2D Alpha Sarcoglycan-related, LGMD R4/2E Bèta-Sarcoglycan-related, and LGMD R6/2F Delta-Sarcoglycan-related communities
Beta-Sarcoglicanopathy.org

Gruppo Cingoli of UILDM – Unione Italiana Lotta alla Distrofia Muscolare
Focusing on all subtypes of LGMD, raising awareness and providing support for the entire Italian community
UILDM.org

Italian Association Calpain 3
Funding research for the LGMD R1/2A Calpain 3-related community
AICA3.org

Japan

Patients' Association for Dysferlinopathy Japan
Representing the Japanese and International LGMD R2/2B Dysferlin-related and Miyoshi Muscular Dystrophy 1 (MMD) communities
PADJ.jp/index.html

Netherlands

Stichting Spierkracht
Raising awareness and supporting the LGMD R3/2D Alpha Sarcoglycan-related community
StichtingSpierkracht.com

South Korea

Korean Dysferlinopathy Patients Association
Providing patients with LGMD R2/2B information and research updates
Cafe.Naver.com/UniteDsyferlinopathy

Spain

Conquistando Escalones Association
Funding research for LGMD D2/1F
ConquistandoEscalones.org

Proyecto Alpha
Funding research for LGMD R5/2C Gamma Sarcoglycan-related, LGMD R3/2D Alpha Sarcoglycan-related, LGMD R4/2E Bèta-Sarcoglycan-related, and LGMD R6/2F Delta-Sarcoglycan-related
ProyectoAlpha.org

Stacy Dixon, MD, PhD

University of Colorado

Meet the Expert

Stacy Dixon, MD, PhD is an Assistant Professor of Neurology, Neuromuscular Division, at the University of Colorado. Her clinical and research interests include muscular dystrophies, spinal muscular atrophy, hereditary nerve disorders, motor neuron disorders, and disorders of the neuromuscular junction.

It can be helpful to work with a physical therapist to design an appropriate exercise regimen and discuss appropriate stretching, warm up, and cool down routines.

Q

We live in Latvia. I am a mom of a 13-year-old boy diagnosed with LGMD1A. He presented with elevated CK 8 years ago. He was very strong, playing soccer several times a week. He is still walking and doing well but gets tired sooner than his friends and cannot run as fast or long distances. What should we do or keep in mind in terms of helping him to slow down progression?

A

It is good that your son is staying active. Some studies have shown moderate aerobic exercise can be beneficial in muscular dystrophies. That being said, it is important to be mindful and for him not to overexert himself with activities. It can be helpful to work with a physical therapist to design an appropriate exercise regimen and discuss appropriate stretching, warm up, and cool down routines. It is also important for him to "listen to his body" and rest and slow down when feeling fatigued.

Q

We are writing from Italy. My 35-year-old cousin was diagnosed with SEPN1 (Selenon) deficiency myopathy at birth. Given the rarity of the disease and following the opinions received from his doctors in Milan, he is losing the will to fight this battle. Is it possible to know at which stage the treatments are? Do you have any valid contact here in Italy? Do you have any general recommendation? Should we have any hope? Would it make sense for us to visit in the USA?

A

I know it can be very difficult living with a rare disorder, but do know there are many researchers and clinicians throughout the world trying to develop treatment options to help patients navigate the journey of life with a muscular dystrophy diagnosis. In Italy, Centro Clinico NeMO is an excellent care center for patients with neuromuscular and neurodegenerative disorders. There are multiple locations throughout Italy.

Q

Some days I feel so exhausted. Is this a common sign or symptom with LGMDs? What is the best thing to do in this case?

A

Fatigue and exhaustion can occur with muscular dystrophies, and it is important to discuss these symptoms with your clinician. Some patients with muscular dystrophy can suffer from neuromuscular respiratory muscle weakness, especially when supine (lying down), which can lead to non-restful sleep at night and daytime sleepiness, due to a buildup of carbon dioxide in the bloodstream. Therefore, assessment and appropriate treatment can be helpful.

Q

I am 69 years old. I have late onset LGMD (LAMA2) diagnosed 8 years ago. I have a neurologist, cardiologist, and a general practitioner. I feel like I have limited support and wish I had a "team" of practitioners who understand LGMD well and can guide me. My best support seems to come from my physical therapists. Is a "team" essential and, if so, how do I form one?

A

It is very helpful to try to form a team with the providers you have by working with them, asking questions, and ensuring they are staying abreast of the latest developments. Additionally, in some places, there are designated multidisciplinary care centers for muscular dystrophies, and it may be helpful to be seen in one near you for specialized expertise, if possible.

Q

What is the benefit of regularly seeing a neurologist? I had a wonderful neurologist who guided me to finally receiving a diagnosis and provided explanation for all that was going on, but since there is currently no cure and no treatment for LGMD2L, how can regular visits with a neurologist help?

A

Continuing to see a neurologist after a muscular dystrophy diagnosis is important. Different limb-girdle muscular dystrophies can be associated with other non-muscular manifestations, and a neurologist can ensure you are getting appropriate care in other subspecialities. Additionally, many neurologists are associated with multidisciplinary care centers. It may be that your neurologist can assess your need for adaptive equipment, facilitate ongoing therapy needs, and keep you abreast of the latest clinical trials and developments.

Q

Is it safe for people with LGMD to take statins? I've heard that some people who take statins experience muscle weakness and wonder if statins could make LGMD worse.

A

This is a difficult question to answer and there is very little evidence from studies. The impact will likely vary with each person and depend on the type of muscular dystrophy and the clinical indication for the use of the statin. In any case, a person should be monitored closely for side effects from the statin.

Continuing to see a neurologist after a muscular dystrophy diagnosis is important. Different limb-girdle muscular dystrophies can be associated with other non-muscular manifestations, and a neurologist can ensure you are getting appropriate care in other subspecialities.

Question

Q

My daughter was diagnosed with LGMD2D through genetic testing when she was in fourth grade. She is now a junior in high school. We have participated in the GRASP LGMD natural history study. Sometimes it feels as though a treatment is never going to happen. When will gene therapy actually be available, and more specifically, what about for her subtype?

A

Unfortunately, I cannot give an exact answer, and it is frustrating that there are currently limited treatment options for any muscular dystrophy. That being said, many thanks to your daughter for volunteering to participate in a natural history study! This is a big first step for the medical community to prepare for the possibility of future treatment trials. There are many researchers and clinicians working on developing new therapies and treatments for muscular dystrophies. You can also intermittently monitor **ClinicalTrials.gov** for new and upcoming clinical research trials.

Q

I am 46 years old and from Brazil. I was diagnosed with LGMD in 2022 after having elevated values of creatine phosphokinase, glutamic-oxaloacetic transaminase, and glutamic-pyruvic transaminase since 2010 (at 33 years old). I have always been very physically active, but on medical recommendation, I considerably reduced bodybuilding activity with excessive load and long distances by bicycle. In 2022, I started using a cane and felt very weak. I was worried and started taking several supplements. I feel that I have noticed improvements. What is your opinion regarding creatine and whey protein?

A

Although some studies show potential benefits of creatine supplementation, the results from multiple studies are not consistent and there are limitations (including small sample sizes, variable doses and durations, and discrepancies in results). Therefore, I recommend you discuss all supplement use with your clinicians. Some supplements and vitamins can be helpful but can cause toxicities at higher doses, so it is important to disclose everything you are taking to your health care team.

Q

One of the biggest questions in our community is which type and intensity of exercise do you think is valuable for people with MD, and are there any things we should avoid?

A

As noted above, some studies have shown moderate aerobic exercise can be beneficial in muscular dystrophies, but it is important to not overexert with activity. Watch for worsening muscle aches, extreme fatigue, and seek emergent medical attention for signs of rhabdomyolysis, such as dark, tea-colored urine. As noted above, it can be helpful to work with a physical therapist to design an appropriate exercise regimen. ■

Watch for worsening muscle aches, extreme fatigue, and seek emergent medical attention for signs of rhabdomyolysis, such as dark, tea-colored urine.

Connect with Us

TheSpeakFoundation.com
ClinicalTrials.gov

Have a Question for Our Experts?

Send Questions To:
ContactUs@TheSpeakFoundation.com

fortify

Fortify is a Phase 3 clinical trial evaluating if an investigational oral therapy (BBP-418) is safe and effective for treating Limb Girdle Muscular Dystrophy type 2I / R9, FKRP-related (LGMD2I/R9)

About Fortify

Fortify is a 36 month randomized, double-blind, placebo-controlled trial for individuals with genetically confirmed LGMD2I/R9 measuring patient response to treatment by measuring both biomarkers and clinical assessments. For every three study participants, two will receive BBP-418 and one will receive placebo.

About the Therapy

In patients with LGMD2I, the enzyme FKRP does not work properly. FKRP is responsible for a critical step in a process called "glycosylation", whereby a crucial string of sugars are added to alpha dystroglycan (α-DG). Without this string, α-DG does not work correctly in its role as a "shock absorber" for muscle fibers. BBP-418's theoretical mechanism of action supplements the FKRP enzyme by adding more of the molecule that FKRP normally reacts with to drive residual activity of FKRP and helping it to stabilize muscle cells and act as a shock absorber. BBP-418 is an investigational therapy and is not yet approved by any health authorities for the treatment of LGMD2I/R9.

Who Can Participate

You may be eligible to participate in Fortify if you:

- Have a genetically confirmed diagnosis of LGMD2I/R9
- Are 12 to 60 years of age
- Have not used ribose or systemic corticosteroids prescribed for the treatment of LGMD or other investigational therapies for the treatment of LGMD within 90 days of screening

There are other requirements to participate in Fortify. A physician or study team member will help determine if you are eligible to participate and if this study is a good fit for you. Speak with your physician about your ability to participate in Fortify.

Fortify Locations:

The trial will be conducted at clinical sites in the United States and Europe.

Additional information about our BBP-418 study is available at **www.clinicaltrials.gov** and at **www.mlbsolutions.com**.

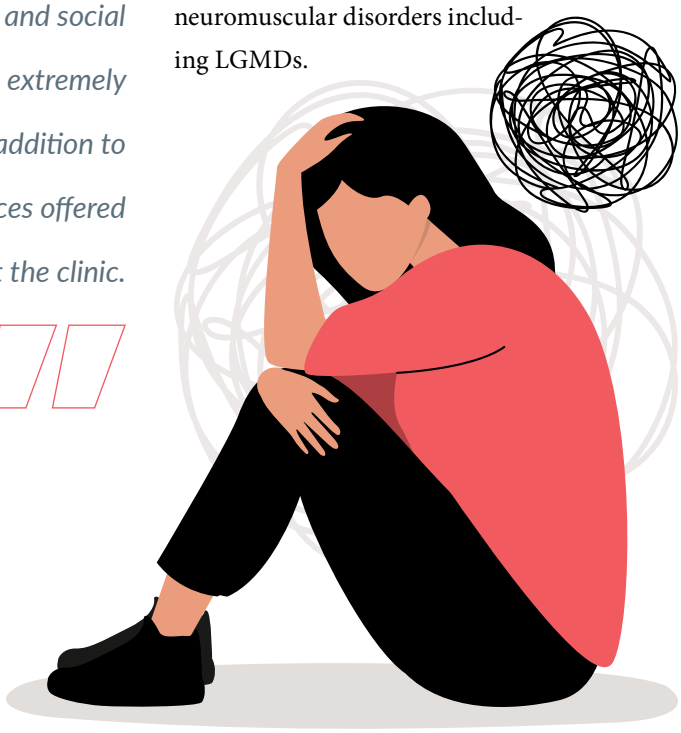
Scan to visit our website

ML Bio Solutions

Addressing Mental and Emotional Health Helps a Multidisciplinary Clinic Better Meet Patients' Needs

Children may have significant impairment in their quality of life and experience coping difficulties leading to distress. Too often, medical teams remain unaware of this until it becomes a severe issue. Thus, providing mental, emotional, and social support is an extremely important addition to the services offered at the clinic.

As director for Carolina's MDA Care Center, I have worked to establish a comprehensive multidisciplinary pediatric neuromuscular care program. Furthermore, I built clinical teams including many pediatric subspecialties such as cardiology, pulmonary, genetics, physiatry, gastroenterology, endocrinology, and palliative care, as well as an allied team of physical, occupational, respiratory and speech therapists, nutritionists, and social workers. Procedures like echocardiograms (echo), pulmonary function testing, and lab work are done in conjunction with clinic visits. This effort has helped to eliminate the need for patients to frequently travel to multiple doctors' appointments and tests. Thus, the clinic has become a flagship, one-stop care center for patients with hereditary neuromuscular disorders including LGMDs.



However, we have realized that many of our patients and their caregivers are impacted at multiple fronts, physically and mentally, due to the burden of their disease. Children may have significant impairment in their quality of life and experience coping difficulties leading to distress. Too often, medical teams remain unaware of this until it becomes a severe issue. Thus, providing mental, emotional, and social support is an extremely important addition to the services offered at the clinic.

To facilitate instituting mental health screening and early intervention, the division of Pediatric Psychology recently introduced a novel, electronic distress screener developed for pediatric subspecialty patients 8-21 years of age termed *Checking IN*. It assesses a wide range of domains in about 5-7 minutes, including: Anxiety, Depression, Anger, Attention, Sleep, Fatigue, Pain, Faith, Body Image, School, Family/Peer relationships, and Medication Adherence.

The screener then provides a summary report which helps us to facilitate conversations with patients and/or their families regarding their mental and emotional well-being. Based on this assessment and discussions, when indicated, a psychology referral is made, and a psychologist typically follows up with the patient within 72 hours. Attending not only to patients' physical but also mental health has improved their care in a multifaceted way. ■

Written by Urvi Desai, MBBS, MS, MD, FAAN
Director of the Carolinas MDA Care Center
Professor of Neurology, Wake Forest University School of Medicine

UPDATED: JANUARY 1, 2024

Active GRASP-LGMD Natural History Studies

Recruiting:

Defining Clinical Endpoints in Limb-Girdle Muscular Dystrophy (LGMD) (GRASP-01-001)

Inclusion Criteria

- Ages 4–65
- Clinically affected (defined as weakness on bedside evaluation in either a limb-girdle pattern or in a distal extremity)
- Genetic confirmation of one of the LGMD subtypes listed below

Exclusion Criteria

- Any other illness that interferes with subject safety or data integrity
- Positive pregnancy test at any timepoint of the study

Subtypes

- CAPN3 (LGMD R1/2A)
- DYSF (LGMD R2/2B)
- DNAJB6 (LGMD D1/1D)
- Sarcoglycan (LGMD R3/2D, LGMD R4/2E, LGMD R5/2C, LGMD R6/2F)

Recruiting:

Defining Endpoints in Becker Muscular Dystrophy (GRASP-01-002)

Inclusion Criteria

- Ages 8 and older
- Clinically affected (defined as weakness on bedside evaluation consistent with BMD)
- Genetic confirmation of a dystrophin mutation

Exclusion Criteria

- >16 hours of ventilatory support
- Any other illness that interferes with subject safety or data integrity

Note: Subjects ages 8-16 must be ambulatory and their dystrophin mutation must be in-frame.

Note: Subjects 17 and older may be non-ambulatory, but must not have lost ambulation prior to the age of 16.

Recruiting:

Trial Readiness and Endpoint Assessment in LGMD R1/2A (GRASP-01-003)

Inclusion Criteria

- Ages 12–50
- Clinically affected (defined as weakness on bedside evaluation in a pattern consistent with LGMD R1/2A)
- Genetic confirmation of LGMD R1/2A (presence of homozygous or compound heterozygous pathogenic mutations in CAPN3)

Exclusion Criteria

- Have contraindications to MRI
- Non-ambulatory, defined as unable to safely walk 10 meters without assistive devices (ankle foot orthotics allowed)
- Positive pregnancy test at any timepoint during the trial
- Have dominantly inherited CAPN3 mutations (i.e. LGMD D4)
- Any other illness that would interfere with subject safety or data integrity

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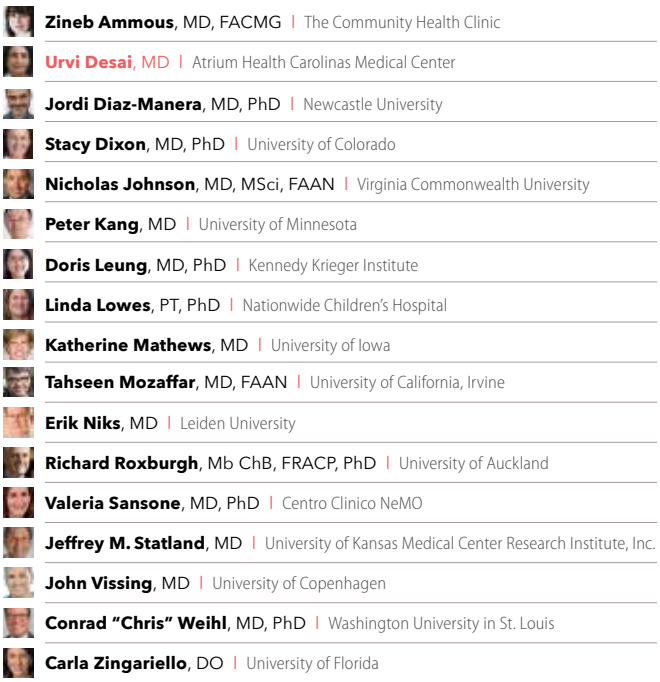
GRASP-LGMD Consortium Members



- **Zineb Ammous**, MD, FACMG | The Community Health Clinic
- **Urvi Desai**, MD | Atrium Health Carolinas Medical Center
- **Jordi Diaz-Manera**, MD, PhD | Newcastle University
- **Stacy Dixon**, MD, PhD | University of Colorado
- **Nicholas Johnson**, MD, MSci, FAAN | Virginia Commonwealth University
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- **John Vissing**, MD | University of Copenhagen
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- **Carla Zingariello**, DO | University of Florida

Spotlight:
Dr. Urvi Desai

Wake Forest University School of Medicine

Dr. Urvi Desai is the Director of the Carolinas MDA Care Center and Professor of Neurology at Wake Forest University School of Medicine. She obtained her graduate medical degree at MS University, India followed by residency in Neurology and fellowship in Neuromuscular Disorders at UNC Chapel Hill. She has established cross-sub-specialty physician and allied health team collaborations in multidisciplinary Adult and Pediatric MDA clinics at Atrium health. She serves on the Advisory Board for the North Carolina site for MD Star Net, a CDC-funded network that conducts public health surveillance of muscular dystrophy. Her research interests include researching overlap of sleep and neuromuscular disorders to help deploy early, non invasive ventilation. She also serves as the principal investigator for multiple trials, in MG, CIDP, DMD, SMA, hereditary TTR Amyloidosis, and LGMDs (dysferlinopathies, 2I/R9, 2E/R4).

SAREPTA THERAPEUTICS

Genetics 101: The Role of Genes in Limb–Girdle Muscular Dystrophies (LGMDs)

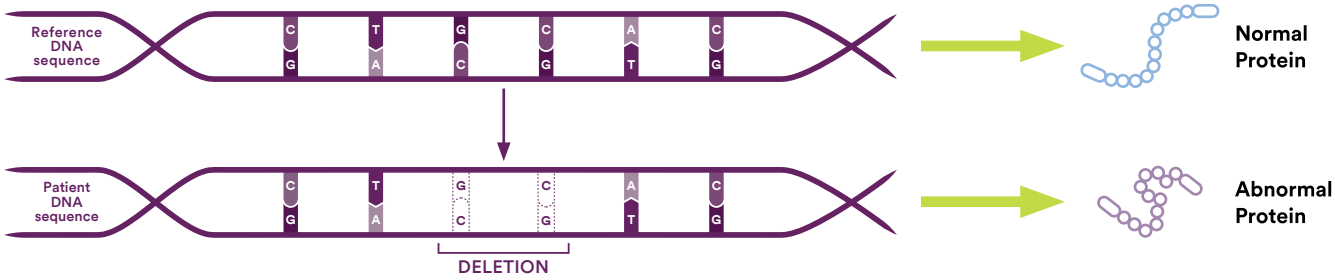
What is a gene?

A gene is a small segment of DNA that contains the instructions for your body to make proteins. These proteins are responsible for carrying out the jobs needed for your cells, tissues, and organs to work properly. There are over 20,000 genes in humans, and no two people have the exact same DNA sequence.

Note: Illustration does not represent a full gene

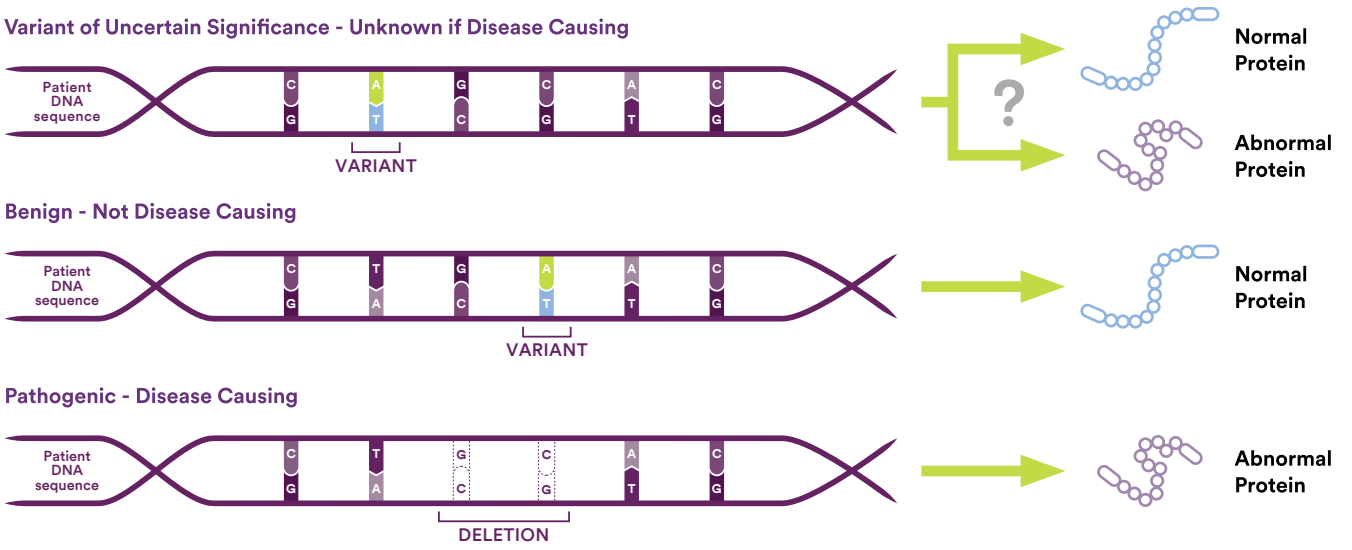
What is a genetic variant?

A genetic variant is a permanent change in a DNA sequence. Variants can occur randomly because cells do not perfectly copy DNA every time. Due to this, not all variants are inherited. A *de novo* variant is an alteration in the genome of an individual that was not inherited from their parents. Different classifications of variants can be found below.



Several types of variants, or permanent changes in DNA, might show up on genetic test reports:

- When that change is causing disease, the variant is called “pathogenic” or “likely pathogenic”. Disease-causing variants are often referred to as “mutations,” though this terminology does not appear in genetic testing reports.
- When that change is not causing disease, the variant is called “benign” or “likely benign”. Some of these changes are what make each of us unique, as our genes control things like eye color and blood type.
- When there is a case in which it is not known whether a specific DNA variant causes disease or not, the DNA change is called a “Variant of Uncertain Significance” or VUS/VOUS.



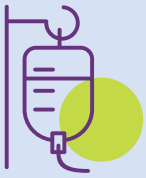
What role does genetics play in LGMDs?

LGMDs are genetic diseases: there are 30+ subtypes of LGMDs, each caused by disease-causing variants in specific genes that code for proteins that are important for muscle function.

Why is it important to know which genetic variant is causing your LGMD?

Knowing which one of the LGMDs you have has many benefits. Since each subtype of LGMD has different risks, rates of progression, and inheritance, knowing the subtype can help your doctor personalize care for your disease and identify which member(s) of your family could be at risk for developing the same condition you have. Knowing your subtype and specific variant may also be required to participate in potential clinical trials, real world evidence studies, natural history studies, or to be eligible for potential future treatments.

Understand Risks and Prognosis



Clinical Trial Options

Family Planning Considerations

How do I learn my genetic subtype of LGMD?

There are many laboratories that offer genetic tests that are appropriate for people suspected of having a form of muscular dystrophy, including many of the LGMDs. Generally, these tests are called “neuromuscular disease” panels. These genetic tests can only be ordered by a healthcare provider: ask your doctor or genetic counselor about genetic testing.

Learn more about genetic testing at limbgirdle.com/genetic-testing

Written By **Robert Muni Lofra**, PT, PhD
Consultant Physiotherapist, Honorary Clinical Senior Lecturer

and Professor **Jordi Diaz Manera**, MD, PhD
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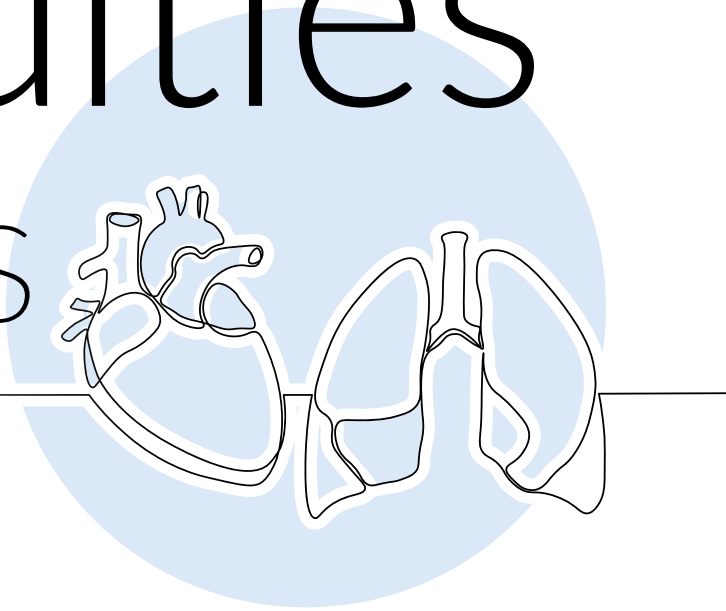
Long-Term Study from Newcastle, UK Shows the Importance of Monitoring for

Breathing Difficulties in LGMDs



Individuals with limb-girdle muscular dystrophies (LGMDs) typically experience muscle weakness, particularly in the muscles around the shoulders and hips. The severity of symptoms can vary among patients, with some facing greater mobility challenges than others. In some genetic types of LGMDs, muscles responsible for breathing and heart function may also be affected, although our understanding of how these complications evolve in most LGMD cases remains limited.

Not feeling rested when you wake up in the morning, having daytime sleepiness or recurrent morning headaches are some of the main symptoms of under-breathing overnight.

The primary objective of our study was to investigate the respiratory function of individuals with LGMDs and how this function changes over time. Understanding these changes may aid in predicting disease progression and improving patient care, as well as facilitating the development of more effective treatments for LGMDs.

Key Points of the Study:

- **Study Population:** The study focused on patients diagnosed with LGMDs who had pathogenic variants in the following genes: CAPN3 (Calpain 3; LGMDR1/2A), DYSF (Dysferlin; LGMDR2/2B), FKRP (Fukutin Related Protein; LGMDR9/2I), ANO5 (Anoctamin 5; LGMDR12/2L), SGCA, SGCB, or SGCG (Sarcoglycanopathies Alpha, Beta and Gamma; LGMDR3/2D, LGMDR4/2E, LGMDR5/2C). The reason for this is that they are the most common LGMDs in our group of patients. Data collection spanned from April 2002 to October 2020, with regular follow-up visits occurring every 12 to 18 months.
- **Approval and Protocol:** The study was approved as a review of services provided by a hospital in Newcastle upon Tyne, United Kingdom. The aim is to utilize the data to inform decisions related to managing respiratory issues in LGMD patients.
- **Respiratory Function Assessment:** The research team assessed respiratory function using a spirometer to measure breathing capacity and check cough strength. Specific values were used to identify breathing difficulties. The study also documented whether patients required respiratory assistance, such as non-invasive ventilation (NIV) or tracheostomy, and if they had concurrent respiratory conditions like asthma.
- **Statistical Analysis:** The data collected were subjected to statistical analysis, which included comparisons between different patient groups and an examination of how respiratory function changed over time.

In simpler terms, the study aimed to track changes in respiratory function over time in people with specific LGMDs. The study evaluated patients' respiratory function through assessments such as spirometry and cough strength tests. The ultimate goal is to gain insights into managing respiratory issues in LGMD patients.

The research focused on 156 patients diagnosed with LGMDs with varied ages and disease duration. At the beginning of the study, only patients with mutations in the FKRP gene displayed respiratory problems, which were more severe compared to other patient groups. Some patients exhibited breathing difficulties when lying down, suggesting issues with their diaphragms. Over time, most patients experienced a decline in respiratory function, with some requiring NIV (bi-level ventilation which can include BPAP or a portable ventilator).

"In simpler terms, the study aimed to track changes in respiratory function over time in people with specific LGMDs."

The graph in Figure 1 shows the predicted respiratory function vs. patient age, which is different for each of the LGMDs. Typically, patients will require breathing assistance when their forced vital capacity (FVC) drops below 50% of the predicted value, but this will vary. Patients should consult their specialist for advice on their case.

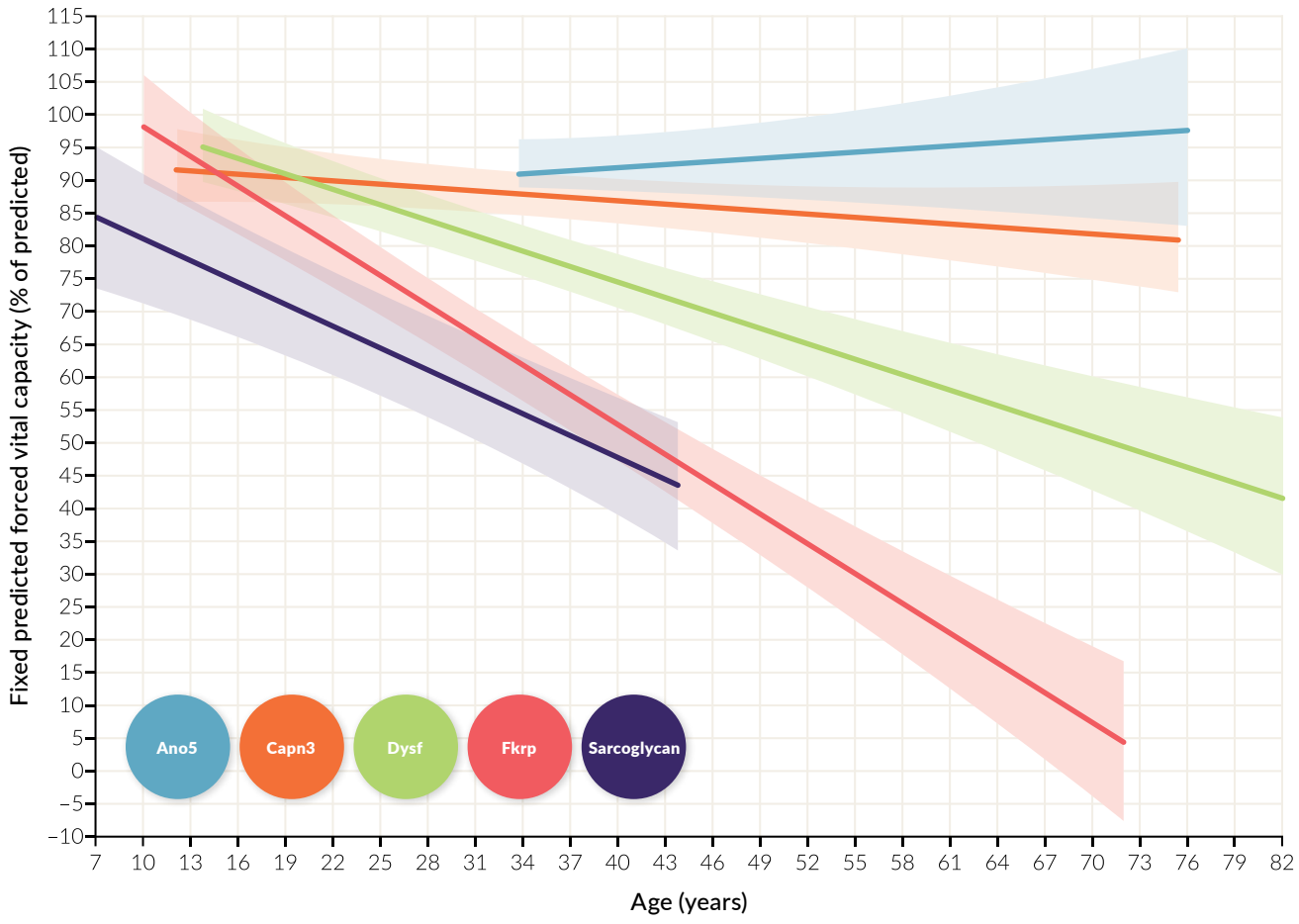


Figure 1: Progression of forced vital capacity percentage predicted values during the follow-up

This study monitored 104 patients for several years, with 36 consistently experiencing respiratory issues throughout the study period. The age at which respiratory function deteriorated varied between LGMD subtypes, with FKRP and sarcoglycanopathy patients exhibiting earlier and more frequent respiratory impairment.

Similar to respiratory function, cough strength also declined during the study. Notably, ANO5 patients were the only group that did not experience a decline in cough strength. All other LGMD types exhibited a reduction in cough strength over time.

Figure 2 shows the predicted progression in cough strength. Patients typically require cough assistance when their cough strength drops below 270 L/min (dotted line in the graph). Again, patients should consult their specialist for advice on their case.

In the study, we attempted to identify variables that could predict which patients might develop respiratory problems or require ventilation assistance, but we were unable to find any variable that could predict this.

In brief, we closely monitored 156 patients with LGMDs over an average period of 8.3 years, specifically tracking changes in their respiratory function and cough strength over time. We observed that certain LGMD types were associated with more significant respiratory problems, which worsened with age. Additionally, the study explored the feasibility of using a predictive test for respiratory issues but found it to be less reliable. Respiratory

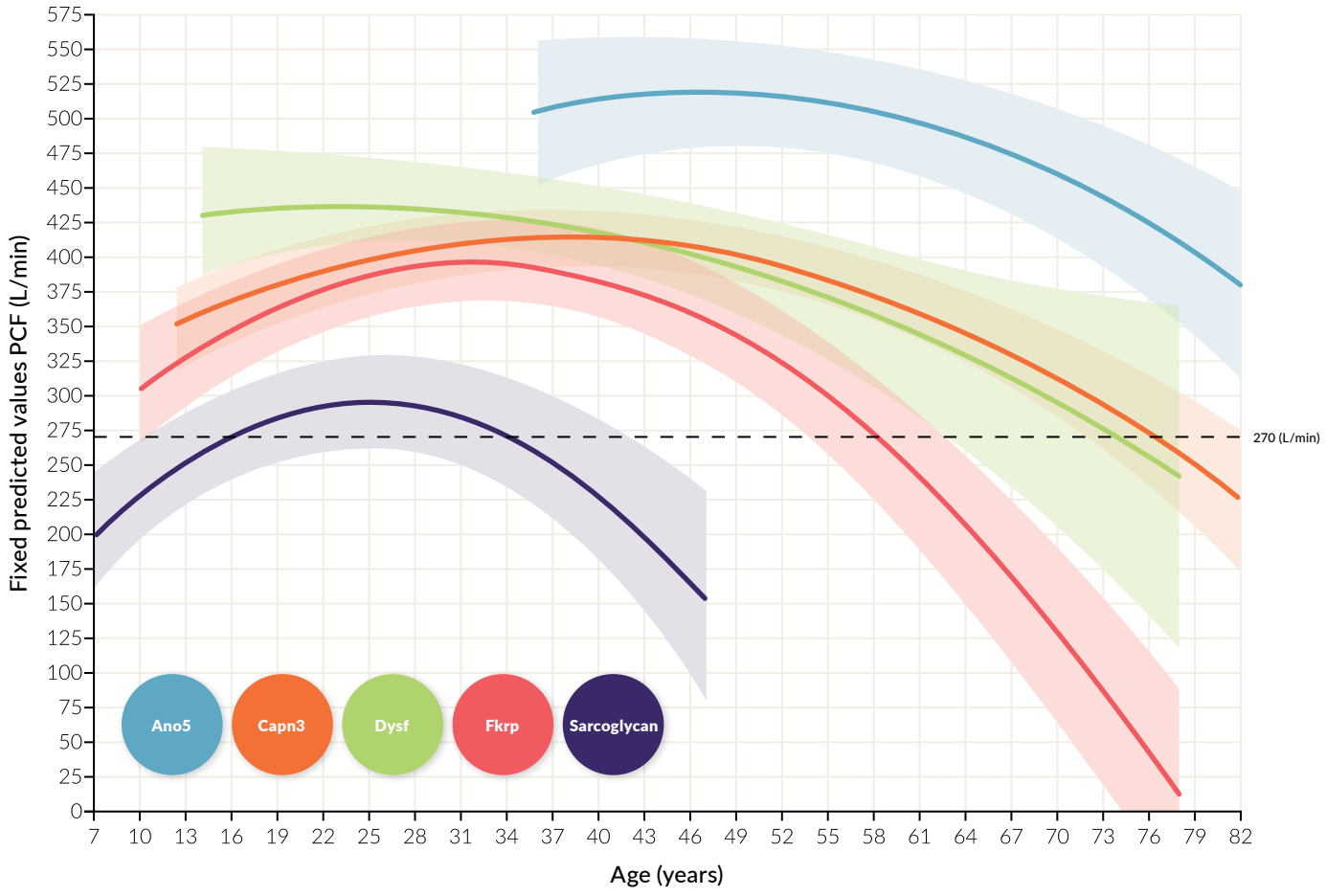


Figure 2: Progression of peak cough flow percentage predicted values during the follow-up

function tests and clinical assessments were employed to discern variation in lung function at the study's outset and its evolution over time, contingent on the specific LGMD subtype.

Patients with gene mutations in CAPN3, DYSF, FKRP, and sarcoglycanopathy genes exhibited a decline in lung function over time. Notably, FKRP and sarcoglycanopathy patients experienced a swifter decline in respiratory function, while CAPN3 and DYSF patients displayed a slower decline. Conversely, ANO5 patients sustained a relatively stable lung function throughout the study.

The study's findings align with prior research indicating that FKRP patients tend to experience more pronounced respiratory issues. Among sarcoglycanopathy patients, a substantial proportion initially presented with respiratory problems, particularly in mucus clearance (coughing), yet the percentage requiring NIV was lower than what was reported in other studies.

DYSF patients exhibited varying degrees of respiratory decline, with some studies indicating a gradual deterioration and others suggesting more severe issues. CAPN3 patients displayed heterogeneous patterns, with some retaining stable lung function, while others experienced a significant decline, with no discernible clinical distinction between these groups. ANO5 patients notably maintained stable lung function, albeit with a marginal reduction over time.

The study identified LGMD subtype, patient age, and ambulatory ability as factors linked to declining lung function. Smoking and other concurrent respiratory conditions did not appear to significantly influence the rate of decline, although only a small number of patients in the study smoked. This is likely related to the small number of patients that smoke, more than to the proven, negative impact of smoking on respiratory function.

Interestingly, spirometry tests did not prove consistently effective in predicting respiratory symptoms or the need for ventilation assistance. Note that the tests in the report were conducted upright, because supine tests were only started more recently, and there is not enough data to include them in the analysis at this point.

“Patients with gene mutations in CAPN3, DYSF, FKRP, and sarcoglycanopathy genes exhibited a decline in lung function over time. Notably, FKRP and sarcoglycanopathy patients experienced a swifter decline in respiratory function, while CAPN3 and DYSF patients displayed a slower decline. Conversely, ANO5 patients sustained a relatively stable lung function throughout the study.”

In conclusion, this study delved into the longitudinal changes in lung function among LGMD patients. It unveiled disparities between LGMD subtypes and identified factors that might aid in predicting the development of respiratory complications. Regular assessments of lung function, even in the absence of overt symptoms, could prove pivotal in the effective management of LGMDs. ▪

Additional Resource: Full Paper

www.ncbi.nlm.nih.gov/pmc/articles/PMC10335843/pdf/NXG-2023-000025.pdf

Do you or does someone you know have LGMD2I/R9?

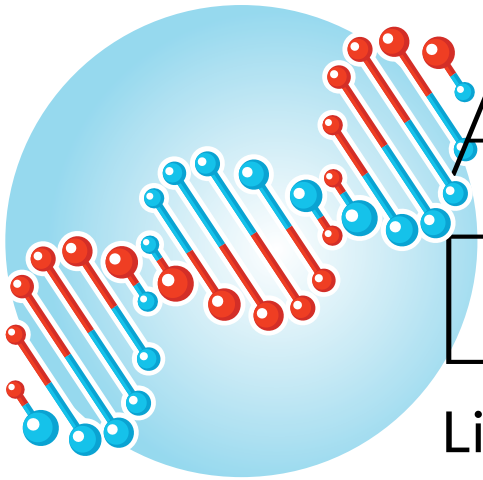
AskBio will be conducting a clinical study of an investigational gene therapy for individuals with a confirmed genetic diagnosis of LGMD2I/R9.

- This is a one-time intravenous infusion of gene therapy designed to produce fukutin-related protein (FKRP) in the body, primarily in muscle.
- Part 1 of the study will assess the safety of LION-101 only in adults (ages 18 and 65 years).
- This is a randomized, placebo controlled, double-blind study.
- The study is designed to investigate at least two different doses of LION-101 versus placebo.
- The initial phase of this first-in-human dose-finding study will be conducted in the US.
- Travel to study sites may be reimbursed; local and home-based testing will be used when possible.
- Information on the clinical trial can be found on clinicaltrials.gov.

To learn more, please visit AskBio.com, email AskFirst@AskBio.com or go to clinicaltrials.gov (NCT05230459)

AskBio™

Written By Andrew Findlay, MD
Washington University St. Louis



Autosomal Dominant

Limb-Girdle Muscular Dystrophies

Clinical Features & Inheritance Patterns of Dominant LGMDs

Dominantly inherited limb-girdle muscular dystrophies (LGMD) have a broad range of clinical features. Dominance refers to the inheritance pattern for this set of disorders. For non-sex chromosomes (X, Y), everyone has two sets of genes, one inherited from each parent. For diseases with recessive inheritance, it takes two pathogenic variants, one on each copy of a gene, to cause disease. For dominantly inherited disorders, it only takes one mutated copy of a gene to cause disease. This means an individual affected by a dominantly inherited disease has a 50% chance of passing the disease on to their child. For recessive subtypes, by contrast, a person generally must inherit a mutation from both parents to have the disease.

Several Broad Generalizations Can Be Made About Dominant LGMDs:

1. They account for about 10% of all LGMD cases.
2. They more commonly have adult onset compared to recessive forms.
3. The diseases typically progress more slowly over time compared to recessive LGMDs.
4. Affected individuals are often in good health at reproductive age. This commonly results in extensive family trees with many affected individuals due to the disease being passed from generation to generation.

Dominant LGMD Nomenclature

In the prior LGMD nomenclature system established in the 1990s, dominantly inherited subtypes were indicated by a 1, followed by a letter based on the order of discovery (e.g., LGMD 1D). With the new nomenclature, dominant inheritance is indicated by a D, followed by a number (e.g., LGMD D1). Several disorders originally labeled as LGMD are no longer classified as LGMDs in the new nomenclature system, as shown in the table. These re-categorized disorders can absolutely cause weakness in a limb-girdle pattern, but their primary clinical manifestations are commonly something different (e.g., distal predominant weakness affecting feet and hands). As new causes for dominantly-inherited muscle disorders continue to be discovered (e.g., mutations in DTNA gene), the list of dominant LGMDs will likely continue to grow.

Old Nomenclature	New Nomenclature	Gene	Protein
LGMD1A	Myofibrillar myopathy	*MYOT*	Myotilin
LGMD1B	Emery Dreifuss Muscular Dystrophy	*LMNA*	Lamin A/C
LGMD1C	Rippling muscle disease	*CAV3*	Caveolin 3
LGMD1D	**LGMDD1 DNAJB6-related**	***DNAJB6***	**DNAJB6**
LGMD1E	Myofibrillar myopathy	*DES*	Desmin
LGMD1F	**LGMDD2 TNPO3-related**	***TNPO3***	**Transportin 3**
LGMD1G	**LGMDD3 HNRPDL-related**	***HNPRDL***	**Heterogeneous nuclear ribonucleoprotein D-like**
LGMD1H		False linkage	
LGMD1i	**LGMDD4 Calpain3-related**	***CAPN3***	**Calpain 3**
Bethlem Myopathy (dominant)	**LGMDD5 Collagen VI-related**	***COL6A1-3***	**Collagen VI**

Table 1: Dominant LGMD Nomenclature

Dominant Disease Mechanisms

Recessively inherited LGMDs are usually caused by mutations resulting in either the absence of the protein or rendering the protein non-functional. These mutations are therefore broadly referred to as causing a "loss of function." In contrast, dominantly inherited disorders can be caused by at least three different mechanisms. In a simplified form, these are as follows:

1. Haploinsufficiency refers to disorders where a mutation on one copy of the gene causes only half the normal amount of functional protein to be produced, and this is insufficient for normal cellular function.
2. A toxic or gain-of-function mechanism results from mutations that either increase the protein's activity, prolong its stability (and thereby increase its effect in the cell), or cause it to gain some additional toxic function unrelated to its normal role.
3. A dominant-negative mechanism results from mutations that negate the activity of the normal copy of the protein. This mechanism is often seen with proteins that group together. The protein complex containing mutant proteins is non-functional, even though it also contains normal proteins.

Therapeutic Strategies for Dominant LGMDs

Currently, there are no approved therapies or clinical trials involving treatments for any of the dominant LGMDs. However, several pre-clinical studies have been completed, investigating treatments for these LGMDs in cells and animal models. The disease mechanisms described above are the basis for the rationale behind the various treatment strategies for dominant LGMDs.

For recessively inherited disorders, gene transfer therapy (where a new, functioning copy of the gene is provided to an individual's cells) will, in theory, be helpful. This approach can also be helpful in the case of dominant disorders caused by haploinsufficiency, where only half the normal amount of functional protein is produced. However, gene transfer therapy wouldn't be expected to help in diseases caused by gain-of-function or dominant-negative mechanisms.

Another approach, called "knockdown," uses chemicals that bind to RNA from the mutated gene to prevent the mutant protein from being produced. This approach is well-suited to dominantly inherited diseases caused by toxic, gain-of-function, or dominant-negative mechanisms.

A variety of knockdown approaches exist. Which approach is best-suited for a disease depends on how much of the affected protein is required for a cell to function normally.

- ➔ If complete absence of the mutant protein is tolerated, a knockdown approach that targets both copies of a gene (both healthy and mutated) can be beneficial for a dominantly inherited disease.
  - LGMD1A is caused by mutations in a protein called myotilin, causing it to misfold and aggregate within muscle. Interestingly, absence of myotilin does not cause abnormalities in mouse skeletal muscle. Mice expressing a mutant *MYOT* gene found in LGMD1A patients were treated with an artificial microRNA (miRNA) targeting human *MYOT* mRNA. This significantly reduced the mutant myotilin levels, improved muscle pathology, reduced protein aggregates, and improved strength in the mice.
- ➔ If at least 50% of the normal protein levels are needed for cellular health, a knockdown treatment that targets only the mutant copy of the gene (allele specific) can be used.
  - LGMDD5 (Bethlem myopathy) is most commonly caused by dominant-negative mutations in the Collagen VI genes. Collagen VI is a key component of the extracellular matrix surrounding muscle fibers. These dominant-negative mutations disrupt assembly of the Collagen VI microfibrils from its three subunits. Collagen

VI is needed for muscles to function correctly, so a total knockdown of the gene isn't a good treatment approach. Selective knockdown of just the mutant allele, however, is a promising treatment strategy for dominant Collagen VI-related dystrophies (and other disorders with dominant-negative mechanisms). Several different approaches are being pursued to apply this strategy to Collagen VI dystrophies.

- Preclinical studies in LGMDD1 have used a slightly different therapeutic approach. LGMDD1 is caused by dominantly inherited point mutations in DNAJB6, a chaperone protein that plays an important role in cellular health by maintaining other proteins in their proper shape and preventing them from aggregating. There are two different versions (isoforms) of the DNAJB6 protein. DNAJB6a is a larger version of the protein that is found mainly within cell nuclei, while DNAJB6b is a smaller version of the protein that localizes to a portion of muscle fibers called the Z-disc. It is thought that DNAJB6b may be primarily responsible for disease pathogenesis in LGMDD1. This is supported by the fact that DNAJB6b is the isoform that localizes to the main site of pathology seen in human biopsies. It's known that an absence of DNAJB6 in mouse embryos prevents them from developing, arguing against using complete knockdown as a treatment strategy. A therapeutic approach involving selective knockdown of the DNAJB6b isoform in LGMDD1 mouse myotubes (muscle precursor cells grown in a dish), resulted in improvement in some of their disease-related abnormalities. The next step will be to test the isoform-specific knockdown in living mice.

→ If more than 50% of the normal protein level is required for cellular health, then a treatment involving complete knockdown of the gene while simultaneously providing a replacement copy of the gene resistant to knockdown can be beneficial. Although it has not been tested in dominant LGMDs, this approach has been found to be beneficial in mouse models of several other dominantly inherited neuromuscular disorders.

Barriers to Developing Treatments for Dominant LGMDs

While the promise of gene-based therapies is becoming a reality, research into these therapies for LGMDs has thus far focused primarily on recessive forms. The gene replacement strategies that are commonly employed for recessive, loss-of-function disorders are not readily translatable to most dominant forms of LGMD, hindering the development of novel treatments for dominant LGMDs. Additionally, dominantly inherited disorders have complex, heterogeneous disease mechanisms as discussed above and, thus, require unique therapeutic approaches. These approaches are not as developed as replacement therapies used for recessive LGMDs.

Also, even if a promising therapy were suddenly available, the natural histories of most dominantly inherited LGMDs are not well characterized yet. Nevertheless, some progress has been made in characterizing the natural history of LGMDD1: recent studies have found that different disease-causing mutations are associated with variable ages of onset, as well as different weakness patterns, where some individuals have weakness in their feet and hands instead of their hips and shoulders. It was also found that particular mutations are associated with different rates of disease progression.

Comparable studies for other dominant LGMDs are lacking and current clinical information are limited to descriptions of individual cases. Characterizing the natural history of disease progression is critically important to identify ideal outcome measures for future clinical trials. Overall, the variability in disease severity and the rarity of all dominantly inherited LGMDs highlight the need for participation in future natural history studies and eventual clinical trials. ■

Assessments in Clinical Trials

By **Douglas Sproule, MD, MSc**
Chief Medical Officer,
ML Bio Solutions

Clinical trials are research studies that evaluate the safety and efficacy of new investigational drugs. Investigational drugs, also called "experimental drugs," are drugs being studied to see if a disease or medical condition improves while taking it. Assessments are medical procedures performed during a clinical study and are an important part of clinical trials. Information (data) obtained from assessments is used to measure the safety and efficacy of a new investigational drug or to gather data about the disease or condition being studied.

Assessments can be performed throughout the duration of the clinical study. Before a clinical study participant receives the investigational drug, a baseline assessment is performed to determine the burden of the disease on the individual before exposure to the investigational drug. For example, the 12-lead ECG assessment is a non-invasive test that records the electrical activity of the heart from 12 different angles. The 12-lead ECG is taken at baseline (starting point) and then again throughout the clinical study at set intervals to monitor the effectiveness of worsening heart disease in people at high risk. Baseline assessments are critical as they serve as a comparator for assessments performed during the clinical trial when the study participant is actively taking the investigational drug or placebo. A placebo can be anything that looks or feels like a real medical treatment but does not contain any active ingredients.

Types of Assessments

There are many different types of assessments that can be used in clinical trials. Some common types of assessments include:

Physical examinations involve a healthcare professional checking the participant's vital signs such as heart rate, blood pressure and temperature, as well as their overall health and well-being.

Blood tests involve collecting samples of the participant's blood. For example, a blood test can measure changes in glucose levels in patients with diabetes.

A muscle biopsy is a procedure to remove a small sample of muscle tissue from the body for examination under a microscope or for measurement of specific substances or markers in the tissue. This can be used to monitor the progression of muscular dystrophy over time or potentially to assess the response to an investigational drug.

Patient-reported outcome measures (PROMs) are questionnaires or other tools that are used to assess the participant's experience of their disease and the impact that it has on their life, and the impact of a potential therapy on their quality of life.

Why are Assessments Done in Clinical Trials?

Assessments are done in clinical trials for several reasons, including:

To measure the safety and efficacy of the investigational drug:

Assessments allow researchers to track the participant's condition over time and to identify any potential side effects of the treatment. They also allow researchers to evaluate efficacy by comparing the clinical study participants receiving the investigational drug to the clinical study participants receiving a placebo.

To gather data to support the approval of the new investigational drug:

If a clinical trial is successful, the data from the assessments can be used to support the approval of the treatment by regulatory agencies, such as the US Food and Drug Administration (FDA).

To advance medical knowledge:

Assessments can help researchers to learn more about the disease and how it responds to treatment. This information can be used to develop new and improved treatments in the future.

Impact of Incomplete or Missing Assessments on Clinical Trials

Incomplete assessments can have a significant impact on clinical trials. If a participant misses an assessment, or if an assessment is not completed properly, the researchers may not be able to accurately assess the safety and efficacy of the investigational drug. This can lead to inaccurate results and can make it difficult to interpret the findings of the clinical research trial.

If a participant is unable to complete an assessment due to illness or other unforeseen circumstances, they should inform their healthcare team as soon as possible. The healthcare team may be able to reschedule the assessment for a later time or to use other methods to collect the data.

Conclusion

Participants in clinical trials should work with their study site healthcare team to ensure that they understand and are able to complete the study assessments. By doing so, they can help to ensure that the results of the trial are accurate and informative and that the investigational drug is able to be evaluated correctly. In this way, clinical study participants can help to advance medical knowledge and to improve the lives of patients with the disease being studied in the clinical trial.

Learn More About Muscle Biopsies in Clinical Studies:

Why are Biopsies Important in Clinical Trials?

LGMD News magazine, Volume 3, Issue 1 | Winter 2023 page 24

The LGMD Awards of Excellence recognize those who are leading the way with excellence in their field or category of service. These submissions were made by individuals living with LGMD who are being served by these companies or providers. We want to give the patient community the opportunity to shout out and celebrate those that they have had the best experiences with across seven categories. **Congratulations to the winners!**

The winner in each category is the provider or company who received the most nominations.

CATEGORY: NEUROLOGIST

WINNER: THREE WAY TIE FOR FIRST PLACE

Dr. Katherine Mathews
MD, FAAN

A neurologist and pediatrics specialist affiliated with the University of Iowa

Dr. Jerry R. Mendell
MD

Clinician-scientist (neurologist) with decades of experience, formerly affiliated with Nationwide Children's Hospital in Columbus, Ohio

Dr. Nicholas E. Johnson
MD, M.Sci., FAAN

Associate professor, division chief of neuromuscular, and vice chair of research in the department of neurology at Virginia Commonwealth University (VCU)

Category: Durable Medical Equipment (DME) Provider

Winner: National Seating & Mobility

About National Seating & Mobility

For more than 30 years, our primary focus has been on customizing chairs to meet the unique needs of our clients. However, we know that mobility goes beyond the chair. That is why we have expanded our mobility solutions to serve more people whose mobility needs range from simple to complex. We deliver personalized solutions to individuals with mobility challenges by bringing industry-leading expertise, uniquely engineered systems and breakthrough technologies. Our products and services provide independence and self-reliance to clients; reassurance to family and caregivers; and responsive, flexible and highly professional clinical support to our referral sources. More information is available at ***NSM-Seating.com****.*

Category: Neuromuscular Disease Center or Hospital

Winner: Nationwide Children's Hospital

About Nationwide Children's Hospital

Named to the Top 10 Honor Roll on U.S. News & World Report's 2023-24 list of "Best Children's Hospitals" (for the 10th consecutive year), Nationwide Children's Hospital is one of America's largest not-for-profit free-standing pediatric health care systems providing unique expertise in pediatric population health, behavioral health, genomics and health equity as the next frontiers in pediatric medicine, leading to best outcomes for the health of the whole child. Integrated clinical and research programs, as well as prioritizing quality and safety, are part of what allows Nationwide Children's to advance its unique model of care. Nationwide Children's has a staff of more than 14,000 that provides state-of-the-art wellness, preventive and rehabilitative care and diagnostic treatment during more than 1.7 million patient visits annually. As home to the Department of Pediatrics of The Ohio State University College of Medicine, Nationwide Children's physicians train the next generation of pediatricians and pediatric specialists. The Abigail Wexner Research Institute at Nationwide Children's Hospital is one of the Top 10 National Institutes of Health-funded free-standing pediatric research facilities. More information is available at ***NationwideChildrens.org****.*

Category: Pharmaceutical/Biotech Company

Winner: Sarepta Therapeutics, Inc.

About Sarepta Therapeutics, Inc.

Sarepta is a global biotechnology company on an urgent mission: to engineer precision genetic medicine for rare diseases that devastate lives and cut futures short. We're ushering in a new era of drug development with the goal of driving efficiencies, including shortening the time from lab to patient and building the world's largest gene therapy manufacturing capacity. We're collaborating with health networks and payers, rethinking pricing models for revolutionary new treatments in development. We are in a daily race to transform genetic understanding into genetic medicine, because every day is an opportunity to save lives stolen by rare disease. Sarepta is at the forefront of precision genetic medicine, with over 40 therapies in various stages of development. Our disease areas include six limb-girdle muscular dystrophies (LGMD). More information is available at ***Sarepta.com****.*

Category: Wheelchair Brand

Winner: Permobil

About Permobil

Our purpose is to innovate for individuals; to create advanced assistive solutions that make the lives of people living with disabilities more enriching. Our dedicated teams work tirelessly to make this happen, no matter if they are designing a new wheelchair, testing seating cushions, or supporting a therapist. Our main focus will always be on the users of our products and services - bringing independence to them by providing the best solutions for their needs. Permobil founder Dr. Per Uddén believed that helping individuals achieve the greatest level of independence is a basic human right and, for over 50 years, that has been the driving force behind our innovative power wheelchairs. As a doctor working in Sweden, Per met polio patients who were confined indoors, and he was passionate about finding a solution to help them. As a result, he created some of the first power wheelchairs! Today, Permobil wheelchairs are highly customizable to meet an individual's needs, and offer power functions, accessories, and connectivity to help end users live life to the fullest. More information is available at ***permobil.com/en-us****.*

Science Always Moves Forward

We will continue to lead future advocacy meetings toward our goal of ensuring that there are no unnecessary barriers to drug development.

There has been amazing progress made in developing therapies for LGMDs. Natural history studies for many forms of LGMD are currently underway and some subtypes already have 15 years of data. There are now potential treatments in Phase 3 trials for the first time for LGMDs. We are also seeing many new drug developers enter the LGMD space. This is a prayer answered and a dream come true for many.

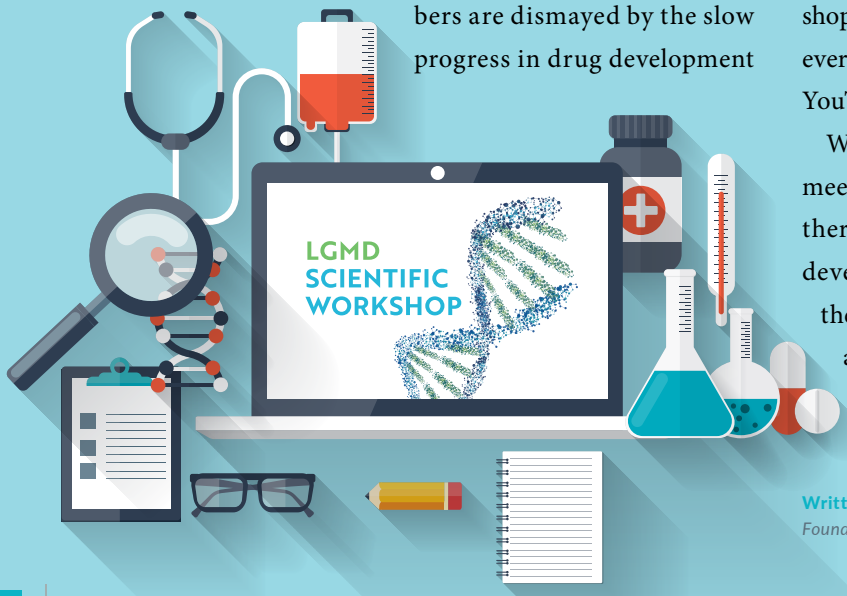
While science continues to move forward, the gears of the drug development process do not always stay in sync with recent developments. We need scientifically rigorous trials, but we must keep in mind the slowly-progressive nature of LGMDs, with variability between patients even within the same subtype. We also know that diseases with small patient populations often require special considerations in clinical trial design.

There are still no approved treatments for any LGMD subtype. Patients and family members are dismayed by the slow progress in drug development at a time when we can treat diseases at the genetic level and are seeing unprecedented advances in science.

To address the promise and the challenges of therapy development for LGMDs, we are convening a LGMD Scientific Workshop with multiple stakeholders on February 8, 2024. This meeting is a natural follow-up to the Externally-Led Patient Focused Drug Development (EL-PFDD) meeting held in 2021. This will be a closed workshop (by invitation only) for various stakeholders in the LGMD community, with FDA in attendance.

Many speakers, including FDA staff, GRASP LGMD researchers, drug developers with active Investigational New Drugs (INDs) for LGMDs, and other regulatory officials will be participating in this all-day event in Bethesda, Maryland. There will also be patient delegates from the LGMD community attending, some of whom will be giving presentations. The proceedings of the workshop will be recorded and made available for everyone to view on the Speak Foundation's YouTube channel.

We will continue to lead future advocacy meetings toward our goal of ensuring that there are no unnecessary barriers to drug development. It is our job as patients to be the loudest voice in the room at any event, and at Speak Foundation, we are supportive of all efforts from the drug development community. ■



Written by Kathryn Bryant Knudson
Founder & CEO, The Speak Foundation

Distinguished Scientific Leaders

in the LGMD community are coming together for a one-day workshop with the FDA to accelerate the path of drug development for Limb-Girdle Muscular Dystrophy.

FEATURED SPEAKERS

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

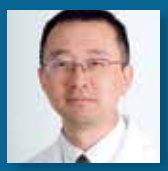
Peter Stein, MD
Director of CDER's Office of New Drugs (OND)
United States Food and Drug Administration (FDA)

Jerry R. Mendell, MD
Former, Attending Neurologist
Nationwide Children's Hospital

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

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

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



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

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

Douglas Sproule, MD, MSc
Chief Medical Officer
ML Bio Solutions

LGMD SCIENTIFIC WORKSHOP

Moving drug development forward for Limb-Girdle Muscular Dystrophy

The SPEAK Foundation
3551 Blairstone Road #105-62
Tallahassee FL 32301

Every Person Deserves Excellent Healthcare







This is why The Speak Foundation will be starting a Health Equity Grant program late Spring 2024

Many individuals with physical health conditions struggle with healthcare insecurity, marked by lack of access to quality care and the financial inability to travel. At the Speak Foundation, we believe that every person deserves excellent healthcare and that financial struggles should not prevent anyone from world-class care. The Health Equity Grant program will provide travel grants for qualified LGMD patients living in the United States to visit approved, leading centers of LGMD excellence. This program is provided in part by a grant from Sarepta Therapeutics.

The SPEAK Foundation

More details to follow in the Spring 2024 issue of *LGMD News*.