Vol 1 / Issue 1

LGMD News

Uniting the Limb Girdle Muscular Dystrophy Community

Respiratory Muscle Weakness in LGMD

Getting Appropriate Respiratory Care Improves Quality of Life and Prolongs Life

GRASP CONSORTIUM
Approaching Potential Treatments for Limb Girdle Muscular Dystrophy

LGMD2B
JAIN Foundation: Building a Registry Community

NATIONWIDE CHILDREN'S HOSPITAL
Advancing LGMD Research from Gene Therapy to Remote Assessments

The SPEAK Foundation

LGMD News

Vol 1 / Issue 1

How To Donate

Visit **TheSpeakFoundation.com** and select "Donate" to support our mission and programs. The Speak Foundation is a 501(c)3 non-profit charity. All donations are secure and tax deductible.

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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Getting Appropriate Respiratory Care Improves Quality of Life and Prolongs Life

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Comments, Questions, or Suggestions?
Jessica@TheSpeakFoundation.com

TheSpeakFoundation.com

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Twitter.com/SpeakFoundation
Twitter.com/LGMDFoundation

Join Our Mission to Cure LGMD

We want, as patients, to be a voice in the field and have an active, helpful role.

How long is this going to take? Like you, it has crossed my mind so many times that the process to obtain a treatment for our LGMD seems long and arduous. However, this magazine was formed to help give you hope, so you can see firsthand the potential treatments that are in development.

We are thrilled to present you with this inaugural issue of *LGMD News* magazine, a project that grew out of our desire to provide individuals with LGMD reliable information from the best sources. This magazine is geared to present only the best research to the population who need to hear it.

We want to trailblaze a path that creates a revolutionary methodology to finding treatments, where patients and researchers meet in the middle to advance treatment outcomes. We want, as patients, to be a voice in the field and have an active, helpful role.

There will come a day when people will say, "Remember when muscular dystrophy was incurable?" Friends, my hope and prayer for our community is we will live to see this day in our lifetimes. Join us as we pioneer a patient-led movement and help to see new treatments get on the market quickly and safely.

The Speak Foundation was established in 2008 with a clear mission in mind, "to speak up for those who have no voice." Nearly thirteen years later, this same mission continues to fuel our passion. Join us as we fulfill it. ■

Kathryn Bryant
Editor In Chief

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

Have you or someone you know been diagnosed with Limb Girdle Muscular Dystrophy Type 2I?

ML Bio Solutions is developing an oral therapy for Limb Girdle Muscular Dystrophy Type 2I (LGMD2I/LGMDR9).

A Lead-in Study (Natural History Study) is currently enrolling participants with LGMD2I. While there is no intervention in this study, participants will be eligible to participate in the late phase clinical trial of BBP-418 (Ribitol).

You may be eligible to participate in the Lead-in Study if you are 10-65 years old and have genetically confirmed LGMD2I.

Remote enrollment is available, all travel/study expenses are covered, and strict COVID safety precautions are observed.

ML Bio Solutions (ML Bio) is a biotechnology company founded by a family whose child was diagnosed with LGMD2I. ML Bio Solutions is a member of the BridgeBio family—a team of experienced drug discoverers, developers, and innovators working to create life-altering medicines that target genetic diseases.

Contact: Brittney.Holmberg@vcuhealth.org | 804-552-0014
info@mlbiosolutions.com | mlbiosolutions.com | clinicaltrials.gov

ML Bio Solutions
a bridgebio company

Looking Beyond Today.

Beyond Labels & Limitations is dedicated to looking beyond the current status of Limb-Girdle Muscular Dystrophy 2A. Our objective is to raise funds for scientific research and educate people about the progression of the disease and how it affects those struggling with it.

We believe there is a cure out there, and we will find it. We are hopeful for the future and the many possibilities it holds.

BEYOND
Labels & Limitations
What Is Your Life Devoted To

BeyondLabelsLimitations.com

Next Steps

Your Starting Point as a Newly Diagnosed Individual with LGMD

Each of these organizations is dedicated to finding treatments and to connecting people through subtype registries. You can contact any of these organizations for unique support to match your personal diagnosis.

The first thing you need to know is you are not alone. This magazine was created by the Speak Foundation to help you get connected into our already existing community of individuals living with Limb Girdle Muscular Dystrophy. There are over 30 different genetically distinct subtypes of Limb Girdle Muscular Dystrophy and it can be hard to find resources and clinical trials that are going on for your subtype. This magazine is the first source for you.

In this issue, on the page to the right, you will find the International Consortium of LGMD organizations that are specific to your subtype and working to find cures. Each of these organizations is dedicated to finding treatments and to connecting people through subtype registries. You can contact any of these organizations for unique support to match your personal diagnosis.

Furthermore, you will find information about researchers who are some of the best in the world, who conduct clinical trials through GRASP-LGMD. GRASP-LGMD is a consortium of doctors united to find a cure for LGMD. Your subtype of LGMD may be one of the forms in a current trial.

Last, the biotech and pharmaceutical companies developing therapies for LGMD are all included in this magazine. There are numerous companies working on a cure for various forms of LGMD. So there is hope. The Speak Foundation — we are a voice for LGMD. ■

LGMD Patient Network

Register at **TheSpeakFoundation.com** to receive updates on the Limb Girdle Muscular Dystrophy patient community. By registering, you will receive our magazine and many important resources to help you. We offer multiple programs to enhance your quality of life, such as the National LGMD Conference and the Personal Care Attendant Stipend Program. The Speak Foundation is a patient-led team of individuals who are living successfully with LGMD — we know firsthand the importance of ***community***.

International Consortium of LGMD Organizations

United States

The Speak Foundation
Uniting the entire LGMD community
TheSpeakFoundation.com

Beyond Labels & Limitations
Funding research for LGMD 2A/R1 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 2S/R18
CamronsCure.com

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

Cure LGMD2I
Funding research for LGMD 2I/R9
CureLGMD2I.org

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

LGMD Awareness Foundation
Join us for LGMD Awareness Day
LGMD-Info.com.org

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

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

LGMD2I Research Fund
Funding research for LGMD 2I/R9 and educating the patient community
LGMD2IFund.org

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

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

Argentina

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

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 1F/D2
ConquistandoEscalones.org

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

Italian Association Calpain 3
Funding research for the LGMD 2A/R1 Calpain3-related community
AICA3.org

Japan

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

Spain

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

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

JOIN OUR FAMILY.

Family Group of Beta-Sarcoglycanopathy

LGMD2E/R4 Bèta-Sarcoglycan-Related

We are families living with LGMD2E/R4 and other forms of limb girdle muscular dystrophies who are dedicated to help promote and finance scientific research projects aimed at treating these devastating diseases.

Keep informed on the latest LGMD2E/R4 news, research activities, and fundraising information by registering with our GFB Patient Registry.

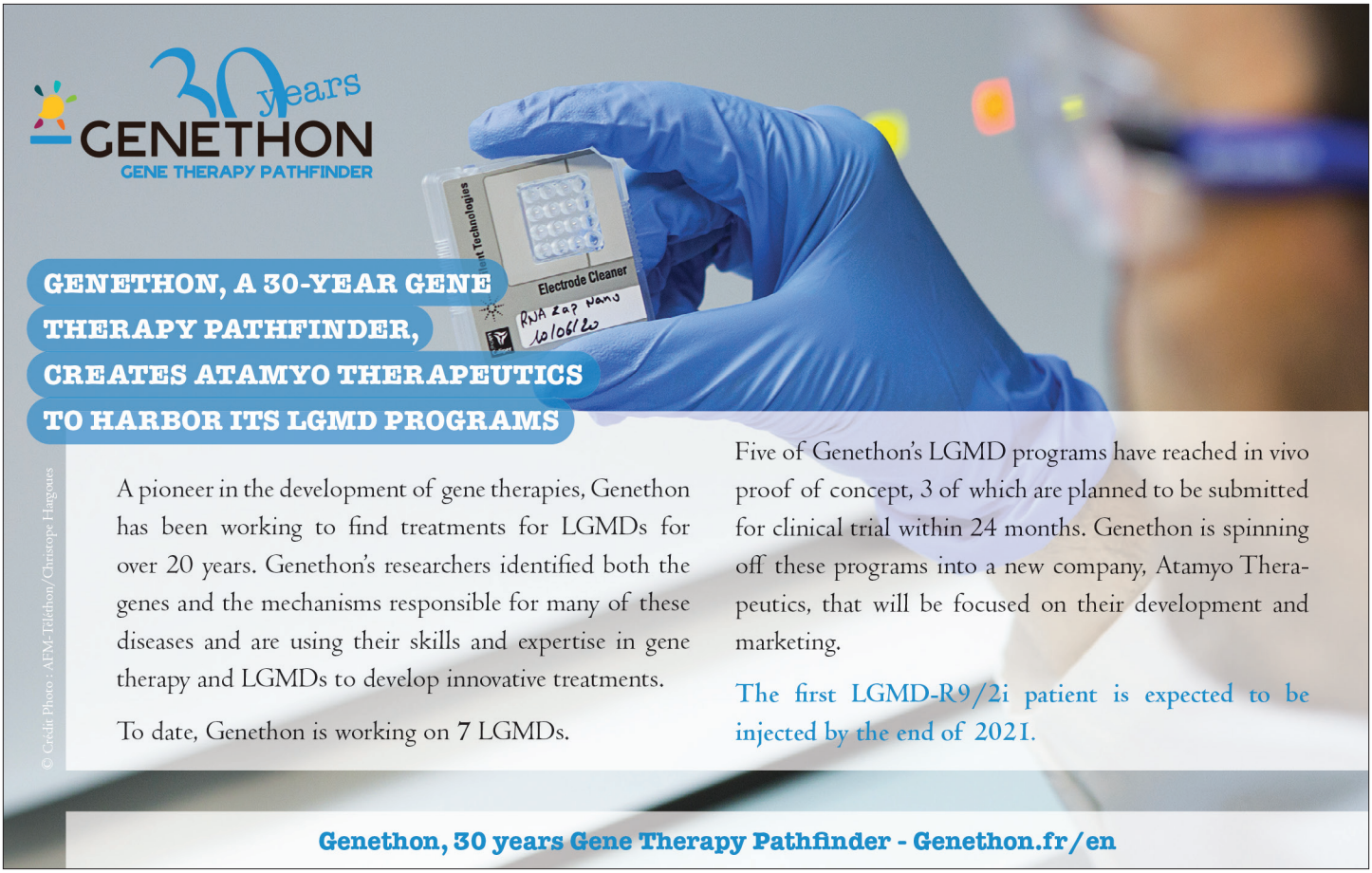
GRUPPO FAMILIARI BETA-SARCOGLICANOPATIE GFB ONLUS

REGISTER TODAY!

lgmd2e.org

30 years GENETHON

GENE THERAPY PATHFINDER



GENETHON, A 30-YEAR GENE THERAPY PATHFINDER, CREATES ATAMYO THERAPEUTICS TO HARBOR ITS LGMD PROGRAMS

A pioneer in the development of gene therapies, Genethon has been working to find treatments for LGMDs for over 20 years. Genethon's researchers identified both the genes and the mechanisms responsible for many of these diseases and are using their skills and expertise in gene therapy and LGMDs to develop innovative treatments.

To date, Genethon is working on 7 LGMDs.

Five of Genethon's LGMD programs have reached in vivo proof of concept, 3 of which are planned to be submitted for clinical trial within 24 months. Genethon is spinning off these programs into a new company, Atamyo Therapeutics, that will be focused on their development and marketing.

The first LGMD-R9/2i patient is expected to be injected by the end of 2021.

Genethon, 30 years Gene Therapy Pathfinder - Genethon.fr/en

Matthew Wicklund MD

Professor of Neurology, University of Colorado School of Medicine

Q

We're hearing about many clinical trials that are currently underway for LGMD. Has the COVID-19 pandemic delayed progress with these trials? If so, in what way?

A

Yes, with surges in COVID-19 cases, academic research centers restricted in-person research to various extents, somewhat slowing progress in clinical trials. For example, with the December 2020 surge in COVID-19, our institution has paused observational trials (e.g., LGMD natural history studies). As a positive outcome from these limitations on research, the research community has innovated, generating new protocols with remote monitoring of research subjects, piggybacking off telemedicine platforms.

Q

I am an individual living with LGMD. Should I consider getting the COVID-19 vaccine?

A

LGMD patients with respiratory and/or cardiac dysfunction own higher risks of morbidity and mortality from COVID-19. It could be unfortunate for someone to hold off on vaccination and succumb to respiratory failure for the hypothetical risk associated with a COVID-19 vaccine. Anyone with LGMD should always consult their own neurologist for specific guidance on medical decision-making.

Q

Would the vaccine affect future gene therapy treatments for LGMD?

A

Death by COVID-19 is a much more serious matter than speculative concerns about future gene therapy. It would be unwise for someone to forestall getting a COVID-19 vaccination for the theoretical, mild risk of future interference of a COVID-19 vaccine with future (still theoretical for most) LGMD gene-based therapy. Individuals with LGMD should also connect with their neurologist for further questions. Companies involved in future gene therapies are also a good resource to connect with on this topic and should have guidance available.

Q

I have an unspecified form of LGMD-type weakness, but still no diagnosis. Are there any free resources available that can help me learn how to get further genetic testing?

A

Free genetic testing is available through Invitae and PerkinElmer. Each of these genetic testing panels evaluate 100+ LGMD genes. You can obtain testing through your neuromuscular provider, a geneticist, or even a motivated primary care provider. These panels provide a diagnosis in 25-40% of persons. On a positive note, over the next year or two, these genetic testing panels likely will expand substantially in size, providing answers for even more persons with LGMD. ■

Meet the Expert

Matthew Wicklund MD, professor of neurology at the University of Colorado, has a 20-year history of research in the LGMDs. His interests span from delineating genetic subtypes to understanding prevalence in the LGMDs. He is zealous about current clinical trials for gene-based therapies.

Have a Question for Our Experts?

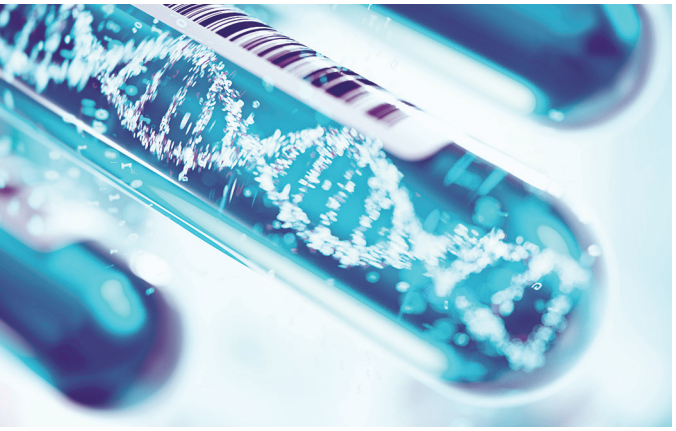
Send Questions To:
Jessica@TheSpeakFoundation.com

Jain Foundation's Story: From Diagnosis to Leading Research and Building a Registry Community

Today, the feeling of urgency to find treatments for dysferlinopathy is as strong as ever for the Jain family and every other person impacted by this devastating muscle disease.

The Jain Foundation story began in 2000 when the Jain family's son was given the diagnosis of Miyoshi Myopathy type 1 (dysferlinopathy, LGMD2B/R2). Upon receiving their son's diagnosis, they also learned that there are no treatment options and the field of dysferlin research needed direction and support. At that time, there were very few researchers studying dysferlin, no clinical studies for this subtype of LGMD, and they knew of no one else with dysferlinopathy. Since officially founding in 2005, the Jain Foundation has been working tirelessly to facilitate progress by developing and directing the field of dysferlin research through the investment of over $35 million dollars in support of 120+ research projects, clinical studies, and other programs. The Jain Foundation created and maintains disease-specific animal models and other research resources, making them available to scientists around the world which greatly expedites progress in the field. The Jain Foundation employs an independent scientific advisory board, leads patient studies, gathers and validates data on disease progression, and is working to support the development of standards of care, as well as the identification of outcome measurements for use in clinical trials. Building a strong patient registry is also instrumental to achieve successful drug development. There are currently 850 individuals with genetically confirmed dysferlinopathy included in the Dysferlin Registry (**Dysferlinregistry.Jain-Foundation.org**). All of these significant milestones in the dysferlin field position the community well for successful trial recruitment and design. Today, the feeling of urgency to find treatments for dysferlinopathy is as strong as ever for the Jain family and every other person impacted by this devastating muscle disease.

There is still much work to be done, especially in the clinic. Individuals with dysferlinopathy are often shocked at the lack of understanding of dysferlinopathy when they speak to neurologists. Many questions are left unanswered, which contributes to additional stress when dealing with this difficult



diagnosis. People want to know how they are going to navigate life as their muscles change. They are not sure how they will deal with relationships, school, picking a profession, and parenting, and they have little to no emotional support or proper social services. It is exciting to see that patient-led organizations like the SPEAK Foundation and the LGMD Awareness Foundation have created incredible advocacy and support programs for people with LGMD. This enables organizations like the Jain Foundation to continue to focus on directing scientific projects and the critical work of developing the Dysferlin Registry.

All who are dealing with dysferlinopathy are encouraged to contact the Jain Foundation to apply for placement in the Dysferlin Registry. If you are unsure about whether you have LGMD2B/R2, the Jain Foundation can help confirm a dysferlinopathy diagnosis. You are not alone! ■

Contributed by Sarah Shira Emmons
Director of Global Patient Outreach and Community Strategies
The Jain Foundation

Opposite:
The Jain Foundation actively seeks to support the development of dysferlinopathy focused **Research**, build a strong patient **Registry**, and supply scientific **Resources** to advance research in the dysferlin field.

Connect with Us

Jain-Foundation.org
DysferlinRegistry.Jain-Foundation.org

Patients@Jain-Foundation.org

(Back, L to R): Kiana Shannon, Megan Iammarino, Lindsay Alfano, Brenna Powers **(Front, L to R):** Natalie Reash, Linda Lowes

From Gene Therapy to Remote Assessments: How Nationwide Children's is Advancing LGMD Research

The multidisciplinary team in the Center for Gene Therapy has a long history of working to better understand LGMD.

The Center for Gene Therapy in the Abigail Wexner Research Institute at Nationwide Children's Hospital has a long history of developing novel gene therapy approaches for the limb girdle muscular dystrophies.

How It All Began

The first human gene therapy trial for LGMD, led by Jerry Mendell, MD, Principal Investigator in the Center for Gene Therapy, targeted children with LGMD2D/R3 α-sarcoglycan-related muscular dystrophy and enrolled its first participant in 2008. Because this was a safety study, the trial only involved injecting the gene in a small muscle in the foot. This was done so researchers could observe whether the gene expressed in the muscle and if there were side effects.

Since that first successful trial, the center has completed two additional clinical trials for children with LGMD. Additional gene therapy programs are in preclinical studies. In the lab of Louise Rodino-Klapac, PhD, previously in the Center for Gene Therapy but currently at Sarepta Therapeutics, the following subtypes of LGMD are being targeted:

- **LGMD2A/R1** Calpain 3-related
- **LGMD2B/R2** Dysferlin-related
- **LGMD2C/R5** γ-sarcoglycan-related
- **LGMD2D/R3** α-sarcoglycan-related
- **LGMD2E/R4** β-sarcoglycan-related
- **LGMD2L/R12** Anoctamin 5-related

An additional treatment targeting LGMD-2A/R1 calpain3-related is also undergoing pre-clinical studies in the lab of Zarife Sahenk, MD, director of Clinical and Experimental Neuromuscular Pathology at Nationwide Children's Hospital. All these gene therapy programs have been licensed or optioned by Sarepta Therapeutics.

Forward Progress

The Center for Gene Therapy continues to lead first-in-human trials in LGMD with a systemic gene delivery study for children with LGMD2E/R4 β-sarcoglycan-related muscular dystrophy (NCT03652259). The purpose of this study is to understand the safety of the treatment at different dose levels.

The neuromuscular physical therapy team, led by Linda Lowes, PhD, a principal investigator in the Center for Gene Therapy and Lindsay Alfano, DPT, a research physical therapist at Nationwide Children's Hospital, is driving clinical outcome measure standardization and novel outcome development. The goal of their research is to evaluate different tests that could be used to measure change in functional abilities. They also test clinical trial participants to understand how a person with LGMD's abilities change over time without treatment.

"If we know a disease causes decline but don't have reliable and meaningful outcome measures to measure that change, we can't determine if a therapy works," says Dr. Lowes.

In preparation for the trials, Drs. Lowes and Alfano have several natural history, or non-treatment, studies ongoing at Nationwide Children's. These studies are enrolling participants with any subtype of LGMD to help prepare for future treatment trials. In response to the COVID-19 pandemic, this team is also working to validate remote assessments as part of these trials. If validated, completing some testing in a patient's home could reduce the burden of being in a trial. Patients enrolled in any natural history trial complete strength and functional testing at visits to determine which outcomes are meaningful and/or to develop new tools for LGMD. If you would like to help move this research forward, you can participate in a natural history study. Please email **NMDTrialInfo@NationwideChildrens.org** for more information.

In addition to developing outcome measures and running natural history trials, Drs. Lowes and Alfano are involved in the LGMD community in other ways. They are currently collaborating with an international consortium of neuromuscular physical therapists to develop a core dataset for LGMD and to inform efforts to develop standards of care for the limb girdle muscular dystrophies. Dr. Alfano served as the local organizer for the first TREAT-NMD LGMD Masterclass to help build knowledge and awareness of the LGMDs among clinicians and researchers providing care for patients with LGMD. Additionally, in an effort to develop standards of care for children with LGMD, Dr. Alfano developed an online survey for families to complete to offer information about the current care and gaps in care they receive. The hope is to reach as many families as possible to gain a global, unbiased view of the current care practices around the world.

The multidisciplinary team in the Center for Gene Therapy has a long history of working to better understand LGMD. This team is driven to provide best outcomes for patients with LGMD through clinical care and advancing research in these diseases. ■

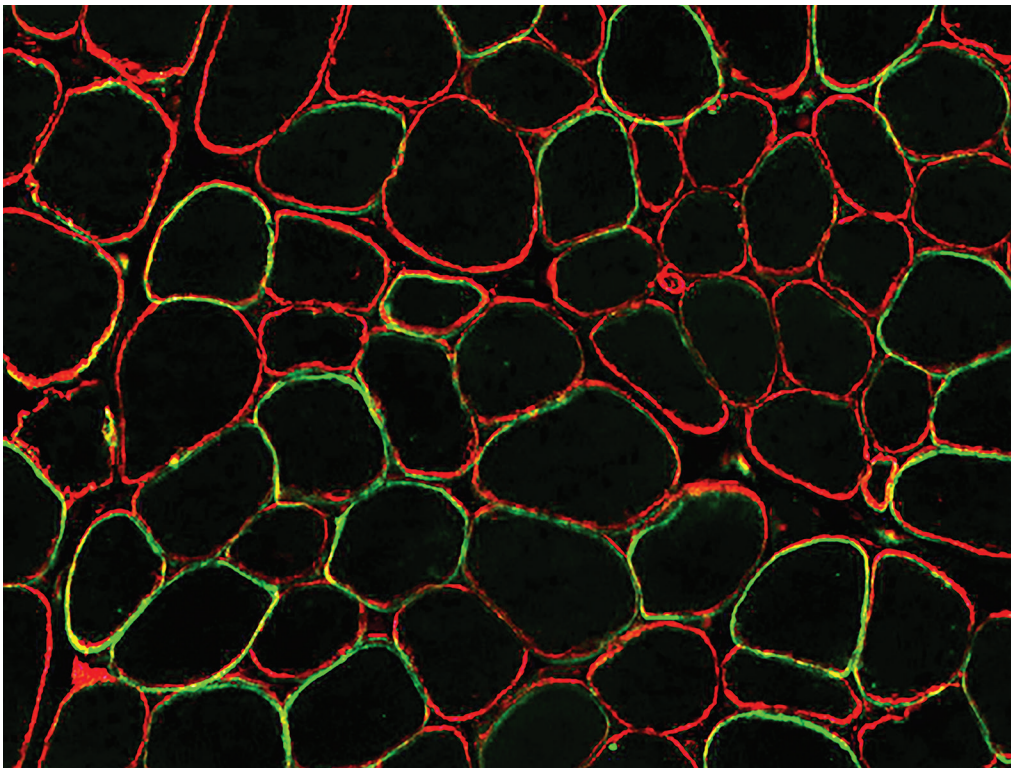
Jerry Mendell MD, Principal Investigator in the Center for Gene Therapy, led the first gene therapy trial for LGMD, targeting children with LGMD2D/R3 α-sarcoglycan-related muscular dystrophy.

Connect with Us

LGMD Standards of Care Patient Survey
redcap.nchri.org/surveys/?s=RWEDRLHNWJ

NationwideChildrens.org

NMDTrialInfo@NationwideChildrens.org



The GRASP-LGMD Consortium

Therapies are likely to emerge in the next 5 years for multiple subtypes, and trials of gene therapy and drugs designed to improve muscle quality or function are expected.

What is the GRASP-LGMD consortium?

Over the last several years, neurologists have been teaming up to collectively approach potential treatments for Limb Girdle Muscular Dystrophy (LGMD). The LGMDs are progressive muscular dystrophies with no FDA-approved therapies that, as a group, represent a large unmet clinical need. The Muscular Dystrophy Association funded the GRASP-LGMD consortium to help address this issue.

Why is this so important? The LGMDs are at a critical juncture. Therapies are likely to emerge in the next 5 years for multiple subtypes, and trials of gene therapy and drugs designed to improve muscle quality or function are expected. LGMDs are divided into over 30 different subtypes, based on a combination of the mutation type and clinical features. Despite the diversity in genetic and clinical presentation, the LGMDs are currently at a crossroads in therapeutic development: the technical ability to target a given mutation or disease mechanism has outstripped the clinical understanding of the natural history of the LGMDs.

Obstacles faced by the LGMD community — as well as other rare disease communities — include: small, geographically distributed populations; imprecise diagnostic testing; a paucity of validated clinical trial endpoints; a need to define coherent inclusion criteria; and the need for facilities and trained personnel for conducting clinical trials. ■

Contributed by Erin DeSpain

Above: Alpha-dystroglycan stainining (in green) and caveolin-3 (in red) surrounding myofibers. Red fibers have loss of alpha-dystroglycan consistent with this patient's diagnosis of LGMD2I/R9.

GRASP-LGMD Clinical Trials

STUDY Defining Clinical Endpoints in Limb Girdle Muscular Dystrophy (LGMD) (GRASP)

Inclusion Criteria:

- Age between 4–65 at enrollment
- Clinically affected (defined as weakness on bedside evaluation in either a limb girdle pattern, or in a distal extremity)
- A genetically or functionally confirmed mutation in ANO5, CAPN3, DYSF, DNAJB6, or SGCA-G
- Ambulatory

Exclusion Criteria:

- Non-ambulatory at the time of enrollment
- Any other illness that would interfere with the ability to undergo safe testing or would interfere with interpretation of the results in the opinion of the site investigator

Subtypes:

- CAPN3 (LGMD 2A/R1)
- DSYF (LGMD 2B/R2)
- ANO5 (LGMD 2L/R12)
- DNAJB6 (LGMD 1D/D1)
- Sarcolgycan (LGMD 2D/R3, LGMD 2E/R4, LGMD 2C/R5, LGMD 2F/R6)

STUDY Biomarker Development in LGMD 2I/R9 (MLB-01-001)

Inclusion Criteria:

- Age between 10–65 at enrollment
- Clinically affected (defined as weakness on bedside evaluation in either a limb girdle pattern, or in a distal extremity)
- A genetically confirmed mutation in FKRP (LGMD 2I/R9)
- Up to 60 participants will complete the10-meter walk test in greater than 4 seconds
- Up to 40 participants will complete the 10-meter walk test in over 12 seconds
- Up to 20 participants may be non-ambulatory

Exclusion Criteria:

- Any other illness that would interfere with the ability to undergo safe testing or would interfere with interpretation of the results in the opinion of the site investigator
- History of a bleeding disorder, platelet count <50,000, current use of an anticoagulant
- Positive pregnancy test at start or at any time during the trial

Subtype:

- FKRP (LGMD 2I/R9)

Contact: **Brittney Holmberg** | Project Manager, Grasp-LGMD Consortium | (804) 997-9384 | *Brittney.Holmberg@vcuhealth.org*

GRASP-LGMD Consortium Members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Doris Leung, MD, PhD
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John Vissing, MD
University of Copenhagen


Katherine Mathews, MD
University of Iowa


Linda Lowes, PT, PhD
The Research Institute at Nationwide Children's Hospital


Matthew Wicklund, MD
University of Colorado Denver


Nicholas Johnson, MD, MSci, FAAN
Virginia Commonwealth University


Peter Kang, MD
University of Florida


Tahseen Mozaffar, MD, FAAN
University of California Irvine


Urvi Desai, MD
Atrium Health


Volker Straub, MD, PhD
Newcastle University


Monkol Lek, PhD
Yale University, Non-Clinical Site

GRASP-LGMD Researcher Spotlight

Dr. Tahseen Mozaffar | University of California at Irvine

Dr. Tahseen Mozaffar currently is the site Principal Investigator for a number of clinical trials and observational studies in muscle disorders, including the ML-BIO natural history study in LGMDR9-FKRP (LGMD2i), the LGMD-GRASP observational study in 4 limb girdle muscular dystrophies, and the COS2 observational study in LGMDR2-dysferlin. Dr. Mozaffar is Professor of Neurology, Orthopaedic Surgery, and Pathology & Laboratory Medicine, and Interim Chair of Neurology at the University of California, Irvine. He is the Founder and Director of the UC Irvine-MDA ALS and Neuromuscular Center and the UC Irvine Neuromuscular Program. His practice focuses on acquired and inherited muscle disorders, and he is widely regarded as one of the preeminent experts on muscle disorders nationally and internationally, especially in the area of rare and ultra-rare myopathies.

JOURNEY

ELIGIBILITY

You may be eligible for this study if you are at least 4 years old and have a confirmed genetic diagnosis of LGMD. Participants may be male or female, and should be receiving routine clinical care from a physician. Both ambulatory and non-ambulatory individuals are able to join this study. Please speak with your doctor about additional enrollment criteria.

MORE INFO

To learn more about this study, including a list of growing global sites, please visit ClinicalTrials.gov (NCT04475926). For additional questions, please contact **ClinicalTrials@Sarepta.com (1-800-690-2003)**, or **Advocacy@Sarepta.com**.

SAREPTA THERAPEUTICS

Transformative therapies rely on informative research.

JOURNEY, the limb-girdle muscular dystrophy natural history study, is an opportunity for individuals across the globe to play a role in understanding their disease to advance future treatments.

JOURNEY is a global natural history study sponsored by Sarepta Therapeutics. A natural history study is designed to inform research by learning how the progression of limb-girdle impacts individuals over time. By participating in this study, individuals with certain subtypes of LGMD will be evaluated by a medical professional and will expand researcher's knowledge of limb-girdle muscular dystrophy.

Joining a natural history study is an opportunity to contribute to research for limb-girdle muscular dystrophy. The insights from your participation will inform future clinical trials and experimental therapies.

The 2019 class of the National LGMD Conference. Over 400 attended the inaugural conference to find a cure for Limb Girdle Muscular Dystrophy.

A Dream that Became a Reality

"The pharmaceutical companies with the best emerging treatments are invited to be present with speakers sharing on the most cutting edge studies."

Have you ever heard the line, "If you build it, they will come?" Dr. Matthew Wicklund of University of Colorado shared that thought with the Speak Foundation in regards to the National LGMD Conference. A little dream of many became reality with the first-ever National LGMD Conference in September of 2019.

The next National LGMD Conference is going international in 2021—dubbed the International LGMD Conference, September 17th-20th, 2021. This international conference will be virtual, where LGMD patients from all over the world will meet together. This event will be of the same caliber as the 2019 conference, with only the best researchers from GRASP-LGMD coordinating with an international consortium of LGMD organizations led by the Speak Foundation. The pharmaceutical companies with the best emerging treatments are invited to be present with speakers sharing on the most cutting edge studies. This event in 2021 will be groundbreaking once again.

What will be accomplished at the 2021 International LGMD Conference? First, you can likely expect to hear from some of the top GRASP-LGMD researchers once again. Second, the top biotech and pharma companies will present their newest research and share the status of current clinical trials for LGMD. Third, we hope to achieve something that has never been done before. Our goal is for every individual in the world living with LGMD to be able to tune into the conference. Since the event is virtual and free, we will be able to bring participants to an online community to watch via live web broadcast. Imagine the amazing ability to connect with other patients from all over the world! Also, everyone who registers will be included to receive key updates and new information on clinical trials.

Registration will go live in April of 2021. Find out more by visiting **InternationalLGMD-Conference.com**. ■

International LGMD Conference
September 17-20, 2021

Registration Begins April 2021
InternationalLGMDConference.com

Conference Administrator **Kathryn Bryant**

Conference Chairman **Brad Williams**

Conference Vice Chairwoman **Carol Abraham**

Our mission is to accelerate and influence the path to a cure.

Including all subtypes LGMD1A to LGMD1H and Autosomal Dominant and X Linked Myopathies.

Muscular Dystrophies not registered (excludes DMD).

Make a Difference.

LGMD-1D DNAJB6 Foundation

Register at **lgmd1d.org**

COALITION TO CURE CALPAIN 3 (C3)

is committed to treating and ultimately curing limb-girdle muscular dystrophy type 2A (LGMD2A, also called LGMDR1 Calpain 3-related or calpainopathy). Our mission is to fund high potential research and clinical trials as we educate the global community about this rare disease.

COALITION TO CURE CALPAIN 3

OVERCOMING WEAKNESS WITH STRENGTH

10 Years of Progress

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LGMD2A/R1 GLOBAL PATIENT REGISTRY
LGMD2A.org

FACEBOOK
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C3 is a 501(c)(3) US-based tax-exempt charity.

Rare Disease Patient Listening Session on Limb Girdle Muscular Dystrophies

Rare Disease Patient Listening Sessions allow patients living with rare diseases to share their perspectives, experiences, and opinions with the Food and Drug Administration (FDA). Several LGMD advocacy foundations jointly organized an FDA Listening Session on LGMDs on October 20.

Listening Sessions are one of several programs that the FDA has implemented over the last few decades to "hear the patient voice" regarding drug development and the testing and approval of new treatments. The FDA's requirement to approve a new drug is that it must be safe and effective. But "safe" and "effective" are subjective. What is effective enough to provide a meaningful benefit is a matter of opinion, so the opinions of patients living with the disease need to be considered. Also, what level of risk might be acceptable depends on several factors, including how the disease affects those living with it, what other treatments currently exist, and how well they work. The FDA looks for input from patients on these topics through Listening Sessions.

The LGMD Listening Session included fifteen presenters who are living with LGMD themselves or are parents of children living with

Above: Dr. Brad Williams, Director of Research at the Jain Foundation, worked with the Speak Foundation and other LGMD advocacy organizations to help organize the FDA Patient Listening Session on LGMDs. Brad lives with LGMD2B/R2 and is a champion for the LGMD community.

LGMD, representing twelve different LGMD subtypes. The Listening Session did not focus on any particular treatments being developed, but gave an overview of LGMDs, and what it is like to live with them, from the patient and caregiver perspectives. The presentations addressed the following topics:

- Background on LGMD: genetic heterogeneity—some 30 different genetic subtypes; most treatments will only apply to one or a few types of LGMD
- The patent population: LGMD affects people of both genders, all ethnic backgrounds, and has onset at a variety of ages, and can have dominant or recessive inheritance. There is no "typical" LGMD patient.
- Impact on activities of daily living, and equipment needed to live
- Impact of LGMDs at different ages: childhood, school, independence, family life and parenting, work
- Impact on cardiac and respiratory function
- Experiences of participation in clinical trials, and patients' thoughts on drug development

The Listening Session was not open to the public, but we have a summary of the session published on the Speak Foundation website and it is now linked on the FDA site. ▪

Contributed by Brad Williams
Director of Research, Jain Foundation

Become an Ambassador for LGMD Awareness Day

LGMD Awareness Day is celebrated worldwide on September 30th of each year, and is an occasion meant to raise awareness for Limb Girdle Muscular Dystrophy.

All LGMD patients, family members, organizations, health care professionals, researchers, drug developers, public health organizations, and any association with an interest in LGMD are invited to join together and become an LGMD Awareness Day Ambassador.

Make an impact! Learn how you can become an Ambassador by visiting **LGMD-Info.org**. ▪

Contributed by Jessica Evans
Assistant Director, The Speak Foundation

Lobby Day on the Hill 2020—A Huge Success

There are times when we need to mobilize. Times when we must come together to create what I call the power of the collectivity. I have spent time in my career lobbying in state capitols and on Capitol Hill. These are opportunities to educate our elected officials on issues that are critical to the lives of so many.

On September 22, 2020, dozens of volunteer advocates across the country joined forces. We reached out to our members of Congress. Led by The Speak Foundation, and other LGMD groups, these advocates sent emails to their U.S. Senators and their U.S. Representative about accessibility issues.

We named this the Right to Access Campaign. We first shared a one-page informational sheet on LGMD basics to help educate our elected officials. Then we focused on the need for accessibility around key issues: healthcare, advanced treatments, personal care assistants, life-saving care during a pandemic, access to housing, and access to airline travel.

We heard back from many leaders saying that they planned to look at these issues more closely. We let them know we plan to be back in 2021 and we are hoping for action on these issues.

Please join our efforts. The power we have is in the power of our group. Numbers matter, and in 2021 we may even be able to do face-to-face meetings on Capitol Hill with our congressional representatives. ■

Contributed by Ralph Yaniz
President, LGMD2L Foundation
Ralph.Yaniz@gmail.com

By Andrea L. Klein
Founder & President of Breathe with MD, Inc.

Respiratory Muscle Weakness in LGMD

LGMD may negatively affect breathing and coughing; understanding this and getting appropriate respiratory care improves quality of life and prolongs life.

Our respiratory muscles, those located over the chest wall, between ribs, the diaphragm, and abdomen, gradually weaken. LGMD onset and scoliosis can amplify this weakness. Coughing requires the diaphragm to engage and take a deep breath in, forcefully contract abdominal muscles, and powerfully expel air. When a cough is weak, mucus builds up and leads to frequent and prolonged respiratory infections.

"We breathe in (oxygenate) and breathe out (ventilate and remove stale air)," said Dr. Hemant Sawnani, a pulmonologist at Cincinnati Children's Hospital.

In sleep, "elimination of carbon dioxide (CO_2), the waste product of metabolism or Oxygen (O_2) consumption, is not as effective," said Sawnani, who treats children and adults with neuromuscular disease (NMD). "Insomnia can be a common presentation. They wake up, go back to sleep, and this happens repeatedly. In the morning they are still fatigued."

Lying on one's back may cause a feeling of heaviness, chest discomfort, and the need to breathe deeper, and/or focus more on breathing. Difficulty concentrating and loss of appetite are other possible respiratory weakness symptoms. Problems may arise later with breathing while awake, even when upright.

"Morning and daytime headaches and fatigue should be evaluated by sleep study that monitors O_2 and CO_2 levels," Sawnani explained. Measuring O_2 alone sometimes results in supplemental oxygen being ordered which Sawnani advised "can be hugely detrimental." Learn more about this on Breathe with MD's "Oxygen Caution" page (**BreatheWithMD.org/Oxygen-Caution.html**).

A CPAP with its single positive pressure helps sleep apnea and upper airway obstruction, and it too may be mistakenly ordered. "There may be some obstruction," Sawnani explained, "but a second pressure in bi-level positive airway pressure is needed."

Often called "BiPAP," the device's two pressures, (inspiratory and expiratory), and the difference between them determines the amount of air delivered in each breath. Enabling a backup pressure rate guarantees a minimum number of breaths per minute.

"The point of non-invasive ventilation at night is to rest breathing muscles, thereby allowing them to be more efficient during the day," Sawnani shared.

Left: Getting appropriate respiratory care improves quality of life and prolongs life.

A sleep study "needs to be interpreted in the context of the disease," he said. "You could easily be poorly served if an untrained eye reviewed the report."

Seeing a specialist in neuromuscular pulmonary medicine can prevent mismanagement. An evaluation should include Pulmonary Function Tests while seated and lying down with measures of Forced Vital Capacity (FVC), Peak Cough Flow (PCF), Maximum Inspiratory Pressure (MIP), and Maximum Expiratory Pressure (MEP). The FVC difference between the two positions will reveal any diaphragm weakness.

> **"Seeing a specialist in neuromuscular pulmonary medicine can prevent mismanagement."**

Sawnani recommends determining "end tidal CO_2," (a measure from exhaled breath), while awake, as some are still ambulatory while developing respiratory weakness. He suggests a fingertip capillary blood gas, an alternative to arterial blood gas, and advises against venous sampling.

Handwashing and avoiding sick people and crowds can prevent infection. Sawnani explained extra hydration to thin mucus and CoughAssist therapy with carefully prescribed settings are critical to recovery from a chest infection. A nasal spray like Afrin may be a helpful decongestant.

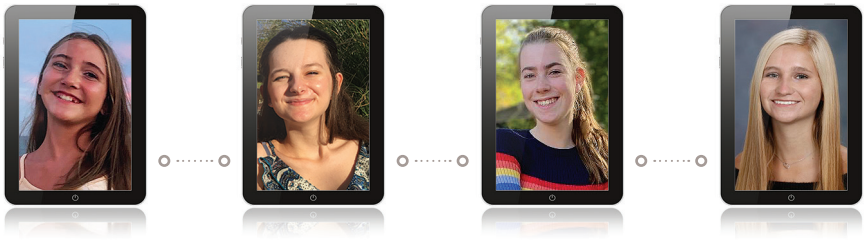
"Over-the-counter (OTC) Mucinex can thin out thick secretions," Sawnani stated. "OTC allergy medicines associated with sleepiness as a side effect should be avoided, as these typically carry another side effect of thickening secretions."

Regarding hospitalization, Sawnani shared, "It's easy to intubate, but by day seven, if you're not off the ventilator, almost as a rule, many [clinicians] do a tracheotomy [surgical insertion of a breathing tube in the trachea]."

While invasive ventilation is a choice for some, Sawnani explained, "In most adult ICUs, patients without NMD who are intubated for illness or surgery are gradually weaned from ventilator support. Once the settings are low enough, the endotracheal tube is removed. In this process, the 'work of breathing' is gradually shifted from ventilator to the patient. In patients with NMD, this is dangerous, as they become progressively more fatigued and experience respiratory failure before or just after tube removal. Instead, transitioning from endotracheal tube ventilation to nasal or face mask ventilation, after a lesser degree of weaning, reduces the patient's fatigue, and ventilation weaning can proceed as progress is made. This requires experience and judgment with a constant focus on patient safety and well-being."

He continued, "There are always options to maximize non-invasive support, but you're sometimes at the mercy of those who don't know how to use it."

Lung volume recruitment, a method to stretch the respiratory muscles and lungs with an adapted ambu bag, Sawnani explained, may slow decline in FVC and allow deeper breathing. Additional studies are needed to fully understand the impact of this component of respiratory care. ■



'Mom ... She Gets Me!'

When you make connections with others who are battling the same condition, you instantly feel supported and the relationships you make quickly become like family.

Samantha (Sammy) Brazzo was five years old when she said these words after she first met Ayla Reilly at the Annual University of Iowa Wellstone Center Dystroglycanopathy Conference. Those words resonate among many people who are battling a rare disease. Sammy, now 12, has Limb Girdle Muscular Dystrophy (LGMD2i), and was diagnosed when she was two years old. Meeting other young people who are battling the same fight has been vitally important to her throughout her childhood.

Due to Covid-19, this year's conference was changed to a virtual experience. Realizing how important those special connections are, Sammy and her mom, Kelly, decided to contact a few families they met at previous conferences, in an effort to get the girls together for a Zoom call.

That Zoom call has now turned into a support group for these young girls. Now, no matter the distance, these young women have a lifeline to each other. The group includes Sammy, Ayla, Maud Cornelissen (who has also attended the yearly conference), Grace Hatfield, and a few others.

Regarding their first call, "We talk about the struggles of living with LGMD, but we also enjoy talking about normal, random topics too," said Maud. "It's nice to be able to just chat with girls about everyday things without having to also educate a curious stranger about LGMD."

Ayla said, "Realizing that other people are going through similar struggles makes it easier to take it on, because they are taking it on with you."

Grace was diagnosed with LGMD2i in April. Her mother, Meredith, joined a Facebook group that includes parents of children with LGMD2i. She said, "These connections have been so helpful, just trying to navigate through this diagnosis. We have already learned so much from other parents in how to best help Grace."

Kelly Brazzo, Sammy's mom and Co-Founder and CEO of CureLGMD2i Foundation, stated, "When you or a loved one are diagnosed with something like LGMD, you can try to navigate this alone, but it can be quite isolating. When you make connections with others who are battling the same condition, you instantly feel supported and the relationships you make quickly become like family."

There are many benefits of being part of a support group for all ages, including finding others who "get you." The common experience among members of a support group often means they have similar feelings, worries, everyday problems, treatment decisions, or treatment side effects. It is important to find the support that will best help you. ■

Contributed by Rebecca Lucas Gregg

Above (L to R): Sammy Brazzo, Ayla Reilly, Maud Cornelissen, and Grace Hatfield

Connect with Us

TheSpeakFoundation.com
CureLGMD2I.com

APPLICATIONS AVAILABLE: DEC. 18, 2020 - JAN. 29, 2021

Personal Care Attendant Stipend Program

Are You Struggling with Daily Tasks to Get Ready for Work?

The Personal Care Attendant Stipend Program offers supplemental grants to employed US individuals living with LGMD who need personal care assistance readying for their work days. Qualified applicants will receive a one-time, $3000 grant per family. Do you qualify? Visit **TheSpeakFoundation.com** for a complete list of eligibility requirements. Get the help you need — apply today!

The SPEAK Foundation

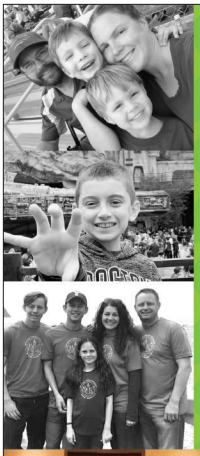
TheSpeakFoundation.com

LGMD Patient Network

The Speak Foundation has been hard at work assembling the first-ever LGMD Patient Network and YOU are invited to be included. To sign up is absolutely free, confidential, and can be done easily by visiting **TheSpeakFoundation.com**.

Don't Miss Out — Join Our LGMD Patient Network Today!

TheSpeakFoundation.com



Even though we're farther from each other this year, we're closer than ever to a cure. Let's

Stay Strong!

Learn More, Donate, or Get Involved at

CURELGMD2i.org

We fight so that our muscles never stop.

Proyecto Alpha is a Spanish non-profit association created to help affected and family members fight LGMD2C/R5, LGMD2D/R3, LGMD2E/R4, LGMD2F/R6.

PROYECTO ALPHA | ASOCIACIÓN DISTROFIA MUSCULAR DE CINTURAS POR DÉFICIT DE SARCOGLICANOS

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The SPEAK Foundation

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International LIMB GIRDLE MUSCULAR DYSTROPHY Conference

2021 International LGMD Conference

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

International Virtual Conference

September 17–20th, 2021

The 2021 LGMD Conference will be going international for 2021 and will be a free event for individuals and families to attend virtually. Due to the unique nature of this virtual event, people from all over the world can meet up for different sessions over 4 days to learn about the best research for Limb Girdle Muscular Dystrophy, as well as hear from leading experts in the field. Emerging research from top industry pharma and biotech will be presented in incredible sessions with new information for the international LGMD community. Don't miss this event!

The SPEAK Foundation

Registration Starts in April 2021

InternationalLGMDConference.com