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MDA® Muscular Dystrophy Association

What is Evrysdi?

Evrysdi is a prescription medicine used to treat spinal muscular atrophy (SMA) in children and adults.

Important Safety Information

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
  - are a woman who can become pregnant:
    - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy
    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi
    - **Pregnancy Registry.** There is a pregnancy registry for women who take EVRYSDI during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving EVRYSDI, tell your healthcare provider right away. Talk to your healthcare provider about registering with the EVRYSDI pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling 1-833- 760-1098 or visiting https://www.evrysdipregnancyregistry.com.
  - are an adult male. Evrysdi may affect a man's ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby
- **Tell your healthcare provider about all the medicines you take**
- You should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement

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A Member of the Roche Group

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Evrysdi—the first and only **oral, non-invasive** treatment for spinal muscular atrophy (SMA)

- **Proven results** in adults, children, and infants with SMA, including infants not yet showing symptoms
- Designed to help produce SMN protein **throughout the body**
- Can be taken **at home, at work, or when on the go**[1]
- **No needles, sedation or hospital stays** required

Talk to your doctor about Evrysdi
Scan the QR code to learn more or visit
EvrysdiResults.com

[1]If refrigeration is not available, Evrysdi can be kept at room temperature up to 104°F for a combined total of 5 days. Please refer to the Instructions for Use for additional information about storage and administration.
SMN=survival motor neuron.

Important Safety Information (continued)

- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water
- **The most common side effects of Evrysdi include:**
  - For later-onset SMA:
    - fever
    - diarrhea
    - rash
  - For infantile-onset SMA:
    - fever
    - diarrhea
    - rash
    - runny nose, sneezing and sore throat (upper respiratory infection)
    - lung infection (lower respiratory infection)
    - constipation
    - vomiting
    - cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
You may also report side effects to Genentech at 1-888-835-2555.

Please see accompanying brief summary for additional Important Safety Information.

If you cannot afford your Evrysdi medication, visit MySMASupport.com for financial assistance information.

Patient Information
EVRYSDI® [ev-RIZ-dee]
(risdiplam)
for oral solution

What is EVRYSDI?

- EVRYSDI is a prescription medicine used to treat spinal muscular atrophy (SMA) in children and adults.

Before taking EVRYSDI, tell your healthcare provider about all of your medical conditions, including if you:

- are pregnant or plan to become pregnant. If you are pregnant, or are planning to become pregnant, ask your healthcare provider for advice before taking this medicine. EVRYSDI may harm your unborn baby.
- are a woman who can become pregnant:
  - Before you start your treatment with EVRYSDI, your healthcare provider may test you for pregnancy. Because EVRYSDI may harm your unborn baby, you and your healthcare provider will decide if taking EVRYSDI is right for you during this time.
  - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping EVRYSDI.
  - **Pregnancy Registry.** There is a pregnancy registry for women who take EVRYSDI during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving EVRYSDI, tell your healthcare provider right away. Talk to your healthcare provider about registering with the EVRYSDI Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling 1-833-760-1098 or visiting https://www.evrysdipregnancyregistry.com.
- are an adult male planning to have children: EVRYSDI may affect a man's ability to have children (fertility). If this is of concern to you, make sure to ask a healthcare provider for advice.
- are breastfeeding or plan to breastfeed. It is not known if EVRYSDI passes into breast milk and may harm your baby. If you plan to breastfeed, discuss with your healthcare provider about the best way to feed your baby while on treatment with EVRYSDI.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Keep a list of them to show your healthcare provider, including your pharmacist, when you get a new medicine.

How should I take EVRYSDI?

See the detailed Instructions for Use that comes with EVRYSDI for information on how to take or give EVRYSDI oral solution.

- You should receive EVRYSDI from the pharmacy as a liquid that can be given by mouth or through a feeding tube. The liquid solution is prepared by your pharmacist or other healthcare provider. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement.
- Avoid getting EVRYSDI on your skin or in your eyes. If EVRYSDI gets on your skin, wash the area with soap and water. If EVRYSDI gets in your eyes, rinse your eyes with water.

Taking EVRYSDI

- Your healthcare provider will tell you how long you or your child needs to take EVRYSDI. Do not stop treatment with EVRYSDI unless your healthcare provider tells you to.
- For infants and children, your healthcare provider will determine the daily dose of EVRYSDI needed based on your child's age and weight. For adults, take 5 mg of EVRYSDI daily.
  - Take EVRYSDI exactly as your healthcare provider tells you to take it. Do not change the dose without talking to your healthcare provider.
- Take EVRYSDI 1 time daily after a meal (or after breastfeeding for a child) at approximately the same time each day. Drink water afterwards to make sure EVRYSDI has been completely swallowed.
- Do not mix EVRYSDI with formula or milk.
- If you are unable to swallow and have a nasogastric or gastrostomy tube, EVRYSDI can be given through the tube.
- If you miss a dose of EVRYSDI:
  - If you remember the missed dose within 6 hours of when you normally take EVRYSDI, then take or give the dose. Continue taking EVRYSDI at your usual time the next day.
  - If you remember the missed dose more than 6 hours after you normally take EVRYSDI, skip the missed dose. Take your next dose at your usual time the next day.
- If you do not fully swallow the dose, or you vomit after taking a dose, **do not take** another dose of EVRYSDI to make up for that dose. Wait until the next day to take the next dose at your usual time.

Reusable Oral Syringes

- Your pharmacist will provide you with the reusable oral syringe(s) that are needed for taking your medicine and explain how to use them. Wash the syringes per instructions after use. Do not throw them away.
- Use the reusable oral syringe(s) provided by your pharmacist (you should receive 1 or 2 identical oral syringes depending on your prescribed daily dose) to measure your or your child's dose of EVRYSDI, as they are designed to protect the medicine from light. Contact your healthcare provider or pharmacist if your oral syringe(s) are lost or damaged.
- When transferred from the bottle to the oral syringe, take EVRYSDI right away. Do not store the EVRYSDI solution in the syringe. If EVRYSDI is not taken within 5 minutes of when it is drawn up, EVRYSDI should be thrown away from the reusable oral syringe, and a new dose should be prepared.

What are the possible side effects of EVRYSDI?
The most common side effects of EVRYSDI include:

- **For later-onset SMA:**
  - fever
  - diarrhea
  - rash
- **For infantile-onset SMA:**
  - fever
  - runny nose, sneezing, and sore throat (upper respiratory infection)
  - constipation
  - diarrhea
  - lung infection (lower respiratory infection)
  - vomiting
  - rash
  - cough

These are not all of the possible side effects of EVRYSDI. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store EVRYSDI?

- Store EVRYSDI in the refrigerator between 36°F to 46°F (2°C to 8°C). Do not freeze.
  - If necessary, EVRYSDI can be kept at room temperature up to 104°F (up to 40°C) for a combined total of 5 days. EVRYSDI can be removed from, and returned to, a refrigerator. The total combined time out of refrigeration should not be more than 5 days.
- Keep EVRYSDI in an upright position in the original amber bottle to protect from light.
- Throw away (discard) any unused portion of EVRYSDI 64 days after it is mixed by the pharmacist (constitution) or if EVRYSDI has been kept at room temperature (below 104°F [40°C]) for more than a total combined time of 5 days. Discard EVRYSDI if it has been kept above 104°F (40°C). Please see the Discard After date written on the bottle label. (See the **Instructions for Use** that comes with EVRYSDI).

Keep EVRYSDI, all medicines and syringes out of the reach of children.

General information about the safe and effective use of EVRYSDI.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use EVRYSDI for a condition for which it was not prescribed. Do not give EVRYSDI to other people, even if they have the same symptoms you have. It may harm them. You can ask your pharmacist or healthcare provider for information about EVRYSDI that is written for health professionals.

What are the ingredients in EVRYSDI?

Active ingredient: risdiplam

Inactive ingredients: ascorbic acid, disodium edetate dihydrate, isomalt, mannitol, polyethylene glycol 6000, sodium benzoate, strawberry flavor, sucralose, and tartaric acid.

Genentech
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EVRYSDI® (risdiplam)

Distributed by:

Genentech, Inc.
A Member of the Roche Group
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South San Francisco, CA
94080-4990

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For more information, go to www.EVRYSDI.com or call 1-833-387-9734.

This Patient Information has been approved by the U.S. Food and Drug Administration. Approved: 3/2023

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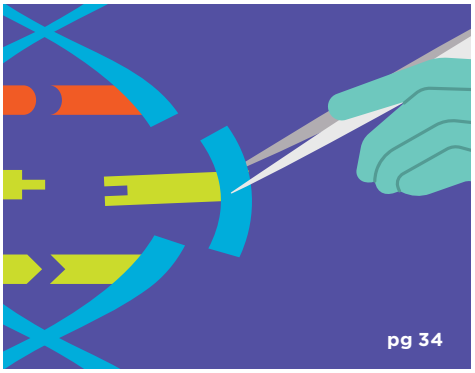

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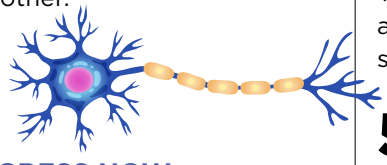

Cover image: Andrei Lishakov/Getty

Year End Leads to New Beginnings

As we close out MDA's 74th year of service and discovery for families affected by neuromuscular diseases, it feels in so many ways like we're just getting started. We're seeing an unprecedented era of breakthroughs in the field of neuromuscular science that MDA established in the 1950s. Highlights in recent months showcase the momentum we're building in research, clinical care, access, inclusion, and community connection.

Donald S. Wood, PhD

This summer in Montréal, Canada, we convened scientists from around the world to discuss a new frontier in muscle medicine: how to recover muscle mass lost to neuromuscular diseases. Researchers are united in their belief that restoring nerves and muscles is achievable, and we are committed to finding the safest, most effective paths forward.

On the advocacy front, we're continuing to work with air travel organizations and regulators on restraint systems that will allow people with mobility disabilities to stay safely in their wheelchairs during flights. Looking ahead, we are focused on the reauthorization of the US Food and Drug Administration's Rare Pediatric Disease Priority Review Voucher program and other pending policies that affect access to safe and effective treatments.

One of the highlights of MDA's year is our inclusive summer camps. Thanks to generous donors who fund the MDA Summer Camp program and the dedicated volunteers and medical staff who treat campers as their own, nearly 1,000 children with neuromuscular diseases enjoyed accessible activities like swimming, crafts, and archery at no cost to their families. This is an experience like no other to help young people discover their independence and make lifelong connections in a community that celebrates them.

As we close out 2024, we invite you to join us in celebrating MDA's 75th year in 2025. The future is bright, and we are grateful for your continued support in making our impact and momentum possible.

Sincerely,
Donald S. Wood, PhD
President and CEO
Muscular Dystrophy Association

THANK YOU, READERS

We received wonderful feedback from readers and listeners in our 2024 Quest Media Audience Survey. Thank you to everyone who told us what they think about Quest Magazine, the Quest Blog, and the Quest Podcast. You help us make Quest a valuable resource for the MDA community. Here are a few things we learned about our audience:

99% read each issue of Quest Magazine

81% read or listen to Quest Media content at least once a month

93% live with a neuromuscular disease or have a family member living with one

95% consider Quest Media a valuable resource for information on daily living and independence

MDA Muscular Dystrophy Association

For more than 70 years, MDA has led the way in accelerating research, advancing care, and advocating for the support of people living with muscular dystrophy, ALS, and related neuromuscular diseases and their families. MDA's mission is to empower the people we serve to live longer, more independent lives.

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FOLLOW MDA ON

PUBLICATION MANAGEMENT: UNLOCK

Doug Clough is a Champion in the ALS Community and Beyond

Doug Clough's commitment to serving as a National MDA/ALS Ambassador has ignited inspiration within the ALS community and beyond. At the heart of Doug's journey lies determination to spread awareness and support for those touched by ALS. One of the cornerstones of Doug's advocacy efforts lies in his partnership with Dutch Bros. Doug's ties to Dutch Bros run deep, having frequented a local stand before his diagnosis. Doug has taken the time to meet with hundreds of employees, expressing his gratitude for their unwavering support of the ALS community.

Dutch Bros and its customers came together May 17, for the 18th annual Drink One for Dane to support the Muscular Dystrophy Association and its mission to end ALS. We're stoked to share the Dutch Bros Foundation donated $2.5 million to MDA.

Mansfield Cares Golf Classic Raises $1.2M

The 38th Annual Mansfield Cares Golf Classic is one of the largest events of its kind. Over 500 golfers, including energy partners and celebrities, come together for this fun event – raising over $11 million for MDA to date. Thank you to Mansfield Energy, and all sponsors and attendees for making the 2024 tournament a success!

CITGO Lake Charles Refinery Raises over $578,000

The CITGO Lake Charles Refinery raised over $578,000 this year for MDA. Their 39th annual Golf Classic brought together sponsors and golfers to enjoy a day on the course with auctions and great food. They also launched an event called Beer, Bourbon, & BBQ, an exclusive networking dinner to benefit MDA.

Burn Boot Camp and MDA: A Powerful Partnership

Burn Boot Camp's Be Their Muscle campaign just concluded its eighth consecutive year, bringing the total raised for MDA to over $3M. Each year, fitness enthusiasts and trainers rally together nationwide for special workout events and challenges, community activities, and personal fundraising efforts.

Carrying Our Hope Forward

Approaching the end of the year is a moment to reflect, recharge, and rekindle hope for the future. Each year brings its own challenges and triumphs, and this year was no exception. The Quest Media team takes its responsibility seriously to share tools and resources we hope you've found helpful, and we have loved sharing stories of determination and resilience, reminding us of the strength we possess when we come together.

The holiday season, with its lights and laughter, offers a perfect backdrop for this reflection. It's a time to cherish connections — whether with family, friends, or new acquaintances who've touched our lives in unexpected ways. Let's embrace the spirit of giving, sharing not just gifts but also kindness and support.

As we turn the page to a new year, let us carry forward the lessons learned and dreams ignited. Together, we can cultivate a sense of hope that fuels our aspirations and inspires action. Let's set our intentions high, knowing that we can overcome any obstacle with determination and community.

In the spirit of the season, we invite you to indulge in the pages of this issue, filled with stories of hope, creative pursuits, and holiday inspirations. May your celebrations be joyful and your hearts light as we close one chapter and step boldly into another.

Wishing you warmth, peace, and a hopeful new year.

Mindy Henderson
Vice President, Disability Outreach & Empowerment
Editor-in-Chief, Quest Media

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DID YOU KNOW?

GIVE THE GIFT OF ACCESSIBILITY THIS HOLIDAY SEASON.

The Quest Holiday Product Guide is a curated selection of products that can make life a little bit easier — and more fun — for people with disabilities.

Each product in the Quest Holiday Product Guide is recommended by an MDA Ambassador, a member of the community who lives with a neuromuscular disease, because they are easy to use, enhance independence, or are beloved in some other way. The guide includes clothing, home, tech, personal care, travel items, and more with adaptive and universal design features.

Use the Quest Holiday Product Guide to treat yourself or find thoughtful gifts for anyone in your life who lives with a disability. MDA Ambassadors recommend the products in the guide, but MDA does not receive any proceeds from purchases.

Shop the Quest Holiday Product Guide at **MDAQuest.org/product-guide**.

Freedom and Opportunity

Adopting a new outlook on life helped Scott Conger excel

BY REBECCA HUME

Human resources (HR) professional Scott Conger is using his experience to help others get the accommodations they need to chase their own success. Diagnosed with an unspecified neuromuscular disease at 12, Scott spent much of his childhood and early adulthood trying to hide his disability. In doing so, he didn't seek assistance that could have helped him on his journey. Now 47, he has learned to embrace his abilities and adapt to the progression of what he now knows is RYR1 myopathy, a diagnosis he received through genetic testing in 2022.

"My path forward has been an evolution — as my muscular dystrophy has progressed, I have progressed, too," Scott says. "I have learned to adapt and pivot, grow, change, and admit to myself that I do, in fact, need help or need to do things another way."

When Scott began working in HR for Bosque Brewing, a New Mexico brewing company and restaurant group, he was not yet using a wheelchair. Bosque Brewing has an inclusive business model centered on celebrating and engaging everyone, including those living with physical or mental disabilities. That culture helped Scott recognize that embracing his disability would empower him to move forward.

"I refused to admit that I needed a wheelchair for a long time. But once I had it, I realized it was not a bad thing but a tool that enables me to do more, be more involved, and go more places," Scott says. "I went from being unable to do what I wanted because of this progressive disability to gaining mobility with a power wheelchair. I had to shift this unhealthy internal point of view that people would see my chair instead of seeing me."

MORE ONLINE
Read more about Scott's journey in an expanded version of this article at **MDAQuest.org/ScottConger**.

Scott Conger enjoys working for Bosque Brewing, an inclusive business.

Scott's manager at that time helped him face his negative preconceptions about using a wheelchair. When he told her he wished he could "just be normal," she responded, "But what is normal? And who is normal? Why can't you just be you? Everyone is normal."

That line of thinking propelled Scott into a new chapter of his life, where he no longer feels the need to hide his disability. Although he can stand and walk short distances, Scott uses a power wheelchair to enhance his mobility at work and in daily life. He finds freedom and opportunity using the supports available to him. As an HR professional, a husband, and a father, Scott says his work is just beginning.

"To me, my muscular dystrophy doesn't mean that I can't do something — it means I need to find a way," he says. Q

Rebecca Hume is a Senior Specialist and Writer for Quest Media.

FACING THE FUTURE: THE CHALLENGES OF TRANSITIONING TO ADULT CARE IN DUCHENNE MUSCULAR DYSTROPHY

As a parent, few things in life can compare to our children moving into the world as independent adults. It's an emotionally loaded event, full of excitement, nostalgia, and anxiety. Everything we've done has led to this moment, and even if we've done all we can to prepare them, we will never stop wondering, "Have I done enough?"

For parents of children with muscular dystrophy, these moments are becoming increasingly common. Improvements in treatment are helping more patients live well into adulthood. Unfortunately, the care systems and resources geared towards pediatric patients haven't kept up with this transition.

Marissa understands this better than most. A mom of three, her youngest son Joseph was diagnosed with Duchenne muscular dystrophy (DMD) at five years old. "In the earliest stages after his diagnosis, my number one priority was saving my son,"
Marissa says.

When Joseph lost ambulation, it brought into sharp focus the challenges they would face in the years ahead. "That was a heavy time," Marissa recalls. "We think about losing the ability to walk as a physical thing…but the emotional toll of navigating this new life was devastating. There were practical questions like getting the best wheelchair for him, modifying our house, transportation, and just helping him navigate this new world and pursue his dreams."

"We were also going through so much in our life at the time—my daughter was about to go to college, I was a newly single parent, my parents were in the final years of their lives and needed care—and it was just too much. I had great support and health insurance, but I was buckling under the weight. I asked a neurologist I know how other people did it, and she told me they didn't, they struggled to make it to doctor appointments because they can't afford train fare into the city. That outraged me, that caring for a child with a life-limiting condition was pay-to-play. So many people suffer without access to resources or even basic care. I needed to do something to level the playing field. That's why I founded Team Joseph, with the mission of funding research and offering direct financial support to families. Even seemingly simple things like wheelchair ramps and shower safe chairs can make a huge difference."

After Joseph's diagnosis, Marissa worked to ensure he had access to the best care they could find. Along with establishing local care, she worked with a renowned Duchenne specialist. At the same time, Marissa was thinking long-term about involving Joseph in discussions about his own care and future.

"My approach was to acknowledge Joseph's medical needs while also talking to him the way I did my other kids," Marissa explains. "We talked all the time about what he wanted to be when he grew up and if he wanted to go to college, which he did. My goal was to help him communicate about his vision for the future and getting him to believe that he had
a future."

It took a lot of work and preparation, but Joseph was ultimately accepted into university. He's currently in his senior year and living in an apartment with his friends.

The summer before Joesph left for college was busy for everyone, Marissa recalls. "I had a lot of anxiety about getting him ready, and I knew I'd have a lot of sleepless nights ahead, just as I did for my other kids. I spent a lot of time coordinating care on campus and focusing on what he'd need to be safe while maximizing the college experience."

While helping Joseph manage his care in college was challenging, there were more challenges ahead as he turned 21. "Some care centers will keep a patient for their lifetime," Marissa said. "But when Joseph turned 21, his local care center stopped seeing him. When he was younger, all his care was coordinated. Now, his care is fragmented by specialty. We're managing 7-10 relationships with different providers, and they

don't talk to each other the way they did in the past. So now we're in the position of reeducating ourselves and working with his care providers as we learn to coordinate all those logistics."

"It's ironic, as patients get older and Duchenne progresses, their needs escalate…but the ability to find or access the care they need diminishes. It's been a beautiful surprise that patients are living longer, but we haven't effectively planned for them living a life of dignity and fullness. We celebrate progress medically and advancements in treatment, but we must balance that with an acknowledgement that some people don't have access to care, treatments, and the necessary medical equipment to maximize their later years."

"Duchenne care for adults should be comprehensive and coordinated among all providers. Ideally, it would also include elements of mental health—not as an option or add-on, but as an integrated part of healthcare. We should also focus on meaning, purpose, and how the patient can contribute to society. That matters, because he has a lot to offer. As long as we have breath in our lungs and our hearts are beating, we have something to contribute."

As for Joseph, he's already found a way to contribute by creating a conference specifically for patients aged 14 and up to help them transition into adulthood with Duchenne. The What Now? virtual conference recruited a roster of speakers that included doctors from across the country, an expert in disability law, a career coach, and so much more. Additionally, every panel was introduced and moderated by an adult with Duchenne.

Joseph is also completing his sports journalism major and hopes to either write sports stories or work in a research department supporting a broadcast team. Overall, he's trying to figure out how to turn his passions into a career, just like any other young adult making their way in the world.

For herself, Marissa would like to see the discussion about the transition of care start earlier. "There needs to be a more coordinated handoff of care, where it's not just the transfer of records and a referral but a conversation between providers and family. And the conversation needs to include the young adult patient so they can talk about what's important to them."

I'd love to see our broader community of parents, HCPs, pharma, and advocacy foster the idea that we may think we represent those living with Duchenne… but when those with Duchenne are living deep into adulthood, the most powerful thing we can do is to create a space just for them—to talk more, to ask more, and to celebrate what they've achieved, while honoring that there is still much more to do.

SCAN TO LEARN MORE ABOUT THE WHAT NOW? CONFERENCE

Catalyst pharmaceuticals

All Together Now

MDA helps members connect with each other

BY MEGAN KRAMER-SALVITTI

Helping members find and build strong relationships with each other is a valuable part of MDA's mission to serve the neuromuscular disease community, which is why we have created multiple programs that give community members opportunities to connect. From asking each other questions about treatments or mobility aids to discussing challenges of daily living or sharing an afternoon of fun, these programs provide safe and supportive spaces, no matter where you are. Find the right program for you here.

Would you like to **connect** with others with similar experiences?

Community Support Groups

MDA Community Support Groups are virtual support groups that provide a safe place for meaningful connection with others within the neuromuscular community. Regularly scheduled online meetings give participants the opportunity to exchange valuable information and resources with others who share similar experiences.

There are multiple active groups at any given time, currently including:

- Pediatric, for children or their parents/guardians
- Adult, for individuals ages 18 and up
- ALS, for individuals living with the disease
- Gene therapy, for parents/guardians of children with DMD or SMA who receive or are interested in gene therapy

Each group is facilitated by an MDA Care Center provider, MDA staff, or other specialist in the community.

To join a Community Support Group, visit mda.org/CommunityGroups and complete an interest form. If you do not find a group that would be a good fit, contact the Resource Center at 1-800-572-1717 or ResourceCenter@mdaUSA.org.

Peer Connections

MDA's Peer Connection program helps community members connect with each other one-on-one. By request, MDA Support Specialists will make introductions between individuals with similar diagnoses or their caregivers, parents, spouses, or siblings.

"Participants can specify that they are open to being connected to others in MDA's community based on criteria including diagnosis, age, interests, and preferred form of communication," says Sara Melton, Senior Family and Clinical Support Specialist. "Once a program entry form is completed, a Support Specialist will work with you to find your match."

Support Specialists will check in to see how the matches are going, but participants decide when, where, and how often they connect. The program has made more than 300 connections since its inception, and is open to Spanish speakers.

"We have fostered connections that decide to meet twice a month for a phone call and others who have decided to meet in person for coffee," Sara says. "It is a joyous experience to be a part of connecting families who are in the same community, in different states, or across the country."

To join Peer Connections, contact the Resource Center at 1-800-572-1717 or ResourceCenter@mdaUSA.org and ask for a program entry form.

Image: kaylabutler/Getty

Are you looking for **fun activities** to enjoy with other MDA community members?

Let's Play

MDA Let's Play members meet online nearly every day of the week to game, host art and design classes, watch movies, play trivia, and more. "It fosters a safe and inclusive online space for members to practice self-expression, share with others, and feel a sense of belonging," says Scott Wiebe, MDA's Director of Community Programs.

Let's Play has its own channel on Discord (a free app for messaging and chatting) that is open only to group members and moderated for problematic behavior or community rule violations. Let's Play activities are streamed on Twitch, a free interactive livestreaming service. Discord and Twitch are open to users ages 13 and up without adult supervision, but parents/guardians can sign their younger children up for Let's Play and are encouraged to watch along.

Scott says most members are ages 14 to 20, so Let's Play programming is aimed to be appropriate for this age group. But anyone who lives with a neuromuscular disease or wants to support the MDA community can join Let's Play. "The only prerequisite is being kind and encouraging toward others," Scott says.

Learn how to join Let's Play at mda.org/lets-play.

Family Getaways

MDA's Family Getaways are three-day all-ages destination experiences for people living with neuromuscular diseases and their families to enjoy accessible recreation activities together. They are held at summer camp facilities, resorts, or adaptive recreation centers in locations throughout the United States.

Getaways are provided at no cost for MDA members and their family unit, such as spouses, siblings, and caregivers. "Anyone registered with the MDA community is welcome to attend with their family, from toddlers to adults," says Kelsie Andreska, MDA's Director of Recreation Programs.

MDA recognizes that everyone's situations are different. "We encourage you to reach out to us if you have questions on who can attend with your family. For instance, if an adult MDA member lives independently with a care provider and considers them family, we absolutely welcome that," Kelsie says.

MDA Recreation Program Specialists are involved every step of the way, from registering people for Family Getaways to planning adaptive activities at Getaway locations, so families can enjoy time with each other and connect with other families there.

"Everyone deserves the opportunity to experience really cool recreation activities and experiences away from home with their loved ones," Kelsie says. Q

Learn about upcoming Family Getaways at mda.org/family-getaways.

Megan Kramer-Salvitti is a writer for Quest Media.

Progress Now

Tracking research updates and breakthroughs that help accelerate treatments and cures across MDA diseases

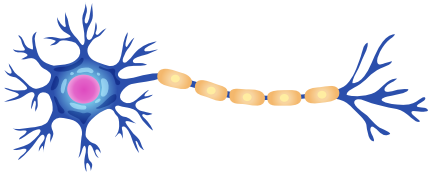
Amyotrophic lateral sclerosis (ALS)

Early PrimeC Treatment Slows Decline

Image: RobinOlimb/Getty

Earlier this year, NeuroSense Therapeutics announced that its phase 2b trial with the ALS drug PrimeC met its primary and secondary endpoints for safety and effectiveness. The drug developer then released further results supporting PrimeC as a disease-modifying treatment when started earlier in the disease.

In the PARADIGM trial, 68 adults with ALS took either PrimeC, an oral (by mouth) tablet, or a placebo twice daily for six months.



After this period, 96% of participants chose to enter an open-label extension in which they all receive PrimeC for up to 12 months. The participants who received one year of treatment with PrimeC lived significantly longer without disease complications and had a slower lung function decline than those who started the treatment six months later.

PrimeC is a fixed-dose combination of two FDA-approved medications: the antibiotic ciprofloxacin and the anti-inflammatory agent celecoxib. The two medications are thought to work together to block key ALS mechanisms, slowing disease progression.

To learn more about the PARADIGM study, visit neurosense-tx.com or go to ClinicalTrials.gov and enter NCT05357950 in the "Other terms" search box.

CLINICAL TRIAL TERMS TO KNOW

Double-blind: Neither researchers nor participants know which participants are taking the drug or placebo.

Multiarm: Comparing several different experimental treatments against a common control group within a single study.

Multicenter: The trial is completed at more than one site.

Randomized: Participants are assigned at random to groups taking the drug or placebo.

Image: miniwide_silver/Getty

Becker muscular dystrophy (BMD)

Phase 2 Study Seeks Adults With BMD

Researchers at Edgewise Therapeutics are seeking adults living with BMD to participate in a global phase 2 study to evaluate the safety and effectiveness of EDG-5506 (sevasemten) in adults with BMD. Sevasemten is designed to prevent contraction-induced muscle damage that occurs with daily activity in BMD.

Participants will be randomly assigned to either sevasemten or a placebo, which will be given orally (by mouth) once daily. The study will last approximately 19 months, which includes up to seven on-site clinic visits.

The effects of sevasemten will be evaluated using blood tests, safety assessments, and functional assessments over the course of the study.

To be eligible, individuals must be 18-50 years old, have a documented dystrophin mutation and phenotype consistent with BMD, and be currently ambulatory, among other criteria.

To learn more, visit BeckerGCStudy.com or email the study coordinator at studies@EdgewiseTX.com.

Duchenne muscular dystrophy (DMD)

Stem Cell Study Gets Go-Ahead

In July, Myogenica announced that the US Food and Drug Administration (FDA) approved an Investigational New Drug (IND) application for MyoPAXon. This allows the company to start a clinical trial testing its stem cell therapy in people with DMD.

In DMD, mutations in the DMD gene cause a lack of functional dystrophin, a protein that protects muscles from damage. When muscle tissue is damaged, muscle stem cells can usually help repair it, but this process is impaired with DMD. MyoPAXon is a line of healthy muscle stem cells generated from human umbilical cord cells. Myogenica aims to inject MyoPAXon into muscles affected by DMD so the healthy stem cells can heal and generate new muscle fibers. In addition, new muscle fibers generated from the transplanted cells would be expected to have functional dystrophin protein, making them less susceptible to the muscle damage typical in DMD.

Image: Bet_Noire/Getty

Peter Kang, MD, FAAN, FAAP, a pediatric neuromuscular neurologist and director of the Greg Marzolf Jr. Muscular Dystrophy Center at the University of Minnesota Medical School, would lead the proposed early-stage clinical trial. Dr. Kang and the clinical research team plan to administer intramuscular (in the muscle) injections of MyoPAXon in nonambulatory adult DMD patients, monitor any potential site reactions or immune response, and assess for the presence of dystrophin-producing muscle fibers.

For more information, visit myogenica.com.

Duchenne muscular dystrophy (DMD)

FDA Expands Approval for DMD Treatment

In June, the FDA expanded approval of delandistrogene moxeparvovec-rokl (ELEVIDYS) to include boys and men ages 4 and older with DMD with a confirmed mutation in the DMD gene. The FDA granted traditional approval for ambulatory patients and accelerated approval for non-ambulatory patients, confirming the benefits and effectiveness of the treatment.

Developed by Sarepta Therapeutics, ELEVIDYS is a gene therapy that targets the genetic root cause of DMD. It is a single-dose infusion delivered into the veins.

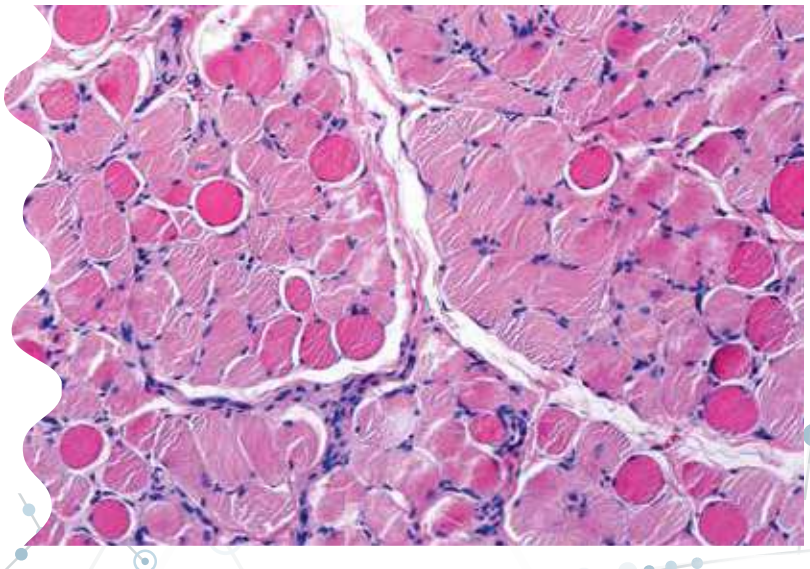


Image: JOSE LUIS CALVO MARTIN & JOSE ENRIQUE GARCIA-MAURIÑO MUZQUIZ/Getty

Friedreich ataxia (FRDA or FA)

FRDA Treatment Chosen for FDA START Program

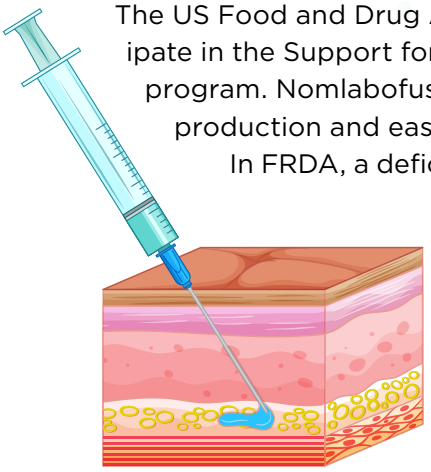


Image: colematt/Getty

The US Food and Drug Administration (FDA) has selected CTI-1601 (nomlabofusp) to participate in the Support for Clinical Trials Advancing Rare Disease Therapeutics (START) pilot program. Nomlabofusp is an investigational treatment for FRDA that aims to restore energy production and ease symptoms.

In FRDA, a deficiency in the frataxin protein impairs the function of energy-producing mitochondria, which affects nerve and muscle cells. This leads to ataxia (a loss of muscle control and coordination), along with heart and neurological problems.

In a phase 2 clinical trial earlier this year, 28 adults with FRDA were given nomlabofusp by subcutaneous (under the skin) injection. Before treatment, participants' frataxin levels were below those of healthy adults but rose to higher-than-normal levels after two weeks.

Launched in 2023, the START program works to accelerate the development of new therapies that address an unmet medical need for rare diseases.

Nomlabofusp is an investigational treatment for FRDA that aims to restore energy production and ease symptoms.

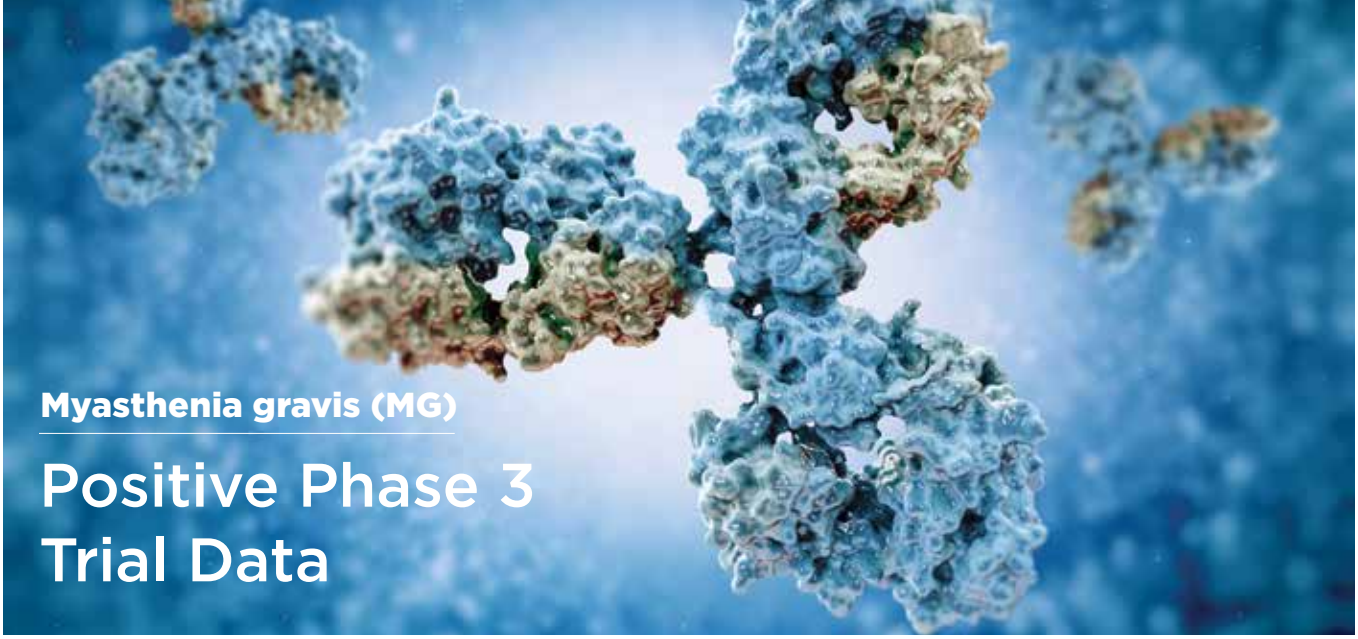


Image: Svisio/Getty

Myasthenia gravis (MG)

Positive Phase 3 Trial Data

Earlier this year, Johnson & Johnson presented findings from the VIVACITY-MG3 trial, which is evaluating the effectiveness and safety of nipocalimab in adults with generalized MG (gMG). Data from the phase 3 randomized, placebo-controlled trial show that treatment with nipocalimab led to significant reductions in disease severity among people with gMG.

The trial met its primary goal, with nipocalimab-treated patients seeing a drop in their MG Activities of Daily Living (MG-ADL) scores, indicating the disease had less impact on day-to-day life.

MG is an autoimmune disease in which antibodies mistakenly attack the connection between nerves and muscles — known as the neuromuscular junction. gMG is a more severe form of MG. Nipocalimab is expected to help ease MG severity by lowering the levels of immunoglobulin G (IgG) antibodies in the bloodstream.

Nipocalimab is administered via intravenous (into the vein) infusions every two weeks after an initial loading dose. The trial met its primary goal, with nipocalimab-treated patients seeing a drop in their MG Activities of Daily Living (MG-ADL) scores, indicating the disease had less impact on day-to-day life. It also met critical secondary outcomes, including a significant improvement in muscle strength and function after 22 to 24 weeks.

The trial is still recruiting patients in North America, Europe, East Asia, and Australia and is expected to conclude in 2026. Based on its findings, Johnson & Johnson expects to submit applications requesting nipocalimab's approval as a treatment for gMG later this year.

For more information on the study, visit ClinicalTrials.gov and enter NCT04951622 in the "Other terms" search box.

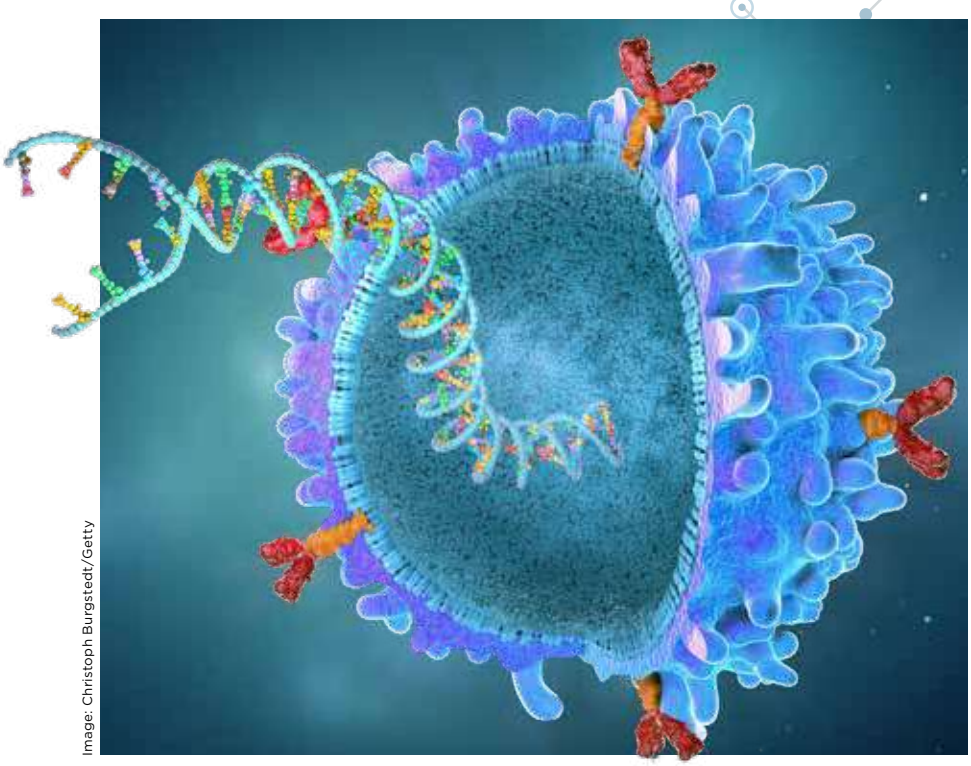


Image: Christoph Burgstedt/Getty

Myasthenia gravis (MG)

Investigational Cell Therapy Shows Promise

Cartesian Therapeutics reported that treatment with CAR T-cell therapy Descartes-08 reduced gMG severity, according to data from a phase 2b clinical trial of the investigational immunotherapy.

In CAR T-cell therapy, a patient's T cells (a type of immune system cell) are changed in the laboratory so they will attack specific cells that cause disease. Descartes-08 is a CAR T-cell therapy designed to destroy immune B cells that produce self-reactive antibodies in gMG.

Most CAR T-cell therapies use DNA to deliver the therapy into cells, and require chemotherapy to deplete existing immune cells before the altered ones can be reintroduced into the body. Descartes-08 is unique in that it uses RNA — an intermediate molecule similar to DNA — to deliver the therapy without the need for chemotherapy.

In Cartesian's randomized, placebo-controlled trial, participants received six weekly intravenous (in the vein) infusions of Descartes-08 or a placebo. Researchers found that after three months 71% of participants treated with Descartes-08 achieved at least a five-point improvement in their MG Composite (MGC) score — a measure of disease severity that combines aspects of several validated clinical scales — compared with 25% of those on the placebo. Clinical responses were sustained for up to six months. Cartesian plans to present this positive data to the U.S. Food and Drug Administration (FDA) by the end of this year and then launch a phase 3 trial.

Earlier this year, the FDA granted Descartes-08 regenerative medicine advanced therapy (RMAT) status. RMAT status is intended for experimental regenerative medicines that treat, modify, reverse, or cure a serious or life-threatening disease and have shown preliminary clinical evidence of being able to address an unmet need for treating that disease. Developers of RMAT-designated treatments receive the incentives of Fast Track and Breakthrough Therapy designations, including more frequent communication with and guidance from the FDA to expedite drug development and review.

Descartes-08 is a CAR T-cell therapy designed to destroy immune B cells that produce self-reactive antibodies in gMG.

For more information on the study, visit ClinicalTrials.gov and enter NCT04146051 in the "Other terms" search box.

Phase 3 Study Seeks Adults with MG

Researchers at Alexion AZ Rare Disease are seeking adults living with generalized MG (gMG) to participate in a phase 3 clinical trial to evaluate the safety and effectiveness of ALXN1720 (gefurulimab) to treat gMG. The researchers are looking into whether gefurulimab helps improve the activities of daily living of people with gMG.

Participants will be randomly assigned to receive either gefurulimab or an inactive placebo control. The drug or placebo will be given by subcutaneous (under the skin) injection. The study duration will be 26 weeks, and regular clinic visits will be required on a schedule outlined by the study team.

The effects of gefurulimab will be evaluated using several outcome measures, and the safety, stability, and tolerability of gefurulimab will be assessed using laboratory testing.

The researchers are looking into whether gefurulimab helps improve the activities of daily living of people with gMG.

To be eligible, individuals must be at least 18 years old and have a confirmed diagnosis of myasthenia gravis (MG), among other criteria.

For more information, visit PrevailMGStudy.AlexionClinicalTrials.com or contact study coordinator Christine Rowe at PatientAdvocacy@alexion.com.

Image: funky-data/Getty

+RECRUITING CLINICAL TRIALS

Find a list of trials actively recruiting individuals to help advance research and treatment development at **mda.org/clinical-trial-updates**.

IMPORTANT SAFETY INFORMATION

Do not use VYVGART HYTRULO if you have a serious allergy to efgartigimod alfa, hyaluronidase, or any of the other ingredients in VYVGART HYTRULO. VYVGART HYTRULO can cause serious allergic reactions and a decrease in blood pressure leading to fainting.

VYVGART HYTRULO may cause serious side effects, including:

- **Infection.** VYVGART HYTRULO may increase the risk of infection. The most common infections for efgartigimod alfa-fcab-treated patients were urinary tract and respiratory tract infections. Signs or symptoms of an infection may include fever, chills, frequent and/or painful urination, cough, pain and blockage of nasal passages/sinus, wheezing, shortness of breath, fatigue, sore throat, excess phlegm, nasal discharge, back pain, and/or chest pain.
- **Allergic Reactions (hypersensitivity reactions).** VYVGART HYTRULO can cause allergic reactions such as rashes, swelling under the skin, and shortness of breath. Hives were also observed in patients treated with VYVGART HYTRULO. Serious allergic reactions, such as trouble breathing and decrease in blood pressure leading to fainting have been reported with efgartigimod alfa-fcab.
- **Infusion-Related Reactions.** VYVGART HYTRULO can cause infusion-related reactions. The most frequent symptoms and signs reported with efgartigimod alfa-fcab were high blood pressure, chills, shivering, and chest, abdominal, and back pain.

Tell your doctor if you have signs or symptoms of an infection, allergic reaction, or infusion-related reaction. These can happen while you are receiving your VYVGART HYTRULO treatment or afterward. Your doctor may need to pause or stop your treatment. Contact your doctor immediately if you have signs or symptoms of a serious allergic reaction.

A prescription medicine for adults with chronic inflammatory demyelinating polyneuropathy (CIDP)

VYVGART® Hytrulo

(efgartigimod alfa and hyaluronidase-qvfc)

Subcutaneous Injection
180 mg/mL and 2000 U/mL vial

NOW APPROVED FOR CIDP

The first new class of CIDP treatment in over 30 years

One injection given weekly by a healthcare professional that takes ~30 to 90 seconds*

Talk to your neurologist about VYVGART Hytrulo for CIDP

Scan the QR code to explore the efficacy and safety profile of VYVGART Hytrulo or visit liveVYVIDLY.com

*After administering your injection (under the skin), your healthcare provider will monitor you for allergic reactions for at least 30 minutes.

Before taking VYVGART HYTRULO, tell your doctor if you:

- take any medicines, including prescription and non-prescription medicines, supplements, or herbal medicines,
- have received or are scheduled to receive a vaccine (immunization), or
- have any allergies or medical conditions, including if you are pregnant or planning to become pregnant, or are breastfeeding.

What are the common side effects of VYVGART HYTRULO?

The most common side effects in efgartigimod-alfa-fcab-treated patients were respiratory tract infection, headache, and urinary tract infection. Additional common side effects with VYVGART HYTRULO are injection site reactions, including rash, redness of the skin, itching sensation, bruising, pain, and hives.

These are not all the possible side effects of VYVGART HYTRULO. Call your doctor for medical advice about side effects. You may report side effects to the US Food and Drug Administration at 1-800-FDA-1088.

What is VYVGART® HYTRULO (efgartigimod alfa and hyaluronidase-qvfc)?

VYVGART HYTRULO is a prescription medicine used for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP)

Please see the full Prescribing Information for VYVGART HYTRULO at VYVGARTHytrulo.com/PI and talk to your doctor.

Please see Consumer Brief Summary on next page.

argenx

CONSUMER BRIEF SUMMARY

Important Information about VYVGART® HYTRULO (efgartigimod alfa and hyaluronidase-qvfc) for subcutaneous injection; Rx only.

The risk information provided here is not comprehensive. To learn more, talk about VYVGART HYTRULO with your healthcare provider. The US Food and Drug Administration (FDA)-approved product labeling can be found for VYVGART HYTRULO by visiting www.VYVGARTHYTRULO.com/PI or calling 1-833-VYVGART (1-833-898-4278).

What is VYVGART HYTRULO?

VYVGART HYTRULO is a prescription medicine used for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP)

It is not known if VYVGART HYTRULO is safe and effective in children under 18 years of age.

Who should not use VYVGART HYTRULO?

Do not use VYVGART HYTRULO if you have a serious allergy to efgartigimod alfa, hyaluronidase, or any of the other ingredients in VYVGART HYTRULO. VYVGART HYTRULO can cause serious allergic reactions and a decrease in blood pressure leading to fainting.

What is the most important information I should know about VYVGART HYTRULO?

VYVGART HYTRULO may cause serious side effects, including:

- **Infection.** VYVGART HYTRULO may increase the risk of infection. The most common infections for efgartigimod alfa-fcab-treated patients were urinary tract and respiratory tract infections. Signs or symptoms of an infection may include fever, chills, frequent and/or painful urination, cough, pain and blockage of nasal passages/sinus, wheezing, shortness of breath, fatigue, sore throat, excess phlegm, nasal discharge, back pain, and/or chest pain.
- **Allergic Reactions (hypersensitivity reactions).** VYVGART HYTRULO can cause allergic reactions such as rashes, swelling under the skin, and shortness of breath. Hives were also observed in patients treated with VYVGART HYTRULO. Serious allergic reactions, such as trouble breathing and decrease in blood pressure leading to fainting have been reported with efgartigimod alfa-fcab.
- **Infusion-Related Reactions.** VYVGART HYTRULO can cause infusion-related reactions. The most frequent symptoms and signs reported with efgartigimod alfa-fcab were high blood pressure, chills, shivering, and chest, abdominal, and back pain.

Tell your doctor if you have signs or symptoms of an infection, allergic reaction, or infusion-related reaction. These can happen while you are receiving your VYVGART HYTRULO treatment or afterward. Your doctor may need to pause or stop your treatment. Contact your doctor immediately if you have signs or symptoms of a serious allergic reaction.

Before taking VYVGART HYTRULO, tell your doctor if you:

- have any of the conditions or symptoms listed in the section **"What is the most important information I should know about VYVGART HYTRULO?"**, any allergies or any medical condition
- have received or are scheduled to receive an immunization (vaccine). It is not recommended to receive a "live vaccine" if you are being treated with VYVGART HYTRULO.
- are pregnant or plan to become pregnant. It is not known if VYVGART HYTRULO may harm your unborn baby.
  - **Pregnancy Registry**: There is a pregnancy registry for pregnant women who take VYVGART HYTRULO. The purpose of this registry is to collect information about the health of you and your baby if you take VYVGART HYTRULO during pregnancy. To learn more, call 1-855-272-6524 or visit https://www.VYVGARTpregnancy.com. You may also talk to your healthcare provider about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. It is not known if VYVGART HYTRULO passes into your breast milk.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the common side effects of VYVGART HYTRULO?

The most common side effects of efgartigimod alfa-fcab-treated patients were respiratory tract infection, headache, and urinary tract infection. Additional common side effects of VYVGART HYTRULO are injection site reactions, including rash, redness of the skin, itching sensation, bruising, pain, and hives.

These are not all the possible side effects of VYVGART HYTRULO. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

What are the ingredients in VYVGART HYTRULO?

Active ingredients: efgartigimod alfa and hyaluronidase (human recombinant)

Each 5.6 mL single-dose vial contains 1,008 mg of efgartigimod alfa and 11,200 units of hyaluronidase (human recombinant). Each mL of solution contains 180 mg of efgartigimod alfa, 2,000 units of hyaluronidase (human recombinant) and histidine (1.4 mg), L-histidine hydrochloride monohydrate (2.2 mg), methionine (1.5 mg), polysorbate 20 (0.4 mg), sodium chloride (5.8 mg), sucrose (20.5 mg), and water for injection, USP, at a pH of 6.0.

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Getting a Handle on Myotonic Dystrophy

Q&A with Nicholas Johnson, MD

BY MYRNA TRAYLOR

Myotonic dystrophy is a multisystemic condition.

Image: sefa ozel/Getty

Myotonic dystrophy (DM) is a form of muscular dystrophy that was first identified by a German physician in 1909. The originally described version is now known as myotonic dystrophy type 1, or Steinert's disease after the doctor who identified the symptoms. Another form of myotonic dystrophy, once known as proximal myotonic myopathy or PROMM, and now called myotonic dystrophy type 2, was identified as a separate disease in 1994.

Nicholas Johnson, MD, is a clinical neurologist and researcher at Virginia Commonwealth University and the Children's Hospital of Richmond at VCU, as well as Director of the Center for Inherited Myology

Dr. Johnson and his research team are excited about the likelihood that effective gene therapies could soon be available to treat DM and other neuromuscular disorders.

Image: Lisa5201/Getty

Myotonic dystrophy type 1 is the most common form of muscular dystrophy in adults, affecting about 1 in 2,100 individuals, and is a multisystemic condition.

Research in the VCU School of Medicine's Department of Neurology. He has a particular interest in inherited muscle disorders, including myotonic dystrophy. Dr. Johnson and his research team are excited about the likelihood that effective gene therapies could soon be available to treat DM and other neuromuscular disorders. Quest Media asked him to share his knowledge about DM.

What is DM?

There are two types of DM. Type 1 (DM1) is the most common form of muscular dystrophy in adults, affecting about 1 in 2,100 individuals, and is a multisystemic condition. It is classically characterized by the development of muscle weakness that starts in the hands and feet; slowly progressive myotonia, which is the inability to relax your muscles; and early-onset cataracts that develop before the age of 50. DM1 also affects many other organ systems in the body, including the heart and lungs.

Type 2 (DM2) is less common than DM1. They share a development of progressive muscle weakness, but this time, the muscle weakness starts in the shoulders and hips. Patients with DM2 also develop early-onset cataracts and often have significant musculoskeletal pain. Heart issues may occur, but this is less common in DM2 than DM1.

When is DM typically diagnosed?

The diagnosis of DM1 and DM2 can be a little challenging, since either type can present with symptoms in any organ system. For example, some patients may develop stomach problems first or sometimes the pain in DM2 can look like fibromyalgia. Often, individuals with DM1 experience an approximate seven-year delay in their diagnosis. And it's even more challenging for DM2, where the delay in diagnosis may be up to 14 years.

In the most severe form of DM1, symptoms can be present at birth or develop in childhood, but sometimes individuals don't develop symptoms until their 40s, 50s or 60s. DM2 is also variable in terms of the age at diagnosis, but symptoms usually appear in early adulthood.

What causes DM?

Both types of DM are caused by changes in genes. In DM1, there's a gene called *DMPK* where a section of DNA with the letters CTG repeats too many times. In DM2, the same thing happens with a different gene called *CNBP*, but the repeated section is CCTG. These extra repeats interfere with how proteins are made, leading to the disease.

These are genetic disorders that are autosomal dominant, which means that you only need to have one mutated copy to cause disease. (We all have two copies of each gene, one from each parent, and in this case inheriting one gene mutation leads to the disease.) They are also passed along to every generation, and there's a 50% chance that future offspring will inherit the repeat expansion. It affects males and females equally.

DM1 is classically characterized by muscle weakness starting in the hands and feet.

Image: magicmine/Getty

DM1 also has a phenomenon called anticipation, where each child who inherits the gene mutation may have more repeat expansions than their parent, and therefore experience more severe symptoms. This difference in severity might also show up in siblings, where one has more severe symptoms than the other.

What are the typical symptoms?

One of the top symptomatic complaints, particularly in DM1, is daytime sleepiness and fatigue, which can be really debilitating. Oftentimes, we'll treat patients with stimulants to try to help keep them awake. In both DM1 and DM2, people may need mobility aids. In DM2, we often need to provide medication to deal with the significant pain that can develop with the disorder. Apart from that, it's important that individuals get regular cardiac monitoring for the cardiac heart rhythm disorders that can develop, and regular lung function testing for the pulmonary complications that can develop. From a combination of those issues, lifespan is usually shortened in DM1. In DM2, it's not yet clear that lifespan is shortened because of the disorder.

How do clinicians help individuals manage the disease?

For DM1, we can treat people with anti-myotonia medications like mexiletine. Current management also includes ankle braces and walking aids, as they are needed, and monitoring for heart rhythm disorders, pulmonary compromise, and early-onset cataracts. There are a number of endocrinological abnormalities that can occur, such as underactive thyroid or an increased risk of diabetes, so we also check for those.

Are there new treatments on the horizon?

We're very interested in the development of genetic therapies that have the potential to modify the course of the disease. Researchers are working on a way to help muscles absorb a special type of RNA (a molecule similar to DNA that is involved in protein production) by attaching it to an antibody or protein that can get inside muscle cells. Several companies have shown that this approach can fix the RNA issues involved in DM, reduce muscle stiffness, and improve strength. Specifically, Avidity Biosciences and Dyne Therapeutics have announced positive phase 1 and 2 results and are expected to move those products forward into phase 3 trials. It's been an exciting time for therapeutic developments in DM1, and of course, many of us in the field are quite hopeful that the same therapeutic approach will be applied to DM2 in the future.

Are there any related diseases whose treatments might help with DM?

Another diagnosis that benefits from a very similar therapeutic technology is facioscapulohumeral muscular dystrophy (FSHD). Q

Myrna Traylor is a writer for Quest Media.

Safe in the Extreme

Tips for winter weather safety with a neuromuscular disease

BY SUSAN JOHNSTON TAYLOR

Extreme winter weather wreaks havoc on everyone's routines, but it is especially disruptive for people with neuromuscular diseases. Many have balance or mobility issues that are made more challenging by wind, snow, and ice. Others rely on electricity to power a wheelchair or respiratory device.

In recent years, even regions of our country that aren't known for cold weather have endured widespread power outages and dangerously icy roads. Millions of Texans experienced this firsthand during the winter storm of February 2021. "It got cold here, and our infrastructure wasn't set up for that type of weather, so our power went out for about a week," says Roger Lopez, a former Safety Officer for the San Antonio Fire Department and current National Coordinator between the International Association of Fire Fighters and MDA.

During a winter weather event, access to needed resources and the ability to use medical and mobility equipment are jeopardized. Sometimes, it impacts even more fundamental needs, like shelter and warmth. "Making sure people with neuromuscular diseases stay warm is important," Roger says. That's because muscle loss and immobility make it harder for the body to generate heat.

Here are five essential tips for people with neuromuscular diseases and their caregivers to prepare for winter weather emergencies.

1. Sign up for emergency alerts.

Your school, workplace, or local community may have phone or email alert systems that notify people of weather-related closures and emergency plans, including warming centers. Roger encourages people to sign up for text messages to ensure they see these alerts and can act quickly.

2. Contact local services in advance.

Call 311, the nonemergency assistance number, to contact your local police, fire, and emergency services and let them know about your medical condition, essential medications, and any allergies. Also tell them if you use special medical equipment or oxygen canisters and where to find those in your home. The dispatch center can keep this information in a file connected to your address and share it with emergency services should the need arise.

Display essential medical information in an easily accessible spot in your home, like the front of the refrigerator. This will expedite getting the help you need if you or a caregiver can't explain your medical needs to emergency responders.

Also, alert your power company if you use a ventilator, power wheelchair, or other electronic medical device. In case of an outage, they may be able to prioritize restoring power to your home.

If you work in an office, talk with your supervisor about emergency plans and mention any concerns or needs. You may want to store a manual wheelchair or backup wheelchair battery at work in case of an emergency.

3. Stock up on medications and emergency supplies.

You may not be able to leave your home during a winter storm. Keep enough extra medication, drinking water, and nonperishable food on hand to last several days in case you're snowed in.

Remember that if you have an electric stove or can opener, you won't be able to use those during

Images: katrink03/Irina Cheremisinova/FANDSrabutan/Getty

a power outage. Shelf-stable foods that don't require heat include:

- Canned tuna or sardines (a pull top doesn't require a can opener)
- Crackers
- Protein bars
- Nuts and dried fruits

On the other hand, if you need to evacuate, have your medications and an emergency kit ready to grab and go. Your winter emergency kit should include:

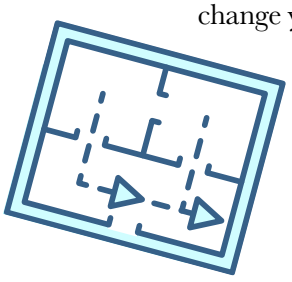
- Backup battery for a power wheelchair or other medical equipment
- Flashlight
- Battery-powered radio
- Extra batteries
- Cell phone charger
- Blankets
- Hand and foot warmers

4. Check smoke and carbon monoxide detectors regularly.

Many people use space heaters or generators to keep warm during the winter. But without proper ventilation, these devices can create the risk of fire or carbon monoxide poisoning. This is especially dangerous during a weather event when emergency services are overtaxed and may not be able to respond quickly.

"Any type of energy-producing device is going to produce carbon monoxide, which is not detectable to human senses," Roger says. Running a vehicle in the garage to keep warm or charge devices also creates carbon monoxide risk.

Test smoke and carbon monoxide detectors at least once a month and replace the batteries at least twice a year unless you have a recent model with long-lasting batteries. "Every time you change your clocks for daylight savings, change your battery," Roger recommends.



5. Plan your escape route.

In case of a fire or other emergency, you should have at least two ways to exit your home and get to safety. If you use a wheelchair, there should be more than one accessible exit in case the main exit isn't safe.

"During a winter storm, if you can leave the house and go somewhere else, like a warming center in a library or school gym, that's probably one of your better bets," Roger says. If you can't leave, being stocked up on medications and emergency supplies will see you through.

Everyone hopes emergency plans and measures won't be necessary. However, being prepared gives you and your caregivers peace of mind no matter what winter throws at you. Q

Susan Johnston Taylor writes about health and general interest topics.

BE PREPARED

Be ready for anything with these MDA resources

Webinar: Preparing for Emergencies
This webinar covers how to make an emergency plan, how to build an emergency kit, and other ways to prepare for many types of emergencies. **youtube.com/watch?v=OI0x41Mm3-0**

Downloadable guide: Emergency Preparedness for People with Disabilities
This guide provides helpful lists of what to do before, during, and after natural disasters and other emergencies. **mda.org/emergency-preparedness-with-disabilities**

Checklist: Preparing for Emergencies, A Checklist for People with Neuromuscular Diseases
Use this checklist to help you prepare an emergency plan that will protect you and your loved ones. **mda.org/emergency-checklist**

Wallet cards: Emergency Room Alert Cards
Disease-specific Emergency Room Alert Cards detail precautions needed in a medical emergency for people with amyotrophic lateral sclerosis (ALS), Duchenne muscular dystrophy (DMD), and myasthenia gravis (MG). They can be printed and folded to fit conveniently in a wallet or purse. The Emergency Room Alert Summary is designed to be filled out with specifics on any neuromuscular disease. Find them under "Emergency Care Resources" at **mda.org/education.**

Advancing Research in ALS and MG Rooted in Community and Driven by Science

Most neuromuscular diseases are debilitating, progressive conditions that significantly impact quality of life for patients, caregivers, and their families. Given the complexity of these diseases, it is critical to understand what is most meaningful to people living with these conditions to adequately address their needs. With roots in neurology, Regeneron recognizes the importance of patient and caregiver insights that can drive critical scientific advancements in conditions like amyotrophic lateral sclerosis (ALS) and myasthenia gravis (MG).

Understanding and Addressing the Unique Challenges of SOD1 ALS in Clinical Trial Design

One form of ALS, called SOD1 ALS, is caused by a mutation in the SOD1 gene and affects a particularly small patient population, accounting for approximately 2% of all ALS cases in the United States. The rarity and genetic nature of SOD1 ALS, combined with its devastating symptoms, present unique challenges in both understanding the patient journey and designing clinical trials.

Engaging the community is one of the most critical first steps, essential to enhancing our understanding of the full spectrum of challenges they face. In the early stages of our clinical development program, the Regeneron Patient Advocacy team proactively partnered with leading Patient Advocacy Organizations to collect insights from patients, caregivers, and advocates on aspects of clinical trial participation that are burdensome to patients and ways to improve their experience. Community members shared numerous pain points and opportunities, including the need for better education on trial participation and the desire for more specific information about what is involved in each study visit. Participants also shared that one procedure, the lumbar puncture, which can be uncomfortable and particularly burdensome but necessary for gathering data.

"Reducing the number of lumbar punctures was evident as a primary concern for patients. Many of them have endured monthly spinal taps for years. Helping to enhance the patient experience – while still considering the integrity of the research is crucial for the advancement of science that truly addresses all patient needs. We were glad, in this case, that we were able to reduce the number of lumbar punctures required in our trial protocol."

– **Oren Levy, MD, PhD**
Medical Director, Regeneron

After reducing the number of lumbar punctures in the clinical trial protocol, we recognized addressing other aspects to clinical trial participation could further improve the experience. Whether it's offering comfort items like eye masks or providing travel assistance and accommodation for patients and caregivers, Regeneron recognizes the importance of the patient experience in our clinical trials, especially when working in a rare disease.

Understanding and Navigating the Unique Challenges of Myasthenia Gravis

Myasthenia Gravis (MG) is a chronic autoimmune disorder that affects the communication between nerves and muscles, leading to generalized muscle weakness, fatigue, and ocular symptoms. This rare neuromuscular condition poses unique challenges for patients, particularly related to receiving a timely, accurate diagnosis and maintaining effective long-term disease management.

Regeneron applied a similar patient-centric mindset to our work in MG. When we launched a Phase 3 clinical program in MG, we were confident in the science—but knew the only way to potentially improve outcomes for patients was to work with the community to understand their experience.

"We were new to this community, and knew we needed to learn a great deal about the patient experience and the unmet needs. The only way to do this was to work with the trusted sources for people living with MG and those trusted sources are Patient Advocacy Organizations."

– **Rosemarie Sellati, MS**
Director of Global Patient Advocacy, Regeneron

Regeneron worked with leading Patient Advocacy Organizations to establish an MG Council of patients, caregivers, and community representatives. The Council serves as a panel of experts, highlighting current unmet needs, providing input into trial participation, and ensuring patient materials align with the intended audience. With input from the panel, we made significant improvements to our patient materials, such as increasing font size, adjusting color contrast, and selecting imagery that better resonated with the community—essential changes given many people living with MG experience ocular symptoms.

We also learned that many patients live in rural areas, making it difficult to access healthcare and information on trial opportunities. To address this, Regeneron partnered with organizations through events like national patient conferences and regional health fairs to support disease awareness and share clinical trial opportunities with local communities.

Keeping trust and knowledge-sharing at the forefront, we are actively collaborating with patient organizations to publish our findings. Publications will include our work detailing the patient experience from symptomology through disease management with a comprehensive resource audit of education and support materials. We believe sharing this information will provide a roadmap for future initiatives for all contributors to the space.

"We are breaking industry norms by sharing findings from our patient advisory boards at upcoming medical meetings. We know first-hand insights from patients are critical to designing patient-focused clinical trials, and are eager to share them with the goal of helping to advance disease management for people living with MG."

– **Ching Lum, PharmD**
Director of Medical Affairs, Regeneron

Regeneron is conducting ongoing research. Study drugs have not been reviewed by any regulatory authority and their safety and effectiveness are unknown. Talk to your doctor to learn more about your treatment options.

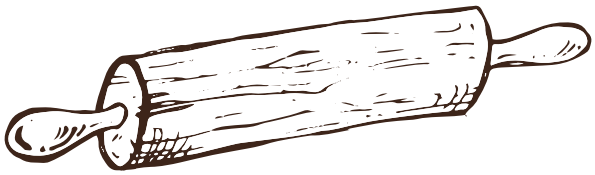
Regeneron is committed to ongoing collaboration with patient communities. To learn more about how we keep patients at the forefront of scientific discovery, visit Regeneron.com.■

Easy Holiday Ent

From Hanukkah to Christmas to Kwanzaa, the holidays bring family and friends together with festivity, food, and fun. It also can be one of the most stressful times of the year for many people, especially when you're hosting and you have a neuromuscular disease.

Fortunately, Quest Media has put together a guide to easy holiday entertaining with a disability. Follow these recommendations from community members and experts to minimize your holiday hosting stress — and remember why you're having that party in the first place.

Illustrations: Margarita Miller/Getty



tertaining

Amber Bosselman

Take the stress out of hosting so you and your guests can embrace the spirit of the season

BY CLAIRE SYKES

Leah Zelaya

Therese Gabriel

Bevi Zelaya (right) gets her youngest son involved in preparing a meal.

Party Profile

THE ZELAYA FAMILY

"The meaning of the holidays is to gather with loved ones and appreciate each other," says Bevi. Her husband, Jaime, and their 16-year-old daughter, Leah, both live with scapuloperoneal spinal muscular atrophy (SPSMA), and it doesn't stop this family of five in Brooklyn, New York, from hosting annual holiday gatherings for friends and family. Even preparing for their guests is a party for Bevi and her three children. "We're building memories," Bevi says.

EMBRACE THE RIGHT MINDSET

To get in the proper holiday party planning spirit, ask yourself a simple question: What kind of party would I enjoy?

"Do what's best for you," says Amber Bosselman, a Disability Life Coach in St. Paul Minnesota, who lives with spinal muscular atrophy (SMA). "I try to entertain in a way that's natural and comfortable. When I feel confident, it's fun for me and others, too."

Here are more ways to maintain a joyful frame of mind while preparing a seasonal gathering:

- **Keep it simple.** "Don't overdo or overthink things," says Leah Zelaya, an MDA National Ambassador living with scapuloperoneal spinal muscular atrophy (SPSMA). "There's no need to feel pressured or try to prove you can do something you can't." For example, it's OK to keep the guest list small, order prepared food, or use paper plates.
- **Pace yourself.** Do the tasks on your to-do list a little at a time in the weeks before the party. Taking on too many tasks at once can lead to fatigue, a common symptom of neuromuscular diseases. Marisa Palandri, OT-L, CLT, CDRS, an occupational therapist at Oregon Health Science University, explains our energy is like a battery. "Before neuromuscular symptoms, you're charged to 100%, but as your disease progresses, maybe you're waking up every day at 50% to 70%. After one or two tasks, you drop to 25% to 50%. At that point, take a break so you can recharge and avoid hitting 10%."
- **Enlist help.** "Often, people feel bad asking for help. However, what is worse is not asking for help when you need it," says Leah. When you allow others to step in, you lighten your load, and you give them a chance to contribute to the fun occasion.
- **Know your guests.** Before you decide on food and beverages, ask guests about any dietary restrictions. Consider who might want to meet or sit near each other and enjoy certain games. "Have something for everybody and plenty of everything," says Ira Walker, an MDA National Ambassador living with SMA.

Ira discovered the benefits of lightweight cookware.

Party Profile
IRA WALKER

Growing up, Ira enjoyed the parties his parents had in their suburban St. Louis home. "My sister, Romanda, also was born with spinal muscular atrophy, and we were both in wheelchairs. Knowing that not everybody's house was accessible, my parents wanted to make sure we were included, so they always raised their hands to host," he says. When Ira moved into an apartment, he started having parties of his own. "I learned from watching my parents how to throw a great get-together, and I've hosted lots of them, of various sizes," he says. "The most important thing is to be together and celebrate with one another."

+ **Go with the flow.** Keep in mind that nothing is going to be perfect. "Don't sweat the small stuff you think people might be bothered by; they won't be," says Ira. Amber says, "You may think the spotlight is on you, so you might feel scared to make mistakes. The truth is, everyone attending feels like the spotlight's on them."

PLAN AND PREPARE

Here are the main elements to get ready for your party.

Your budget

Decide on a budget, then determine what type of party you can have within that. "Don't add unnecessary stress by overspending," Ira says. "Most of your expenses will go to food and beverages. The last should be decorations."

Your home

In the weeks before your holiday party, clean your home (or hire someone to do it), designate a place for guests' coats, set up tables or arrange small group

Therese chooses décor that makes her home feel welcoming.

Party Profile
THERESE GABRIEL

"I love making people happy. And they are when you feed them good food and provide a welcoming home," Therese says. She's been spreading happiness for more than 40 years. Up to 18 friends and family come to her home in St. Louis for Thanksgiving dinner. For Christmas, she hosts a dinner/cookie party where, instead of gifts, guests bring cookies and items to donate to a local charity. Therese assures that no one is left out: "If plans have changed for any neighbors, friends, or family, and they have no place to go, all are invited to join us!"

Therese asks guests to bring desserts and charitable donations to her holiday party.

sitting areas, get out serving dishes, and make room for the food and beverages.

The kitchen

If you like to cook or bake but muscle weakness slows you down, consider investing in some new kitchen equipment. Ira recommends lightweight pans and countertop appliances, such as a small grill, crockpot, and a toaster oven/air fryer combo. Leah's family has purchased adaptive kitchen equipment, such as a rocker knife, nonslip cutting boards, and vegetable choppers, from wellness4ky.org/resource/adaptive-kitchen-equipment.

The menu

Love homemade? "Stick to what you know and do well," says Therese. "Now is not the time to try a new recipe unless you give it a trial run first." You can ease the burden on yourself by making one or two dishes you enjoy and rounding out the meal by asking guests to bring other dishes or ordering food.

The food and drink

Think about what you can prepare ahead of time. "You can cook and bake things a day or even weeks before and freeze them," recommends Leah's mom, Bevi. Then, you'll just need to thaw or heat them on the day of the party.

YOU ARE NOT ALONE

Everyone feels lonely sometimes. That feeling can be especially difficult during the holiday season. Learn how you can take healthy steps to lessen or avoid loneliness in a Quest Magazine online exclusive article at **MDAQuest.org/not-alone**.

The table

Will your dinner be sit-down or self-serve? Either can be formal or casual, but one is a lot easier, at least for Leah and Bevi, who prefer buffet style. For a potluck, have empty platters, bowls, and serving utensils waiting for guests who bring dishes.

You!

Yes, you are an essential element of the party, so don't neglect your own care. Get plenty of sleep, especially the night before. Marisa, an occupational therapist, suggests using the evening before the party to shower and fix your lunch for the next day. On the day of the party, do as little as possible so you can save your energy for your guests. If you live alone and think your home will feel too empty and quiet once everyone leaves, ward off loneliness by asking a friend to call you afterward.

HAVE A GREAT TIME

When it's time to mix and mingle, follow these tips to make sure your guests — and you — enjoy the occasion.

- **Be welcoming.** "Warmly greet each guest and let them know how happy you are that they're there," says frequent hostess Therese. Designate someone to help you take their coats and offer drinks as they arrive.
- **Get comfy.** "As host, you want to create an environment for people to enjoy themselves," says Amber. This might involve helping quieter people mingle and bringing those who don't know the other guests into the fold. "When you introduce guests to each other, say lovely things about them," suggests Therese. This makes each person feel special and can spark conversations.
- **Take breaks.** It's OK to leave the party for a few minutes. Privately ask someone to play substitute host during those moments. "No one needs to know you're gone except the person privy to your 'code phrase,' so they can take over the host job for a little bit," says Marisa.
- **Stay put.** Don't be flitting around cleaning up as the party is happening. Conserve your energy so you can give your full attention to your guests.
- **Have fun.** Why entertain unless you do? "It's not your home or the food that matters most. But rather, if you're relaxed and enjoying yourself, then your guests are, too," says Therese.

Leah chooses simple, crowd-pleasing recipes.

CHEERFUL OR CHALLENGING?

How do Quest readers feel about the holidays? See the latest Quest Poll on page 48. If you're feeling holiday stress, listen to the Quest Podcast at **MDAQuest.org/podcast/holiday-stress**.

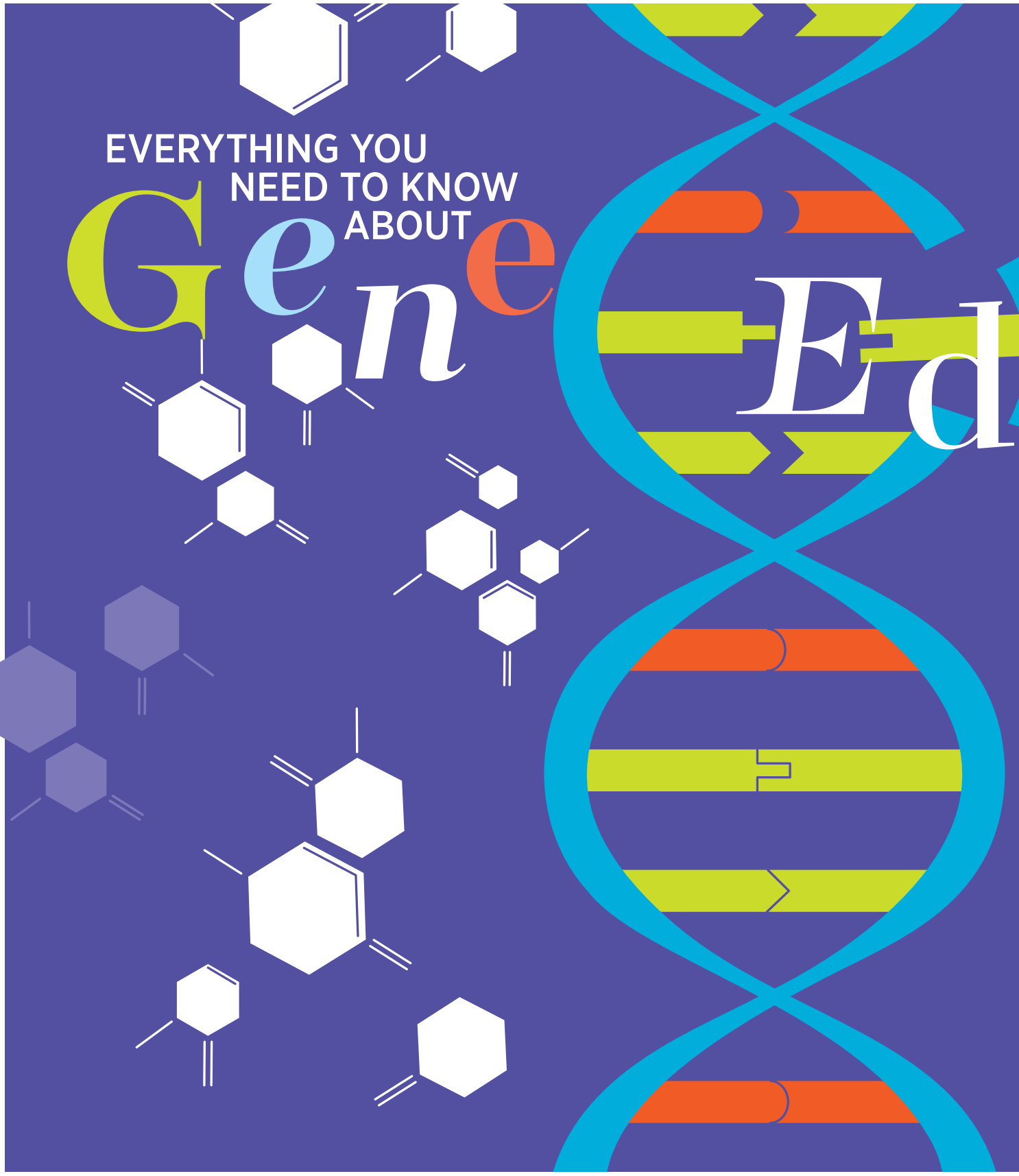
GIVE GRATEFULLY

In hosting a holiday gathering, you do more than open your home to others. "You give them a peek into your life and share how you've adapted to some of the challenges you face every day," Therese says. This may seem like a small thing, but it matters in ensuring that people with disabilities are visible and represented in our society.

Entertaining can also have benefits for the host: "You create more opportunities to continue building deep connections, which is also a great antidote if you're prone to feeling lonely," Amber notes.

When you make entertaining easier on yourself, the stress you alleviate opens up your heart to spend quality time with those you love more generously. There's no better gift than that. **Q**

Claire Sykes is a freelance writer in Portland, Oregon, who covers health and the human side of bioscience.


EVERYTHING YOU
NEED TO KNOW
ABOUT
Gene Ed

iting

This gene therapy technique holds unique promise

BY LARRY LUXNER

Gene therapies for neuromuscular diseases are creating quite a buzz these days. This is a promising therapeutic area, with two such therapies approved and many more in clinical trials. Some experts would argue that gene editing holds even more promise, as it can truly alter a genetic mutation at its source and avoid some of the limitations current gene therapy methods have.

At the moment, gene editing is still in the early stages. In 2023, the US Food and Drug Administration (FDA) approved the first gene editing-based therapy for the treatment of sickle cell disease. Although no therapies using gene editing are currently approved or in clinical trials for neuromuscular diseases, it's beneficial to understand what it is and why the scientific world is excited about it.

Image: LadadikArt/Getty

How does gene editing work?

Gene editing involves altering a targeted section of **DNA** within cells. This approach can precisely target **genetic mutations**.

The most well-known gene editing tool is **CRISPR-Cas9**. This technology can enter cells, cut a specific section of DNA and then remove, add to, or replace that section. This change becomes permanent, allowing cells containing the repaired DNA to make functional **proteins**.

Another method being explored is base editing. This is an ultraprecise gene editing method that targets just one of the four base chemicals that make up DNA. These bases are called adenine (A), guanine (G), cytosine (C), and thymine (T). Certain bases pair with each other — A with T and C with G — to form units called base pairs. A base that is missing, mismatched, or out of order can alter how cells make proteins.

"Typical CRISPR-Cas9 editing involves cutting both strands of the DNA helix. With base editing, there's no cut in the DNA; we simply modify a single letter in the DNA," says Eric Olson, PhD, Founding Chair of the Department of Molecular Biology at the University of Texas Southwestern in Dallas and a pioneer in the gene editing field. "We are very excited about this approach, which we're taking, as it does not have the concerns associated with making a double-stranded DNA break."

Words in blue are defined in "Words to Know" on page 38.

MDA has funded several research studies on promising new approaches to gene editing, including base editing.

How is gene editing different from other gene therapy methods?

Gene editing is a type of **gene therapy**. Most of the currently available gene therapies work by delivering a working **gene** into the body using an adeno-associated virus (AAV) **vector**. The AAV is not harmful, but it can enter cells to deliver a working gene that provides new instructions to produce a needed protein. This is called gene replacement.

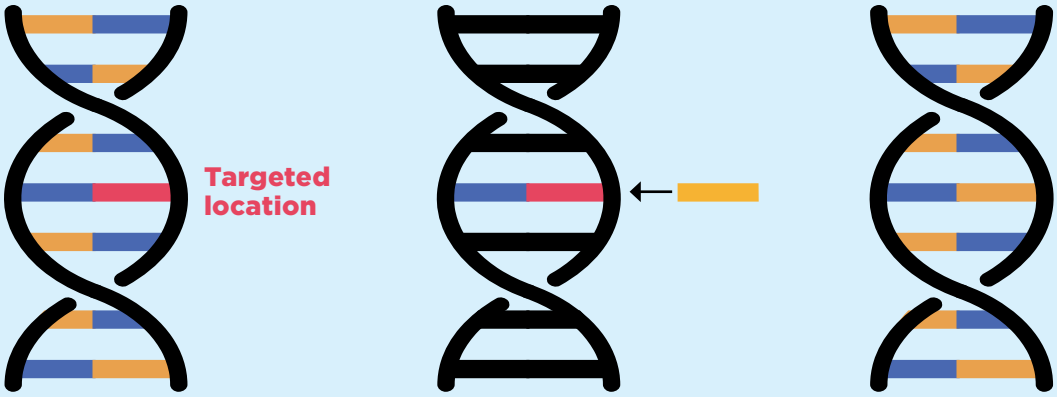
CRISPR-CAS9 GENE EDITING

1. Find
A CRISPR molecule finds a specific DNA section containing a genetic mutation.

2. Cut
The Cas9 enzyme cuts both strands of DNA at **the target location**. DNA can be removed from or added to that location.

3. Repair
The cell's **natural DNA repair** process makes the change permanent.

BASE EDITING



1. Find
The base editor finds a **targeted location** on the DNA with an incorrect letter in the genetic code.

2. Modify
The base editor chemically changes the incorrect letter to **the correct letter**.

3. Restore
The correct **DNA sequence** is restored, allowing cells to make functional proteins.

"With gene replacement, we're trying to add a functional copy of a gene. We're not fixing the mutation or changing anyone's DNA," explains Sharon Hesterlee, PhD, Chief Research Officer at MDA. "The person still has the mutated gene in their chromosome; we're just putting in a healthy copy. The idea is that this healthy copy can stand in."

This method of gene therapy is used in onasemnogene abeparvovec-xioi (Zolgensma®), approved by the FDA in 2019 to treat spinal muscular atrophy (SMA). This therapy has had demonstrable benefits. Some children who were identified with SMA through newborn screening and given Zolgensma as infants have not yet developed symptoms of the disease.

It's possible these benefits will last a lifetime, but gene therapy has not been around long enough to know. Our bodies are constantly making new cells to replace old cells. With gene replacement, the new cells still contain the genetic mutation. As new cells replace older cells that received the functional copy of the gene, the effects of the gene therapy may become "diluted." Dr. Hesterlee points out this is especially concerning with a muscle disease like Duchenne muscular dystrophy (DMD). "The child who receives gene therapy will continue to grow muscle, and that new muscle will not have the gene you delivered," she says.

MDA has funded several research studies on promising new approaches to gene editing, including base editing.

Among the biggest issues with current gene therapies usinge AAV vectors is that they can only be given once, even if they wear off.

"Once patients have been dosed with AAV, they can't be dosed again — at least not currently — because of the body's immune response," Dr. Olson says. "There may be ways to bypass that response, but we're not there yet."

In addition, because AAV is a naturally occurring virus, some people have been exposed to it without knowing it and have developed immunity. They would not be eligible for any gene therapy using an AAV vector.

Advantages of gene editing

The biggest advantage of gene editing is that it truly "fixes" a genetic mutation.

"Gene editing offers the opportunity to correct a mutation within the patient's DNA," explains Dr. Olson, who directs UT's Hamon Center for Regenerative Science and Medicine, as well as the Wellstone Center for Muscular Dystrophy Research. "This is particularly attractive for a disease like DMD because the dystrophin gene is one of the largest genes in the human **genome**," he says. To develop an AAV-delivered gene therapy for DMD, researchers have to use a miniaturized dystrophin gene that doesn't have the full functionality of the whole gene.

The biggest advantage of gene editing is that it truly "fixes" a genetic mutation.

"When one uses gene editing, the corrected gene is then expressed at the right time, in the right place, and at the right level," Dr. Olson says. "This is why we think it's the ultimate solution for many neuromuscular diseases — but it's going to take time and careful experimentation to ensure a safe approach."

Challenges of gene editing

Because gene editing permanently changes DNA, it might not require redosing, but it does raise safety concerns.

"You're introducing into the patient an enzyme that can modify the genome, though so far, we and others have not seen significant off-target editing," Dr. Olson says.

A chance that a gene editing therapy might result in an off-target edit (an unintended genetic modification) may be considered too risky. "Even if it's cutting in the right place 99% of the time, the problem is the 1% where it doesn't," Dr. Hesterlee says.

WORDS TO KNOW

Here is a guide to terms used in this article.

CRISPR-Cas9: A tool used to "edit" pieces of a cell's DNA. Also called CRISPR, this tool uses a specially designed RNA molecule to guide an enzyme called Cas9 to a specific sequence of DNA. Cas9 then cuts the strands of DNA and removes a small piece, causing a gap where a new piece of DNA can be added.

DNA: A long molecule that carries a cell's genetic information.

Genes: Segments of DNA that act as blueprints for making proteins for virtually every structure and function in the body.

Gene editing: A type of gene therapy in which a particular segment of DNA is removed or altered.

Gene therapy: Adding, removing, or changing genetic materials in a person's genetic code to treat or cure a disease.

Genetic mutation: A flaw in a sequence of DNA that alters gene function.

Genome: The sum of all genes in the body.

Messenger RNA (mRNA): A molecule that contains instructions for cells to make proteins.

Proteins: Complex molecules that play many critical roles in the structure, function, and regulation of the body's tissues and organs.

Vector: A delivery vehicle that carries new genes to cells.

Image: LadadikArt/Getty

Despite these concerns, neuromuscular disease researchers continue to pursue gene editing because of the promise it offers. "If you can get it right, then you've done a permanent correction," Dr. Hesterlee says.

Where gene editing research is heading

Dr. Olson's lab is working on solving one of the major challenges of gene editing: how to deliver gene editing *in vivo*, or inside the body. The only FDA-approved gene editing therapy is performed *ex vivo*, or outside the body — cells are extracted from the person being treated, modified in a lab, and then implanted back into their body.

Currently, AAV vectors are the most effective way to deliver gene therapy *in vivo*, but gene editing materials are difficult to fit in an AAV. According to Dr. Olson, the long-term solution may be a combination of gene editing with nonviral delivery. This would accommodate the size of gene editing materials while lowering toxicity associated with large doses of viral vectors, which in the past has resulted in some adverse reactions in DMD gene therapy clinical trials.

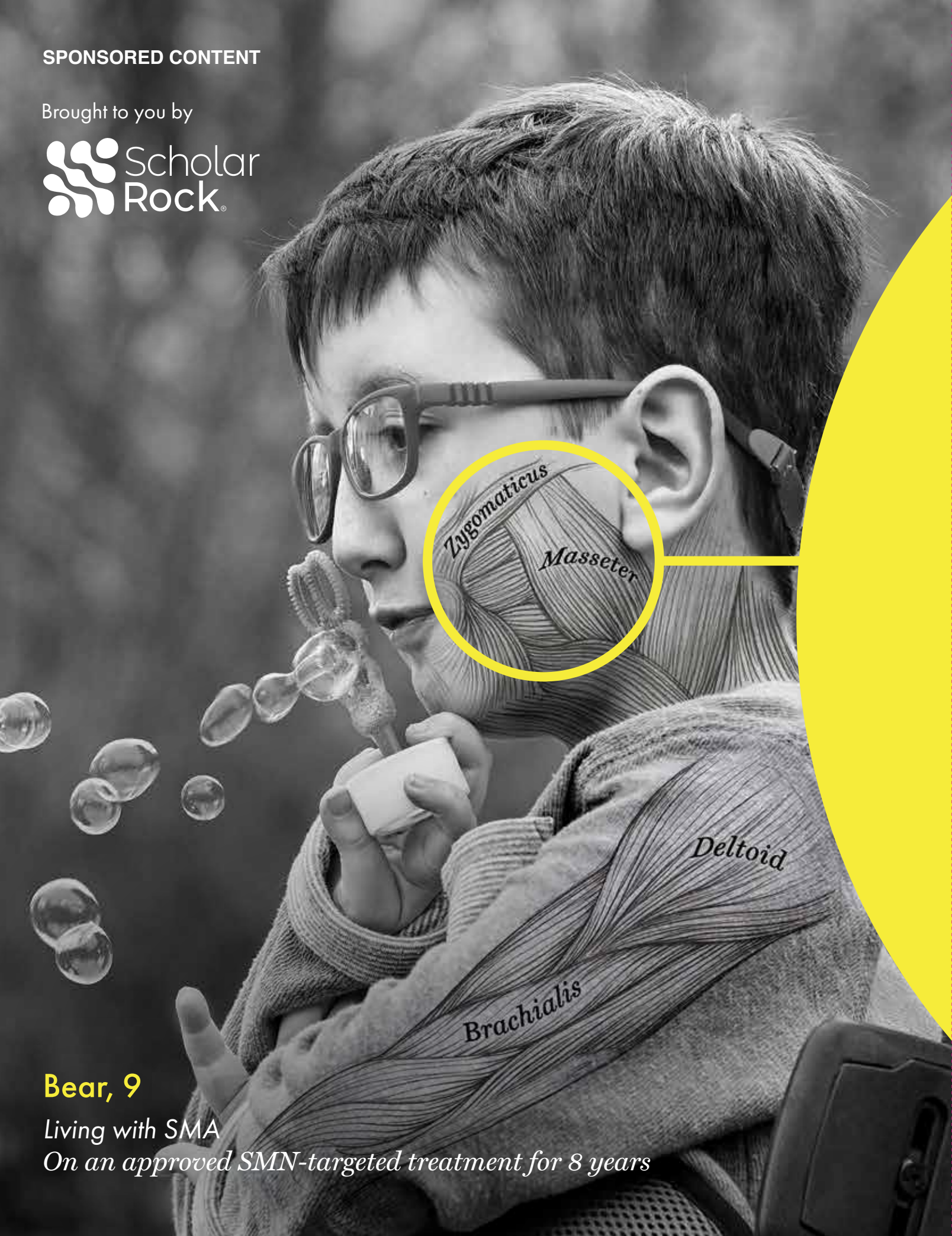
The long-term solution to delivering gene therapy *in vivo* may be a combination of gene editing with nonviral delivery.

Dr. Olson is encouraged by the highly successful Pfizer and Moderna COVID-19 vaccines, which rely on **messenger RNA (mRNA)** technology as a delivery method. Inside the body, mRNA gives instructions to cells, and it has proven to be a safe, effective, and precise way to deliver vaccines and, potentially, treatments for genetic diseases.

"We've certainly seen the transformative impact of nonviral approaches with COVID vaccines, though there are other challenges with muscle, which comprises 40% of the human body mass," he says.

Dr. Olson believes he and others are close to breakthroughs on these challenges. "I'm hopeful that gene editing and other approaches will bring long-term benefits to the many patients in need," he says. Q

Larry Luxner is a freelance journalist based in Israel. He writes frequently about rare diseases.



Bear, 9

Living with SMA

On an approved SMN-targeted treatment for 8 years

LIFE TAKES MUSCLE

STOP **SMA** FROM DOING THE SAME

Muscles work together to power almost everything we do, from breathing, to sitting upright, and even blowing bubbles. By definition, spinal muscular atrophy (SMA) is a neuromuscular disease that results in the loss of both nerve cells and muscle. Survival motor neuron (SMN)-targeted treatments have made great strides in treating people living with SMA; however, progressive muscle weakness persists. The community is looking for more, and that starts with a focus on preserving motor function and improving muscle strength.

See how muscle matters to people living with SMA at **LifeTakesMuscle.com**.

Learn more about the latest in SMA

US-SMA-0002 08/2024

IS VOCATIONAL TRAINING

This alternative to college streamlines entry into the workplace

BY STEVE WRIGHT

If you hear the phrase "vocational training" and think, "That's not for me," then you might not be considering the full picture.

Vocational training, sometimes called trade school or technical education, provides job-specific instruction that equips trainees with skills needed in the workforce. Unlike traditional academic education, it focuses on practical knowledge and on-the-job training related to a particular trade rather than broad exposure to the liberal arts and sciences.

Vocational training can be a desirable option for people with disabilities who are interested in entering the workforce for the first time or wish to develop new skills. In addition to saving time and cost over four-year college, vocational training can capitalize on common skills in the disability community.

Image: Artis777/Getty

ONAL FOR YOU?

"From junior year on, I spent every day of the week training for what I wanted to do. I lived and worked in Los Angeles for about three years — as long as I could after being diagnosed with limb-girdle muscular dystrophy at age 20."

—Cassidy Nilles

Vocational training gave Cassidy Nilles a flexible career.

Benefits of vocational training

People may assume vocational training is for manual labor (think plumbers or mechanics), but that isn't always the case. Increasingly, many vocational jobs rely on technical skills rather than physical abilities — think of a civil engineer technician who helps an engineer draft building plans and analyze materials and costs using special software.

The shorter timeframe and lower cost of vocational training can mean lower student loan debt and a fast track to employment. With employers much more supportive of remote work after the pandemic, vocational programs can open a wide range of careers that can evolve and grow.

According to Alice Muterspaw, Vice President of Vocational Services at The Viscardi Center, traditional vocational training fields, such as mechanical, culinary, and cosmetology, still exist, but there is a growing number of well-paying jobs that are not focused on physical labor.

"You can get IT training and be hired to work at a remote help desk," she says. "Call centers are a large market right now, and people can be set up to do that remotely."

The Viscardi Center in New York offers a range of services for people with disabilities, including vocational training and job placement. Alice believes that in a rapidly changing workforce, vocational training can make a worker just as attractive to employers as a person with a four-year academic degree.

She also notes that state vocational rehabilitation agencies, which provide services to help people with disabilities pursue employment, often fund vocational training programs and provide tools or support needed to complete them, such as transportation.

A flexible career

MDA Ambassador Cassidy Nilles launched her career through vocational training and plans to take that route again when she reenters the workforce.

A SAMPLING OF VOCATIONAL TRAINING JOBS

Occupation	What they do	Projected growth rate	2023 median annual pay
Audio and video technicians	Set up, operate, and maintain sound and video equipment	Faster than average	$54,160
Civil engineering technologists and technicians	Help civil engineers plan, design, and build projects	Slower than average	$60,700
Claims adjusters, appraisers, examiners, and investigators	Evaluate insurance claims	Slower than average	$75,020
Court reporters and simultaneous captioners	Transcribe speech for legal proceedings, television program, or presentations	Average	$63,940
Hairdressers, hairstylists, and cosmetologists	Provide services related to hair and makeup	Faster than average	$35,080
IT security analyst	Implement security measures to protect an organization's computer networks and systems	Much faster than average	$120,360
IT support specialists	Maintain computer networks and provide technical help to computer users	Faster than average	$60,810
Medical assistants	Complete administrative and clinical tasks, such as scheduling appointments and taking patients' vital signs	Much faster than average	$42,000
Medical records specialists	Compile, process, and maintain medical records	Faster than average	$48,780
Property managers	Oversee many aspects of residential, commercial, or industrial properties	Average	$62,850
Real estate brokers and agents	Help clients buy, sell, and rent properties	Slower than average	$56,620
Tax preparers	Prepare tax returns for individuals or small businesses	Average	$49,010
Travel agents	Sell transportation, lodging, and entertainment activities to individuals and groups planning trips	Average	$47,410

Source: US Bureau of Labor Statistics, Occupational Outlook Handbook

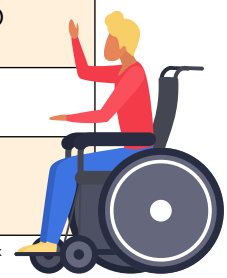


Image: Artis777/Getty

While growing up in the Chicago suburbs, she wanted to be a hairstylist. She liked the idea of being her own boss and having a career right out of high school.

"From junior year on, I spent every day of the week training for what I wanted to do," Cassidy says. "I lived and worked in Los Angeles for about three years — as long as I could after being diagnosed with limb-girdle muscular dystrophy [LGMD] at age 20." She liked controlling her destiny and earning money via talent and hard work.

CHOOSING A PATH

Deciding what to do after high school is challenging for everyone. Read about strategies to help teens with disabilities think about their next steps or future careers at MDAQuest.org/career-path.

The Viscardi Center in New York offers a range of services for people with disabilities, including vocational training and job placement.

Cassidy is currently a stay-at-home single mom to her 6-year-old daughter and uses a power wheelchair for mobility. She observes that vocational training can be easier for a single parent, as well as a person with a disability, to afford and manage around their needs.

"There are many options for certification programs and opportunities to expand the career you're in," she says. For example, although Cassidy can no longer work as a hairstylist, she plans to stay in the beauty industry, perhaps as a licensed colorist who creates custom hair color formulas for an online company.

+MENTORSHIP PROGRAM

Teens and young adults with neuromuscular diseases can join the MDA Mentorship Program to connect with mentors in a variety of fields and get hands-on learning in a supportive environment. The aim is to help youth discover their strengths and interests and increase the number of people living with neuromuscular diseases in the workforce. Learn more at **mda.org/mentorships**.

"If my daughter wanted to go into vocational training, I'd say, 'heck yeah,'" she says.

Adaptable skills

Another advantage of vocational training is that it allows an individual to focus on their interests and adaptable skills.

"If you are a great problem solver, into computers, or love travel, there are careers, many remote, that can be attained via vocational training that leads to certification," Alice says.

Lori Becker, CEO of the Starkloff Disability Institute in Missouri, is also a graduate of the Starkloff Career Academy. She has seen firsthand how vocational training can leverage transferable skills.

"Every disability is unique and has different impacts on the body," she says. "I'm legally blind. Our chief financial officer has congenital muscular dystrophy [CMD]. The great thing is that there are plenty of vocations that are not the typical carpenter or electrician."

She gives an example: "Cybersecurity is a booming field that can be done on your computer at home. You could get a certification in as little as six months and get an entry-level job. Then you can grow in increments — whether it is going back for a higher IT certification level or pursuing a master's degree."

While each person's interests and needs may be different, people in the disability community commonly have skills that are adaptable to just about any job.

"Many people with disabilities are great at planning, organizing, and problem-solving because they live in a world not designed for them," Lori says. "Employers are looking for more diverse talent. They want to hire a workforce that reflects the community."

Richard Vagen, who has a type of muscular dystrophy and uses a wheelchair for mobility, works part time in enrollment for continuing education at St. Louis Community College, which delivers professional development and vocational opportunities. After earning a bachelor's degree in art history, Richard attended a Starkloff career program aimed at honing job interview skills for people with disabilities.

"I think the number of programs offered in the vocational space and the way they adapt with the times gives people with disabilities the opportunity to discover fields in which they can rise," he says. "My job evolved into virtually all remote work, with flexibility that allows me to help raise my kids and manage my disability."

Presenting oneself to employers as a person with a disability who is confident in their skill set and has the certification to back it up can be a pathway to a career, not just a paycheck.

Steve Wright is an award-winning writer and advocate based in Miami. He lectures throughout the US and abroad on creating a better built environment for people with disabilities.

"I think the number of programs offered in the vocational space and the way they adapt with the times gives people with disabilities the opportunity to discover fields in which they can rise."

— Richard Vagen

Richard Vagen attended a Starkloff career program.

Reporting Back from MDA on the Hill

For three days in September, MDA staff and grassroots advocates came together in Washington, DC, to ensure lawmakers heard their voices. This event, called MDA on the Hill, featured advocacy training, networking, meetings with members of Congress and their staff, and much more. Take a look at all the action.

Image: smartboy10/Getty

By the numbers

+ 95 advocates and staff attended
+ 24 states were represented
+ MDA advocates had 97 meetings with lawmakers and staff

Making voices heard on key issues

MDA advocates encouraged lawmakers to support three key bills that are important to the neuromuscular community:

1. **SSI Savings Penalty Elimination Act:** A bill to eliminate the savings penalty for Supplemental Security Income beneficiaries by raising outdated asset limits.
2. **Rare Pediatric Disease Priority Review Voucher Reauthorization:** A vital program that incentivizes the development of treatments for rare pediatric diseases, which will expire without Congressional action.
3. **Accelerating Kids Access to Care Act:** A bill to streamline the process for children with complex medical needs to access care through Medicaid across state lines. Right now, there is a lot of red tape if a child on Medicaid needs to obtain medical care in another state.

We hope these three bills will pass Congress by the end of the year.

More than lobbying

Increasing support for legislation that benefits our community is the main objective of MDA on the Hill, but we know that participants get a lot more out of the event. Advocates routinely take home the speaking skills and important connections they made in Washington, DC, and continue to advocate on MDA issues where they live. In addition, participants build invaluable friendships with fellow advocates.

To learn how to join a future MDA on the Hill event, contact MDA Advocacy at advocacy@mdausa.org.

Quest Poll: Holidays

How do you feel about the winter holidays?

(531 responses)

- Love them! I look forward to them all year
- I have mixed feelings — mostly joy with a little bit of stress
- I can take them or leave them
- They're a little more stressful than joyful
- I dread them

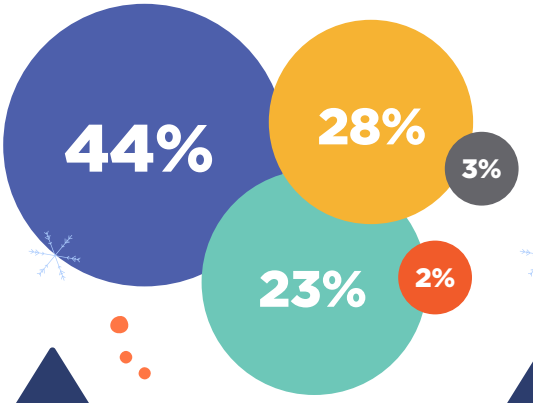


Image: Yevgeniya Kolnobritskaya/Getty

Quest Marketplace

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Image: Brandon Laufenberg/Getty

Access MDA

A Look Back at 2024

2024 was a big year for MDA, our members, and the neuromuscular disease community. We saw a lot of progress and successful efforts from each of our departments. Here are some of our notable wins:

+ A suite of MDA-supported **accessible air travel** reforms was signed into law.
+ MDA launched the **Access the Vote campaign**, a nonpartisan effort to ensure the neuromuscular disease community is informed and prepared to vote.
+ MDA launched **MDA Community Groups**, a virtual place for members of the neuromuscular disease community to safely gather resources, interact meaningfully with one another, and exchange valuable information.
+ MDA launched the **MDA Scholarship Program**, awarding scholarships to 10 college-bound students with neuromuscular diseases.
+ **MDA funding** led to FDA approval of givinostat (Duvyzat), an HDAC inhibitor that slows Duchenne muscular dystrophy (DMD) progression in children and adolescents
+ MDA launched a **collaborative grant** aimed at advancing gene editing research for Friedreich's ataxia (FA).
+ MDA research led to **expanded approval** of delandistrogene moxeparvovec-rokl (ELEVIDYS) gene therapy for DMD.

Image: Skathi/Getty

The Power of Speech

I talk to people for a living. Myotonic dystrophy is making it harder.

BY ANDREW ZALESKI

I'm lucky, I remember thinking to myself, my iPhone wedged between my left shoulder and cheek, that this isn't a more important story. It was late January 2022. About two weeks before, on a Friday afternoon, a genetic counselor from the Johns Hopkins Hospital called me to confirm news I had dreaded for almost two months. Several weeks before Christmas, I sat in the office of a Johns Hopkins neurologist describing to her a series of symptoms I had lived with for just under two years: Cataracts. Clawing in my hands. Pulsing aches along both arms, running from elbows to fingertips. A seemingly inexplicable need, on many days, to take a nap at 3 p.m. because if I didn't, I wouldn't be able to stay awake until dinner. And, most notably, unending pain in my mouth.

Andrew Zaleski was diagnosed at age 32.

By then, for months, when I bit into food or tried speaking, sometimes my jaw just wouldn't move, and my tongue would twist and contort into a position so cumbersome and sideways that I couldn't even form a sentence. This symptom, where muscles contract and cannot relax, is called myotonia. In an article published in 2023, I characterized the sensation of myotonia in my mouth as taking "the worst shot of tequila you've ever had" — cheeks sunken in and lips puckering — and then being told to start speaking.

That Friday afternoon conversation with the genetic counselor made sense of it all: I had — I have — type 1 myotonic dystrophy (DM1) and all the classic symptoms of that disease. I was 32 years old.

Suddenly, the question "What's your number?" took on a whole new meaning. DM1 is caused by abnormally expanded stretches of the *DMPK* gene, which is composed of strands of the DNA bases cytosine, thymine, and guanine (CTG). These bases repeat, and, with few exceptions, anything over 50 repeats results in DM1. Generally, the greater the number of repeats, the more severe the disease. My CTG count clocked in at 140, and while that sometimes means just a mild case of DM1, I am absolutely classic. It was appropriate, I thought, given my taste for jazz and expensive bourbon.

Which brings me back to the phone. I'm a freelance journalist and a writer for many magazines: Outside, Bloomberg Businessweek, Popular Mechanics, Washingtonian, and a slew of others, including GQ, where I've written a column on health and nutrition since

2020, long before I experienced any signs or symptoms of my condition.

This interview was for a column about deficiencies in vitamin D, and how many Americans possess levels far below the norm. (Incidentally, in 2018, my primary care physician ordered a test for me just to check. Swimming through my vessels was a mere 21 nanograms of vitamin D per milliliter of blood, which is considered insufficient. Hindsight, as the saying goes, is always 20/20, and if I had known then that low vitamin D is common in DM1, I might've taken that as a sign. Still, it's not as if I knew in 2018 what would be revealed to me four years later.)

The doctor on the phone with me was explaining the usefulness of vitamin D in the body. Yet I could barely move my mouth. Which is kind of a problem for someone whose ability to do his job depends on his being able to ask questions. And I just couldn't. At one point, I recall using my left index finger and thumb to form a vice grip on my jaw and move my mouth up and down just to put words together.

I've often felt more relieved than overwhelmed in the years following my diagnosis. Knowing what is happening to me is its own form of catharsis. And I know this could be worse. I hope it doesn't get worse.

Andrew's father, John (right), has mild DM1.

But in every interview I go into, whether on the phone or in person, the thought lingers at the back of my mind: Is my mouth going to cooperate? What a strange game of chicken I continually play, my psyche and my myotonia locking eyes, wondering who's going to blink first.

"What a strange game of chicken I continually play, my psyche and my myotonia locking eyes, wondering who's going to blink first."
— Andrew Zaleski

I've looked for ways to deal with this. Usually, I try to set up phone calls for the afternoon, when the muscles in my face are more warmed up. When I'm out on assignment, I try to meet in the afternoon, although it's not always possible.

In fall 2022, well after I'd been living with the knowledge of my DM1, I went gallivanting around old orchards in Washington state for an Outside story about apples. The guy I was profiling told me before I even flew out there that we'd begin the day at 9 a.m. Which means at 8:30 a.m., I was sitting on the couch in my hotel room wiggling my jaw around. Opening and closing my mouth. Moving my face side to side. Rubbing my cheeks like I was trying to start a fire with my beard. All so that when I stepped into his truck, I could actually say, "Hey, nice to meet you finally."

My cardiologist, a wonderful doctor at Johns Hopkins named Andreas Barth, is always quick to tell me that mexiletine, a drug that might temper my myotonia symptoms, is an option. I've tried putting it off — which is probably a subconscious stubbornness more than anything else. I'm willing to bet that by the time you read this piece, I'm on the drug, hoping that it works.

But this, I suppose, is why I write. As long as I can string sentences together, I'll have my voice.

Andrew Zaleski, 35, is a freelance journalist living near Washington, DC. He wrote about his DM1 journey for GQ in February 2023.

Love in Motion

Congratulations to our 2024 Quest Media photo contest winner, Liliana Ceccotti, of Landenberg, Pennsylvania. She took this photo of her son, Santino, and his fiancée, Gill, for their engagement announcement.

The couple got engaged in January 2023 and planned a party in the spring. "I took my son and Gill to Longwood Gardens to take some engagement photos," Liliana says. The public garden in Kennett Square, Pennsylvania, has many beautiful wheelchair-accessible spaces, and they shot this photo in the historic conservatory building.

"It was Gill's idea to ride the back of the wheelchair," Liliana says. "We took a lot of different photos, and this one was the most fun because he had to go a little bit fast, and she kicked her leg up. We took several shots of it, and we had a blast." She made the photo into a poster for the engagement party.

Santino, who lives with spinal muscular atrophy (SMA), is an appellate attorney in Delaware. Gill is a legal assistant. They were married in June 2024. "It was a beautiful wedding," Liliana says.

She still looks at this photo and sees the pure happiness of the moment. "We had so much fun that day," she says. Q

+MORE PHOTOS

Congratulations to the runners-up in our reader photo contest: Alec Chapman of Perry, Michigan; Rebecka Croxall of Carson City, Nevada; and Jeffrey Gibler of Vail, Arizona. See their photos at **MDAQuest.org/2024Photos**.

ADVERTISEMENT

GRAND CANYON

Do you have Becker muscular dystrophy? Have you considered the Grand Canyon Trial?

The GRAND CANYON Trial

Edgewise Therapeutics is seeking individuals living with Becker for the pivotal cohort of the GRAND CANYON trial of sevasemten (EDG-5506)*, an investigational treatment for adults with Becker. The GRAND CANYON trial aims to evaluate the effect of sevasemten on how the disease is affecting your muscles and its impact on daily activities like getting up from a chair, walking and climbing stairs. Safety, biomarkers, and pharmacokinetics are also being evaluated.

The Investigational Therapy

Sevasemten is an investigational therapy in the form of a daily oral pill. Sevasemten is designed to prevent muscle injury caused by contraction that occurs with daily activity in Becker. Sevasemten is designed to limit this damage and help prevent the functional decline that accompanies disease progression in Becker.

Has Sevasemten been studied before?

Sevasemten has been given to 115 healthy volunteers, 130 adults and adolescents with Becker, some more than 2 years, and 98 children.

What side effects have been seen so far?

The most common side effects were mild and transient dizziness and drowsiness.

Can I join the GRAND CANYON Trial?

Approximately 120 adults living with Becker are expected to be enrolled in the trial. To participate, you must fit the following criteria:

- Genetic diagnosis of Becker muscular dystrophy
- Not taking corticosteroids
- Male, ages 18-50
- Ambulatory with the ability to complete functional activities, such as a 100-meter timed test*
- Able to meet other criteria as specified

*Select assistive devices such as orthotics or a cane can be used during the 100-meter timed test. For reference, 100 meters is the length of a football field.

Edgewise is committed to reducing trial burden for participants

- Compensation for your time participating, payable as a stipend per visit completed
- Travel concierge services to coordinate all aspects of travel for participants and a caregiver
- Reimbursement for childcare
- Geographic coverage of clinical sites was expanded, and number of site visits limited to ease travel burden

Participation in the GRAND CANYON trial is for approximately 20 months and will require up to 7 in-person site visits over the duration of the trial. Sites across the United States, Europe, Israel, Australia, and New Zealand are enrolling for now. For more information, please go to clinicaltrials.gov (NCT05291091), scan the QR code to access the GRAND CANYON study website (beckergcstudy.com) or write us at studies@edgewisetx.com!

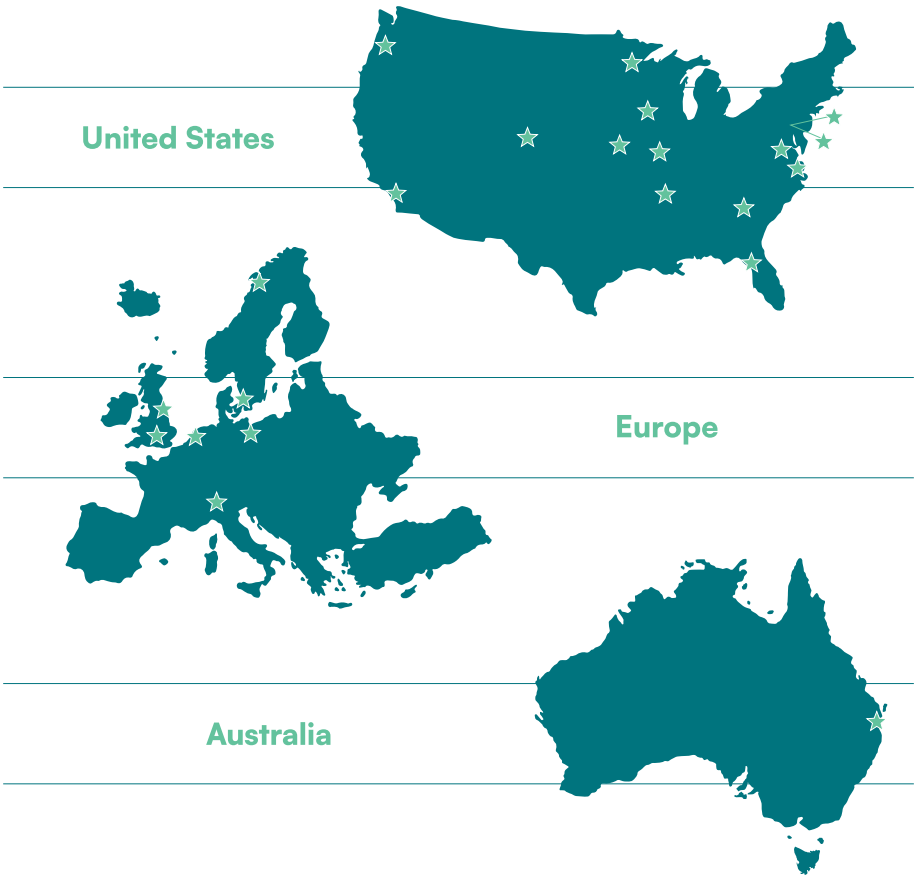
***Sevasemten has not been approved by any regulatory authority and the safety and effectiveness have not been proven**

Edgewise THERAPEUTICS

fortify

Thank You

to the participants and clinical sites in FORTIFY, our Phase 3 study. We appreciate the entire LGMD2I/R9 community for all you do on behalf of LGMD drug development.



Stars indicate approximate location of participating Fortify study sites. For a list of trial sites please visit clinicaltrials.gov.

MLBioSolutions

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