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Welcoming Remarks

MS. CLAIRE SIMON: Hello, everyone, and thank you all for joining us for our RegenMedEd Webinar: Finding Your Support Team While Participating in a Clinical Trial. Today's webinar is hosted by the Office of Therapeutic Products (OTP) within the Center for Biologics Evaluation and Research (CBER) at the U.S. Food and Drug Administration (FDA). My name is Claire Simon. I am a Project Manager in OTP, and I lead the RegenMedEd program and support OTP's many outreach and engagement activities. I will also be your host for today's event.

Some of you may have joined us for previous RegenMedEd events. If that's you, welcome back, and thank you so much for being here. If today is your first time attending one of our events, we're happy that you've joined us, and we hope you find today's event engaging and informative.

The theme of today's webinar is support for patients who choose to participate in a clinical trial. I'm really excited to say that the theme for today's event was actually a suggestion we received from an attendee at one of our previous events. We always appreciate when you share topic ideas with us. For those who are interested and have potential topic ideas for future events, we'll have more information on how to share those in just a few slides.

As many of our audience members know, there are many factors that may affect a patient's decision to participate in a clinical trial. One of those is often how much support a patient has or will need outside of the clinical trial setting. Clinical trials may involve travel to medical centers — sometimes far from home — requiring participants to take time off work or school. Additionally, patients may need assistance getting to and from appointments, scheduling appointments, tracking symptoms, managing day-to-day tasks, and more. Friends, family members, colleagues, and others often provide support for patients as they take part in these crucial studies that help advance understanding of and treatments for many diseases.

Today we are fortunate enough to be hearing from three panelists, all of whom have direct experience with participating or caring for a loved one participating in a clinical trial. Our panelists today will share how they built and managed their support systems during their own experiences, and how they have done the same for others through their work with patients and patient organizations. Before we get started, I'd like to offer a sincere thank-you to our panelists for spending time preparing for today's webinar and for being here to share your stories.

A quick preview of today's agenda: We'll kick off today's webinar by hearing from Ms. Laurie Adami, who is a cancer veteran and patient advocate. Next, we'll hear from Ms. Heidi Edwards, who is the President and Founder of Sisters' Hope Foundation, and she will talk about her experience advocating for various family members with adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP). Lastly, we'll hear

from Dr. Maria Kefalas about her experience advocating for children with metachromatic leukodystrophy. We'll then move into our panel discussion, which will have a question-and-answer (Q&A) format. This panel will feature some questions that were submitted during registration. We'll also leave some time for live questions from our audience.

As some of you heard earlier, this event is part of a series of virtual events called RegenMedEd. The RegenMedEd series includes educational webinars and workshops where we invite patients, caregivers, and advocates to learn about topics related to regenerative medicine therapies. Our previous RegenMedEd events can be found on the FDA website. I also invite you to use the hashtag #RegenMedEd on your social media channels if you'd like to share your thoughts on today's webinar or share an idea for a RegenMedEd topic that you'd like to learn more about in the future. We'll also share a survey after today's event where you'll have an opportunity to submit those ideas and other feedback. At the end of today's event, I'll touch on more about the survey next steps.

A few notes about today's event: This webinar is being recorded. The recording and slides will be posted on FDA's website in the next few weeks. Closed captioning for this event is available directly in Zoom. As I mentioned earlier, we will have some time at the end for questions. If you have a question for our panelists, please type it directly into the Q&A box in Zoom. The Q&A box can be found on the bottom of your screen in Zoom.

Regarding your questions, please note we are unable to answer questions about specific medical conditions or diagnoses. We encourage you to discuss those questions directly with your health care team. We also understand people may have questions about the status of specific investigational products or drug applications. However, there are laws that FDA must follow that limit the information we can provide about investigational products. We do very much appreciate questions and comments and will do our best to address as many as we can. Finally, please use the chat box if you want to share a general comment or are experiencing technical difficulties.

Panelist Presentations

Now I'm excited to hear inspiring stories from our panelists today. Our first panelist is Ms. Laurie Adami. Ms. Adami was diagnosed with incurable stage 4 follicular non-Hodgkin's lymphoma at the age of 46 and spent 12 years in continuous cancer treatment. In 2018, she received a CAR T cell therapy (CAR T) in a clinical trial and finally achieved complete remission. After her own experience, Ms. Adami now dedicates much of her time to assisting cancer patients and navigating the challenges a cancer diagnosis brings. She's very involved with the Leukemia & Lymphoma Society, serving as a first connection volunteer, a public policy volunteer advocate, and more. Ms. Adami resides in Los Angeles with her husband, Ben, and they have a son, August, who graduated from college in 2022. Through her advocacy work, Ms. Adami's goal is to raise awareness and funding for CAR T research and to provide hope to patients navigating a terminal illness.

With that, Ms. Adami, I will turn it over to you.

MS. LAURIE ADAMI: Thank you so much. I have no conflicts of interest, and I have nothing to disclose.

I wanted to first thank FDA for inviting me to share my experience today. I appreciate being here with all of you. As was mentioned, I was diagnosed in 2006 at the age of 46, so 18 years ago. I spent 12 years fighting my disease, and I had seven lines of treatment, including three clinical trials over the years. When I was diagnosed, my son was only in kindergarten, which was an incredible motivator for me to stay alive. It was as if a bomb had gone off in my head. None of us ever expects to hear those words: "You have cancer." When I did, I realized I had no idea where to start, how to function, or what to do, as I never expected that I would be the one getting a cancer diagnosis.

I want to share today my experience and what I did when I heard those awful words and I had to deal with a cancer diagnosis. I would say that whether or not you're in a clinical trial or you're doing a standard-of-care, already FDA-approved therapy, your building of a support network is identical any way you look at it. The first thing I did when I was diagnosed 18 years ago was, I thought, "I don't have a clue what to do; I need to find a smart person I know who has a cancer diagnosis and who can help me with what I do — someone on the road ahead of me." I reached out to someone I had previously worked with, who said: "Laurie, the most important thing is making sure your diagnosis is correct and that you're seeing a specialist in your disease, because only a specialist will know what treatments exist, what treatments are coming, and what you should do." That was one of the first things I did. I also got connected through a work associate with another cancer patient who had the same diagnosis. Finding someone on the road ahead of me was really helpful to give me hope that I could stay alive. So I encourage patients to look beyond their medical community to find people who can help.

Find your team of supporters. I have my husband. I have my son. I would say to avoid negative people as much as you can. I remember somebody said to me: "Oh, my uncle had that same disease, and he died right away." That's not helpful, so get rid of negative people and find the positive people who can help you. You may be surprised who steps up and who doesn't. I was very disappointed in some friends who vanished on me, but people you don't think are terribly close may step up and help. Initially, because I was so overwhelmed with phone calls and emails, I started sending a weekly email to tell people what was going on. It started with my close family and friends — initially 9 people — and I had more than 200 by the end.

A little word about online activity: When I was in my clinical trial for CAR T, I used CaringBridge to post as a way to let people know what was going on with me. Also, it was a great way to set up a meal train, to request meals, and to ask for help with my son. One caution about social media and Facebook: There's a lot of drama and a lot of false information, so you want to be careful where you're getting your information. It can be kind of crazy-making, so just be careful. I would say CaringBridge was a great way for me to communicate.

Find your communities. Are you in a church? Do you belong to a temple? At your work, do

you have a community? Do you have kids? Do you have kids who are in school? Use that network as a way to get support. I had a little boy, and childcare can add stressors, so build a network to help. Arrange for somebody to pick up your child to go to school. Arrange for meals. Arrange for playdates at friends' houses. I had a great girlfriend, and my son was really good friends with her son. They would just take him for the weekend when I was in treatment and I wasn't feeling well, so that my husband and I could focus on me. Also, nonprofits are incredibly important and vital.

Most of us don't know about nonprofits, because they tend not to advertise; they're putting their money into their mission. Look for those nonprofits. I did a lot of relying on the Leukemia & Lymphoma Society, but the cancer support community is a great source. They can provide you education. They can provide in-person and now increasingly remote support groups, so that you can meet other patients who can help you on your journey. They often offer in-person or virtual exercise programs, meditation, yoga, and even art classes. They have free clinical trial location services, which I found to be much better than ClinicalTrials.gov, which is full of outdated information.

Often, these nonprofits offer individual counseling for patients, their caregivers, and even their children. They can provide financial support for out-of-pocket expenses, including travel. In addition, a lot of cancer drugs are now provided in oral form as a pill, and they're very expensive. A lot of times, your insurance will not cover all the costs of these trials or these medications, so these nonprofits will reach out to pharmaceutical companies on your behalf to negotiate or even eliminate financial costs for these drugs.

These nonprofits offer free services to the patients, so it's incredible. Find the biggest nonprofit that will help with your disease and reach out to them. This is very important. As I say, most of us don't know about these nonprofits until we're diagnosed. Go find them because they will potentially be lifesaving.

There are some obvious support systems you can reach out to. The first is your employer. What are your benefits? What's your sick leave policy? How about disability, short- and long-term? I was very lucky. Over my seven lines of treatment, I had great insurance and great support from my employer. I worked part-time for a bit; see whether your employer will let you do that. Then when I had to go out on leave, my employer was very helpful at putting me out on short- as well as long-term disability. You may have employee benefits you don't know about; check into that. You may have leave polices. Also, health insurance is obviously very important. I had very good coverage. I had a preferred provider organization (PPO) plan, and then I had my long-term disability. I was switched to original Medicare and got a secondary payer, so everything for me was covered through standard of care, as well as all my clinical trials. Find out what you've got.

A lot of times, your insurance plans might have social workers and people to help you navigate through your trials or your standard-of-care treatment. But again, if you don't advocate for yourself and you don't ask, these are not going to come to you. So I encourage everybody to be their own advocate. If you can't advocate for yourself, find a family member or a close friend who can help you do it. Or go to one of these nonprofits that can

often provide help in a number of different ways.

As to medical systems, I live in Los Angeles, and I had a lot of cancer centers nearby. I had treatment at four different large cancer centers, so I was very lucky as far as that was concerned. I do want to stress it's very important to find a specialist in your disease. When I was diagnosed, I thought I could just to go a hematology oncologist, because I had a blood cancer. But then this friend of mine in the beginning said, "No, Laurie, you need to find a lymphoma specialist, because they will know about all the latest and greatest, and a general oncologist who's supporting all kinds of cancers cannot possibly know everything about your cancer." So find a specialist and use them.

Also, I wanted to comment that doctors are very busy, so when you're in a clinical trial, you will be assigned a clinical trial specialist who will support you. They will get you through all of it and they will help you, so use them. Also, find nurse practitioners and nurses who are responsive. Get their cell numbers and use them, because the doctors don't have time to interact with you on a regular basis. Also, many cancer centers offer free services to patients. I used the Simms Mann Center at UCLA (University of California, Los Angeles) when I was in my two trials there. That's very, very helpful.

As for why I participated in trials: For me, the standard of care didn't always work well and gave me long- and short-term bad side effects. So I was in trials that were typically more targeted, and I found that the trials were actually better for me. I also ran out of care during my standard of care, so I had to use clinical trials, or I would have been dead. I found the medical support in my trials much better than in standard of care. They rolled out the red carpet for me, and it was just amazing compared with standard of care, where I was just one of many. I was contacted regularly in trials, so I found it much better. I encourage patients always to do clinical trials.

As I said, I live in L.A. and had a lot of options. I waited 6 years for my CAR T trial, so I had to just stay alive until I could get that CAR T, which ended up being my cure. I'm 6 years out now and still clean.

Other costs of trials are trial location and costs of participation. Mine were always free. I never had to pay a penny for my three clinical trials, where I had out-of-pocket costs for standard of care. Also, I never did a placebo: I always wanted to make sure I was doing the drug. Is the trial delivered by infusion or orally? If it's orally, you might be able to do it at home. Is it one time or ongoing?

Okay, I'm going to conclude my comments, because I know I'm out of time. Sorry, all, for running over.

MS. SIMON: Thank you so much, Ms. Adami, for that very informative and inspiring presentation. It's really remarkable to see how much you've turned your own experience into hope for others. So thank you so much.

Now I'd like to introduce our next panelist, Ms. Heidi Edwards. Ms. Edwards is the President and Founder of Sisters' Hope Foundation. She holds a bachelor of arts in

psychology from Alvernia University and a master of arts in human resource management and labor relations from St. Francis University.

Ms. Edwards is an active member and advocate for ALSP patient communities. She works with multiple industry partners, has been named to the FDA Total Product Life Cycle Advisory Council, serves as an advisory board member for Jura Health and Share4Rare, led an ALSP FDA patient listening session, and presents to clinicians, investors, and biotechnology companies around the globe. Ms. Edwards is passionate about raising awareness and advocating for those affected by *CSF1R*-related ALSP. Her journey with the disease started more than 20 years ago, when her aunt was diagnosed.

Ms. Edwards, thank you so much for being here today.

MS. HEIDI EDWARDS: Thank you. Hi, I am Heidi Edwards, President and Founder of Sisters' Hope Foundation, and I have lost five family members to ALSP. It's a devastating genetic neurological disease. Today I am sharing my family's experience with gene and cell therapy and what I have learned through losing my sister Heather and my twin sister Holly. For a list of my disclosures, please refer to the slide on the screen.

ALSP is a rapidly progressive neurological disease that typically strikes between the ages of 30 and 50, bringing with it a combination of cognitive, behavioral, and motor symptoms. ALSP is caused by a dominant mutation in the *CSF1R* gene, wiping out generation after generation of families. There is no FDA-approved treatment or cure for this disease, which causes death within 1 to 6 years of symptom onset. It is a whole-body, whole-person disease that affects every aspect of the lives of the patient, care partner, and family.

My sisters and I embarked on a journey to save their lives. A new experimental treatment was being offered: a stem cell transplant using bone marrow. The treatment was not FDA approved and was used off label in hopes of being a viable option. The closest medical institution offering this treatment was the University of Minnesota, a thousand miles away from our homes in Pennsylvania. Heather, as big sisters do, went first. Heather desperately wanted to save her life and see her two young children grow up. She did what was necessary despite the thousand-mile separation from her kids and the exorbitant cost of the transplant. Unfortunately, 2 days after engraftment, Heather went into cardiac arrest and was placed on life support. As it became clear, Heather wasn't going to survive the transplant, and she would die a thousand miles away from her family. My twin, Holly, was faced with not only the loss of her sister but the decision of whether to pursue the same transplant for herself.

Everything was ready for Holly's transplant, and we were 2 days away from bone marrow harvest. Holly needed to make a final decision. Amidst all of the grief of Heather's imminent death, Holly and I were grappling with difficult questions regarding Holly's transplant. Would Holly's body be strong enough to undergo this treatment? Or would she also die a thousand miles away from her home and family? Holly decided the risk of transplant was too great, and she wanted to go home and live out the remainder of her life at home in Pennsylvania with her only child. She gave up her only chance at saving her life. She went home to her son and to me and my family, and she passed away 11 months

after walking away from the transplant.

Logistical hurdles definitely affected Holly's decision to participate in the trial. If the trial were close to home, I do believe it may have been a different decision. Because of Heather's outcome, some of the protocol for the transplant was tweaked. Would that have been enough to save Holly's life? We will never know, because she wanted to go home and be with her son.

Clinical trial and study participation is a balancing act, but it is especially challenging with a disease that affects people in the prime of their lives. Heather was 45 years old, and Holly was 43. Heather was lucky enough to have a spouse to help her, but it still put strain on their children and his job. Holly was a single mom raising a teenager.

It is so important to remember that a trial cannot be a one-size-fits-all plan. Not every family is the same, not every disease is the same, and not every disease population is the same. What you think will work for a childhood-onset disease doesn't work for a young adult-onset disease. When weighing the possibility of participating in a clinical trial, the care partner must take into account a wide variety of issues:

- The cost of the trial. The trial itself was expensive, because it was not backed by a pharmaceutical company. We also had the cost of travel and long-term housing, as Heather and Holly would have needed to remain near their hospital for 4 months after transplant.
- Childcare. Heather's two children and Holly's only child stayed in Pennsylvania. They had to continue with school and their activities. We had to have trusted adults who could step in for a long period of time to help maintain some sense of normalcy and be emotional support for these kids, who were forced to grow up quickly, face realities most adults don't have to, and recognize that they might carry the same genetic fate.
- Loss of time at work and potentially reduced pay. Heather's husband was self-employed, which made this a little easier. But his clients would wait for the job to be completed only for so long. And if he wasn't working, he wasn't getting paid.
- Extra care partners for the patient. In our situation, Heather's husband and I tag-teamed caring for Heather and Holly. Caregiving is unrelenting and exhausting. One person cannot be expected to shoulder the whole burden.

When considering whether to participate in a clinical trial, please take into account the expenses that are not covered, such as childcare, and the emotional toll this will take on the patient, care partner, and children. Be prepared for the best and worst outcomes, and have a plan in place. If the patient is unable to make decisions, know what they would want. Have in place a power of attorney and a living will.

Tragedies happen. Bodies respond differently to medications. People may not survive trials, and you want what is best for them. Make decisions based on their wishes, not on your emotions. Consider future challenges that may exist, such as paying for long-term

care and ongoing therapies. Ask yourself: “Does the clinical trial consider the patient and the care partner?” Care partners, if you feel it does not consider the patient and you, please know it is okay to say no to participation in a trial.

I found that arming myself with education about the procedure and knowing the risk and benefits allowed me to feel empowered and have a sense of control over each day. I researched the medications, the side effects, and what to expect each day. When you are informed and educated, you are better prepared to ask questions as they arise. One of the best resources we received was a binder filled with medication schedules, daily expectations, and medical departments involved. This became my daily guide. I could open the binder and see what Heather’s treatment plan was for that day.

Lean on the support available from the medical center. Heather and Holly’s care team was phenomenal. Contact a social worker as often as needed to help with local resources. The social worker in Minnesota helped us find an apartment within walking distance to the hospital. This is an extremely vulnerable time in your life. Privacy goes out the window, because you need so much support. The friends and family who wanted to provide support were kept in the loop. Meals were accepted. Help with the kids, homework, drives to practice, and cleaning assistance were all welcome gifts.

The biggest challenge I encountered when building a support system for Heather and Holly was that not everyone was as invested or reliable as I expected — even those who were being paid to provide a service. My sisters could not care or advocate for themselves. They needed a voice, and that voice had to come from someone other than themselves. The primary care partner must always be prepared to step in, step up, and pick up the slack. Caregiving is difficult, and if you are caring for an early-onset dementia patient like I was, there may come a time when it’s too much for you. Know your limits.

I knew my limit when I was Holly’s primary care partner. I needed to hire a full-time care partner to help not just Holly but me during the final 6 months of her life. I still had to continue functioning so I could help raise Holly’s son, raise my own son, work full-time, and care for my husband, who also has dementia. Knowing your limits is the best thing you can do for yourself and the patient.

Through my experience, I am able to help companies make more informed decisions on how to set up clinical trials or studies to better accommodate patients and families. Rare diseases and early-onset dementia trials need to meet the patient and care partner where they are and provide in-home and close-to-home study sites, wearable devices and other cutting-edge technology, and convenient services for the patient and care partner.

Through Sisters’ Hope Foundation, we work tirelessly to put the patients first and make sure their voice is heard. At the end of the day, if you are designing a trial, it must work for patients and their care partners. I started Sisters’ Hope Foundation to honor my sisters and to provide resources and support for those affected by ALSP. Since there were no ALSP-specific groups available to help guide me, I now make sure others do not have to navigate this alone. I work to make sure the patient voice is heard in every aspect, including clinical trial design. I am fortunate to be collaborating with biotechnology

companies from the beginning of the drug development process. My lived experience and the lived experiences shared with me by others with ALSP allow me to make recommendations directly to those designing clinical trials. This input will make trials for ALSP more accessible to our unique patient population.

Thank you.

MS. SIMON: Thank you so much, Ms. Edwards. It's truly amazing to see the work you've put into Sisters' Hope Foundation, and we're so appreciative that you're willing to share your experience here with us today.

Our final panelist for today is Dr. Maria Kefalas, a professor at St. Joseph's University and the cofounder of the Calliope Joy Foundation and Cure MLD. On July 5, 2012, she learned that her youngest child, Calliope (or Cal for short), suffered from a fatal degenerative neurologic disease called metachromatic leukodystrophy (MLD).

Cal's 9-year-old brother, PJ, suggested that the family start selling cupcakes to raise money and to help kids like Cal. Over the next several years, the family would sell 50,000 cupcakes, and the money would help establish the nation's first Leukodystrophy Center of Excellence at the Children's Hospital of Philadelphia. The story of Cal and the cupcakes has been featured on national television and recognized by many, including the National Organization for Rare Disorders (or NORD), in which Dr. Kefalas received the 2018 Rare Impact Award. Today, Dr. Kefalas and her family continue to sell cupcakes and have raised more than a million dollars to help children impacted by leukodystrophies.

With that, Dr. Kefalas, I'll pass things over to you.

DR. MARIA KEFALAS: Thank you. This slide has a list of my disclosures.

As Claire mentioned, in 2012, my youngest child was diagnosed with MLD. On the 1-year anniversary of her diagnosis, there was a paper published in the *Journal of Science* that reported results from a lentiviral-based gene therapy in Milan, Italy. It was a remarkable achievement to see three presymptomatic babies who had no symptoms of the disease several years after being treated with this therapy. It was at this moment, in 2013, that my life changed forever. It was one of my late daughter's doctors, Amy Waldman at the Children's Hospital of Philadelphia, who said: "We take the money that you've raised selling these cupcakes to get as many children to Milan, Italy, as possible." And that is what I've been doing for the last 10 years. We have sent about 20 children for treatment in Milan, and more recently at the University of Minnesota, as an FDA site was approved there.

The challenges of this trial are quite immense. The only way to identify a child who's eligible for treatment is to basically have an older sibling diagnosed with MLD, and then there's a 1-in-4 chance that a younger sibling might have it. Once the children show symptoms (such as gait issues, loss of speech, balance issues), the disease is too far progressed to benefit from gene therapy. As many of you know, gene therapy often works only by stopping disease progression. In the case of neurologic disease that affects the

white matter of the brain, nothing can reverse the damage; you can only prevent it from happening. This meant that for every single trial participant, the family had to watch one child suffer and die in order to save a younger sibling.

This meant, for us, that we were dealing with young families in crisis. We were telling them that while it was absolutely horrifying and tragic what was happening to an older sibling, the clinical team could not help that child, but we would be able to help the younger one. In some cases, the children were identified while mothers were pregnant with children who were identified as having MLD. The burdens of this on our families and our clinicians were extraordinary.

The trial began in 2009, and I'm happy to say that we were able to get FDA approval for the drug in 2024. I guess that while I'm very grateful for the FDA's approval, I want to point out that this is a marathon. This is a very long haul.

What I have learned working with patient families in trials is that trial design is very much a patient advocacy concern. I think a lot of families, when they're diagnosed with a disease like MLD, focus on raising money to sponsor research. What a lot of us don't understand is that the actual design of the trials and how to recruit patients for the trials are, in many ways, even more important than raising funds. I think that we, as patient advocates, can advise on efficacy point goals for the study that are meaningful. For example, while many researchers want to focus on children with MLD being ambulatory and walking, for many of our families, communication is much more important. These children are nonverbal. We would consider a drug successful if our children lived longer and were able to have more trunk control. We are not necessarily that concerned with walking, so those issues about what is a meaningful outcome for the clinical trial should be part of those discussions and of what we talk about with our research teams, regulators, and the families who participate.

A huge challenge in the rare disease community is also in research trial design. Placebo control arms are the gold standard. These are the ideal ways to run clinical trials. In rare diseases, having a placebo control arm is often impossible and downright unethical. Certainly, that was the case for MLD. You could not run a placebo control arm, so we had to rely on retrospective natural history data.

The use of natural history data and having FDA regulators understand this type of data are crucial for designing clinical trials. I think we patient advocates can make the case to regulators that we don't want to have a placebo control arm. I think industry partners are often very timid about that pushback from FDA on the issue of placebo control arms. But in the rare disease space, it's really important for us advocates to make sure that if they're not a useful tool, if they're not an ethical tool, they should not be used. Again, as a patient advocate supporting clinical trials, I often tell families: "While we want to help your child and your family, we must look at this as a collective research endeavor. This is not a treatment that will guarantee a healthy child for you. What we are doing is trying to understand this science, understand this treatment, and collect data that, over the long run, will convince regulators around the globe that this is a meaningful therapy."

I often struggle to communicate to my fellow advocates in the rare disease space that

clinical trials are not treatments, that we must as advocates protect the integrity of the science and protect the integrity of the data. I feel like, as an advocate, I'm uniquely positioned to make that case to my families.

For the past 10 years, I have scoured the world looking for children who can benefit from this gene therapy, which is now, after the FDA approval, known as Lenmeldy. For about 10 years, I have waited for emails and phone calls from families, and the minute we get a call that there is a child who can benefit from gene therapy, we deploy our team. We call them "the war room." These folks will do everything, from help people get passports to wire about $5,000 in funds. This trial particularly, in Italy, would require families to be away for 6 months minimally. This was economically devastating. People had to walk away from jobs. People were selling all their belongings to get on a plane to go to Italy. We worked with families from Brazil, Australia, the United States, New Zealand, England, and Switzerland, and we were absolutely committed to making sure that every eligible child could access this therapy.

What this has meant is that we have raised a lot of money to help families get to Italy. We have also had to engage with payers here in the United States to get reimbursement under compassionate use. We've had some really remarkable advocates who have made the case that while this treatment was not approved in the United States, it was promising and miraculous, and that the ethical and right thing to do was for a payer to reimburse. As you can imagine, that has been an uphill battle. We recently had a pretty public and ugly battle with Medicaid in Texas, and we were able to triumph and get the child to Minnesota for treatment. But I can tell you that was a 3-month battle, and we were racing against the clock to make sure the child would even be eligible for the treatment.

As a patient advocate, it's also so important to understand that we have to manage expectations. As Laurie and Heidi spoke about, when you're talking to families, you can tell them that it's okay to walk away, that they don't have to get on a plane and go to Minnesota or Italy and spend 6 months away from their loved ones. We also say to families that, if you're going to do this, you must be willing to commit to the 10-year follow-up of data collection. We have found that when families walk away because they've just gotten the treatment and they're done — thinking "This is just about my family" — those families undermine this work because we can't have the data that we need to make the case to FDA.

I made it very clear to families, and I think I was uniquely positioned to do this as a parent of a child who had died from MLD: "Please don't take this slot if you're not willing to make a commitment on behalf of all the other families." I know the doctors and researchers would never say that, but I could say that. And I feel that was very important, given all that had been sacrificed and all the work that was being done to advance this therapy.

As an advocate, I'm so proud that I was able to help nearly 20 children from around the world access this therapy. It has provided me tremendous comfort and hope to see this new era of gene therapy ushered in. I have raised a lot of money, but I actually didn't sponsor the trial. The money I raised mostly helped get children to Italy and, more recently, Minnesota. In all of this, I have been very clear about my true north. My true north was not

only launching this trial or raising money; I wanted to have a trial where we had really robust data that we could use to convince payers over the long haul that this is a commercially viable and transformative therapy.

As folks who are supporting clinical trials, while it is immense work to fund a trial and to get folks enrolled, you must protect the integrity of the data and you must advocate for your families and help them accept the challenges and burden of being in a clinical trial. But I promise you that this work is absolutely meaningful and transformative, and I remain so proud of the fact that there are now dozens of kids in the world who are walking around and enjoying life because of my late daughter.

Thank you so much for your time.

MS. SIMON: Thank you so much, Dr. Kefalas. You and your family are truly such an inspiration to those with MLD and the MLD community.

Panel Discussion

MS. SIMON: We'll now shift into our panel discussion. Panelists, you all are welcome to go ahead and unmute yourselves. Feel free to turn your camera on if you feel comfortable doing so.

A reminder to all of our attendees that the Q&A box is open in Zoom. Feel free to submit your questions there. We'll also have some questions teed up for our panel that were submitted during the registration process. With that, let's go ahead and get started.

Our first question is for all of our panelists. As you all have shared today, having a support system is a big part of someone's clinical trial experience and potentially even part of their decision making when determining whether they will participate in a clinical trial. During your own experiences as a patient, a caregiver, or an advocate, what type of support was most impactful to you? I'll open it up to all of our panelists.

MS. EDWARDS: I think what was most impactful to me was any support that gave me a break. I was grieving the loss of my older sister. I was caring for my twin sister, who was going to pass away from a terrible, terrible dementia and movement disorder. And I had a family of my own and a husband with dementia. I knew what my limits were, and it was really important to have someone offer support. If it was a meal, that meant I didn't have to make a meal for everyone. If it was a night shift, I need my sleep. That is no secret. If I was not able to get sleep through the night, I couldn't function the next day to take care of everything that needed to be done. When it comes to the support and needs of someone in a caregiving role, nothing should be out of the question. Nothing should seem too small.

MS. ADAMI: I would say in a similar vein that over my 12 years, where I got specific offers of help, it was somebody calling to say, "I'm going to bring you dinner tonight, and I'm going to set up a meal chain, and we're going to arrange for August to have rides to school." At one point, I was radioactive for 8 days because of one of my treatments. So I

couldn't be around my family. I couldn't prepare meals. I couldn't take my son to school and pick him up. People knew that, and they called and said, "Okay, we're going to just take care of it." So a specific offer. Just getting stuff done so I could do what I had to do for my health and deal with what I was dealing with, because of the side effects of the clinical trial. Or because of the side effects in the standard of care, actually.

DR. KEFALAS: I think, as an advocate, one of the most important things I did was help families accept the decision — whether they had gotten a slot on the trial and were going to have to leave an older child who was sick, or they had not been eligible. I think some of the most amazing conversations I had with families were just helping them process the medical teams' decisions, good and bad, in terms of eligibility for the trial and assuring them that they were amazing to even try to get to Italy or Minnesota and be in the trial, that they should have no guilt at all or feel sadness that they didn't do everything they could to help this child, and that the decisions that were being made were really for the safety of the children and for the advancement of the science. We would not have an FDA-approved therapy if the PIs had not held the line. If they had let in every kid who came to their door, we would not have had the data to convince FDA this was a safe and transformational therapy.

I think that when you're doing this advocacy work as a patient advocacy group (or PAG), you have to remember it's not about the family that you're talking to. It's about the science. And that's an odd thing to say. Of course, I love these children. I love these families. I had lost a child too. I understood what they were going through. But I also know that we would not have this drug, and that gene therapy would be on life support in the United States, if our community hadn't made those difficult decisions.

MS. SIMON: Thank you so much, all. I think those were great first answers to kick off our panel discussion.

Dr. Kefalas, we have a question for you. You have experience working with families all over the world. You shared a little bit about that during your presentation. As you know, and as many people here know, there can be so many logistics when participating in a clinical trial, let alone one overseas. Can you share a little bit about what might be helpful for patients and families to know when they're considering participating in a clinical trial in a different country?

DR. KEFALAS: Yes. Our team in Milan is remarkable, they are the most fabulous people. But it was a huge culture shock for families to come from around the globe and work with an Italian team. For example, this was very funny: They didn't have hospital gowns for babies, so they would wrap the babies in adult hospital gowns. So one of the moms said, "Can you get me some gowns that fit the babies?" So this volunteer here in Pennsylvania hand-sewed a bunch of hospital gowns, and we shipped them to Milan.

In all seriousness, I think that you have to prep families for how tough this is going to be. We have an amazing team on the ground in Italy who would call me and say, for example, "We have a family that eats only halal food. Can you help us make sure that this family is taken care of?"

We used the power of social media to raise awareness. There is no such thing as a closed trial. People are live-streaming on Instagram on our trials all the time. I laugh at the thought that there are probably investors in companies that are tracking our families when they participate in clinical trials. But in all seriousness, social media is a really powerful tool for telling your story and connecting with folks from home.

The most important thing I do when I send families overseas is I get them money and I get them an adapter so they can use the electronic equipment. It's funny, the small things that really matter. And having a great relationship with those teams that you can talk to them and say, "We have a family from Brazil, and they need $3,000 to fly from Brazil to come to Milan," and we were able to do that.

I think I would say the key is having a really open relationship with the clinical teams and then respecting what we as patient advocates can offer and do to support. I think they came to rely on me a great deal, and I came to have great respect for them and trust in them.

MS. SIMON: Thank you, Dr. Kefalas.

A follow-up question to that: Ms. Edwards, zooming back into our virtual map over here, no longer overseas, but your experience in caring for your sisters was across different states. How can family members or friends who live in a different state support loved ones participating in a clinical trial?

MS. EDWARDS: It takes a really deep bench. I will say that.

With a disease like ALSP, my sisters were not out of the norm. They were in their mid- or early 40s, and you have children at home. You need to take care of them as well and travel halfway across the country to try to save your life. What we did was we were open and honest with everyone. We needed support. We needed help. We tag-teamed a lot of it. We knew that if Heather survived, she would have to stay in Minnesota. So we knew the schedule of everyone who was willing to help us and travel to Minnesota and stay in the apartment and care for her. And it's okay, there were some people who were not able to do it, but they would stay back, and they would help with the kids. You need to trust other people. You need to rely on them and ask for a lot of help.

In Holly's situation, she was a single mom. I had power of attorney for her and I was her caregiver, so I bore the brunt with most of the work that needed to be done for Holly. But again, I had an amazing support system to help myself and my family at home.

Logistically, it's not going to work for everyone. But we made it work for us, because it was our only option going into this. We knew it was our only option to save their lives, so we made sure it worked. But just know — go in very open-minded — that you cannot do this on your own and the patient cannot go through this on their own.

MS. SIMON: Thank you so much, Ms. Edwards.

We have another question for all of our panelists. One thing that you all have in common is you've taken your experiences and you've really turned them into action, whether that's

advocacy, support, or education — such as starting your own patient organization, helping connect and talk with other patients and their families as they consider their options for treatment or clinical trials, and participating in this webinar today and sharing your story. When you're talking with patients and their families, what type of information or support do you offer to them first? What does that first conversation look like? I'll open it up to anyone.

MS. ADAMI: It really depends upon the patient and what they're dealing with. I'll get patients at all different points of their journey, so the first thing I do is find out, obviously, their diagnosis. Have they been in treatment? The important thing is to get the patient to talk. It's not about my story. It's about hearing what they're going through, and their needs are going to vary.

For example, I was connected with a patient recently who was going to do CAR T for her refractory relapsed cancer. With CAR T, the patient needs to have a caregiver for the first 30 days, and this individual didn't have a caregiver. Her friends and her family were outside the country in Asia, and they couldn't travel here to help her. She was at risk of not being able to get this treatment that could save her life, because she didn't have a caregiver. The important thing there was to try to figure out how to patch together care for her and reach out to her community, and it ended up being really interesting. The cancer center she was being treated at for her CAR T had not encountered this situation before. Rather than see this patient walk away and likely die, they decided to recruit from their nursing students, who would act as caregivers when the patient needed a caregiver outside of the hospital setting.

There's still a lot of innovation happening. There's no one-size-fits-all. I'll get a patient with pancreatic cancer who has a very different circumstance from someone with a blood cancer. I would say each one is individual, and the important thing to do is listen to their journey and figure out what they need and how I can help them.

DR. KEFALAS: Actually, a little plug: We wrote a book to explain gene therapy to children, because no one knew what gene therapy was. The medical teams were speaking at this really high level, so one of the most important things we did as advocates was to explain what this therapy was and what the experience was going to be like and that we didn't know what it was going to do. I'm happy to say that the oldest U.S. child to receive this therapy is 14 years old, looks amazing, and has no signs of MLD. But even with that success, there's still a great deal of uncertainty.

I think the most important thing we do is deal with the disappointment and grief of not being able to help and save your kid. We've all watched so many Hollywood movies, and we all want that miraculous happy ending like Laurie has had. My late husband actually had multiple myeloma (MM), so I know the CAR T world very well. CAR T is amazing, and so is gene therapy. But as my friend often says to me: "We're not going to be able to save everyone. It's always enough to do something." Having families accept that and come to terms with that is difficult.

MS. EDWARDS: When a patient or a family contacts me, I always offer hope, because

finally, for the first time, I can say to them, "What your local neurologist may not know about ALSP, I do know. I'm the expert, and I'm going to walk you through this." Even if they said, "Go home and get your affairs in order, because you're going to die from ALSP," that may not be the case in the near future.

So I always provide hope. They're so desperate. They can read about the devastations of this rare neurological disease. But what they can't read about is the fact that we have industry partners working on treatments and potential cures, and there is hope for a future with ALSP.

MS. SIMON: Thank you so much to all of our panelists for answering that. I think one of the main takeaways I've heard from all of you is that there's always someone out there to reach out to. An advocate, an organization, and tools to learn more and to connect with.

Ms. Adami, a question for you. As you shared in your presentation, you were diagnosed when your son was very young and then participated in a number of clinical trials and received different lines of treatment up until your son was in his teens. Can you share a little more about the types of resources and support for caring for children while either a parent or a sibling may be participating in a trial? I know you touched on some of these in your presentation, but anything else in terms of working with schools, teachers, guidance counselors, and so forth, I think, would be very helpful to hear.

MS. ADAMI: It's really interesting, because my son spent his entire elementary, middle, and high school with me in treatment. The day after I got out of the hospital — he was, at this point, 18 — he flew to Washington, D.C., from Los Angeles to start his freshman year of college by himself. So he went through a lot.

I remember, when he was in kindergarten and I was diagnosed, the only option for me was a chemotherapy and monoclonal antibody treatment. That was all there was at the time. The first thing I realized was, my hair was going to fall out. There was no way we could not tell my son what was going on, because I would take him to school and everybody would be like: "Your mom is bald! My grandpa was bald, and he died of cancer." So we had to get in front of it. What it also meant was, everybody who saw me in a scarf knew that I had cancer, so there was no way I could not share it.

One of the first things I did was I went to his teacher. He was, at this point, in kindergarten, so I had a meeting with her to say, "I'm very worried about the effects on my son of what I'm going to be going through." I had an open dialogue with her, saying that she could share with me if she saw any signs in August that he was going through a difficult time because of this. Obviously, it was very scary for him, and he was still not really able to understand what was happening.

Throughout my journey, I always communicated with his teachers each year, because I went through it for 12 years. I was in treatment the whole time. I lost my hair three times. I always had side effects. And then getting the school community on board, talking to the principal, finding out about after-school programs. It turned out I was lucky, because a lot of the parents of his classmates would reach out and ask: "Can we pick up August for

school? Can we take him for a playdate after school? Would that help?" I got the specific offers of help.

Also, through these nonprofits, there's a lot of support for family and children. I remember talking to my son, because the cancer support community in Los Angeles where I lived had therapy for children and support groups for children. So I offered this proactively to my son, and my son's response was, "Mommy, I'm fine. We need to take care of you. But I'll tell you if it changes."

I think the important thing is to reach out and to let people know. There are a lot of patients who don't want people to know and don't want to share, and they don't want pity. Patients are worried that if they tell someone else "I have cancer," people are going to look at them with pitying eyes. To me, it was always that the more people who knew, the greater the chance I might get to a better doctor, a better treatment, and obviously offers of support.

MS. SIMON: Thank you so much, Ms. Adami. I want to open it up to Ms. Edwards and Dr. Kefalas, if there's anything you want to add to that question.

DR. KEFALAS: Can you repeat the question again?

MS. SIMON: Of course: Any type of information about types of resources and support for caring for children while a parent or a sibling may be participating in a clinical trial?

DR. KEFALAS: My late husband had MM, and my daughter had leukodystrophy. The trauma on children is immense. It is hard on marriages. It is hard on relationships. It is bad for your career. It is a nuclear bomb blowing up in your life. I do think that clinical trial participants, clinical PIs for clinical trials, and advocates need to recognize this as a traumatic experience, and that we should lead with trauma-based interventions.

We have a psychologist who works with our families. We have support groups. I work with an amazing team of child life specialists whom I regularly refer to families to work with over the long haul. What Laurie is describing — my children were like that too. When your 16-year-old daughter is making dinner for you because she's worried, because she's taken on this role of caregiver, that's not good. That is not a good situation to be in. I made that mistake as a parent, so I'm really very supportive of us as advocates being quite honest about the fact that this is traumatic and needs to be handled, and that the hero mom, the hero cancer patient, the hero caregiver is a wonderful myth that needs to be taken down. People need help, and they need to deal with this trauma very seriously.

MS. EDWARDS: Yes, I agree with that, Maria. In my family, because it's an early-onset dementia and movement disorder, there's children involved. And it's a dominant mutation, so there's a 50% chance that they're going to inherit this disease as well. We were always honest and transparent with the children.

You can't hide the progression of a neurodegenerative disease. "Why is nanny walking like a penguin?" "That's shuffled gait, and this is why. There's something wrong with her brain." Kids see it. They see the changes. "So and so isn't the same anymore. What's

happening?" "Why is mom yelling at me all the time? She's agitated and angry." We were always really up front, from the very first diagnosis, and then talked through it as a family and made sure the children understood at their age level what was happening and what potentially could happen.

MS. SIMON: Thank you so much, Ms. Edwards, Dr. Kefalas, and Ms. Adami.

Ms. Edwards, a question for you. You shared during your presentation a little bit about how your sisters were diagnosed with the same disease. One of your sisters participated in a clinical trial; the other did not. For others who are deciding whether to participate in a clinical trial, what might be some considerations or questions they need to think about as they weigh that decision?

MS. EDWARDS: One of the questions you should think about is logistics, of course. The decision for Holly, if it was in Philadelphia, say, would have been a very different decision. She lived in Philadelphia, so going to a local university would have been an easier option. When participating in a clinical trial, you have logistics to think about.

In our situation, it wasn't pharmaceutical-backed, so we had to come up with money. The insurance company wasn't going to pay for it; it was coming out of our pocket. You need to think about those expenses. GoFundMe was huge for us. That's the only way it was possible. But for some families, that's not an option. They don't receive enough funds, so they're not able to participate in something that's off label.

If you're going into a clinical trial that is pharmaceutical-backed, you need to take into account everything that is not covered, and there are going to be expenses that are not covered. Who's going to take care of your children while you're away? Who's going to take care of your dog? If you can't afford to pay for parking at the airport, how are you going to make this work? If you can't afford to put food on the table because you're paying for parking at the airport to travel somewhere or because you have to pay to board your dog, you really need to think through all the details. Because not everything is going to be covered.

MS. SIMON: Thank you, Ms. Edwards. I think those are all very important points.

We have time for one more question for all of our panelists here. I believe this one also came in through one of our registrants for this event. You've all touched on, of course, different types of support — logistical, emotional, and whatnot — but thinking about clinical trial sponsors, what is the best type of support that they can give to participants and caregivers?

DR. KEFALAS: The role of industry is really complicated and nuanced. In gene therapy, it is an expensive, high-risk investment, and I think that their contact with the patients has to be separate. I feel as if GlaxoSmithKline and later Orchard have been wonderful partners and that they, on more than one occasion, were committed to donating the drug in cases of compassionate use. I have tremendous admiration for the decisions they made that were not good for the bottom line but have resulted in children getting a chance to live, because they

did the thing that was good for the science and for the family. For industry, their true north ought to be advancing the science and research, but also caring for the families. And they have an ethical obligation to us as well. It's a tough line.

I don't know about CAR T; it's a different business model. But for us in the gene therapy space for ultrarares, we still don't have a sustainable model for commercial reimbursement. So I'm always thinking MLD has to prove as a concept that an ultrarare gene therapy can make money. It's an absolute tension that I haven't figured out yet.

I'm sorry, Laurie. I didn't mean to cut you off.

MS. ADAMI: I was going to talk about my experience in clinical trials a little bit, as far as pharmaceutical companies. All three of my clinical trials — one was phase 1, and two of them were phase 2 — were delivered by a pharmaceutical company. In my experience, the information went one way, from the patient to the doctor to the pharmaceutical company. The reporting of side effects — all of that.

At the same time, I have a lot of gratitude for the pharmaceutical companies, because without them, I would be dead. A lot of these treatments I have were developed in academic cancer centers (such as UCLA, Penn, and M.D. Anderson), but they cannot commercialize the products. Once they've developed the products, they've got to get into a partnership or an ownership model through the pharmaceutical companies.

Gene therapy and CAR T are different, because these are not just off-the-factory, one-size-fits-all pills and infusions. They are actually handling a patient's life. At the CAR T center, my cells arrive at the facility and come out engineered for me only. There's a lot of issues around HIPAA. For example, I've spoken at multiple CAR T companies and cell and gene therapy companies, and initially, I couldn't say my last name. I was just Laurie. I was at the company that made my CAR T right in California, and I was only allowed to say, "Laurie, a CAR T patient in this clinical trial." One of the attendees came up to me afterward and said, "Laurie, if you Google 'Laurie and CAR T,' you can find out who you are," because I became kind of a public figure.

Companies also don't want to be seen as providing support to one family and not another. They're all working on it. I'm now on two panels that are working with pharmaceutical companies on how to better support the patients and the caregivers through these trials, because — remember — the caregivers play an incredibly important role in cell and gene therapy treatments, to the extent that the caregiver has to monitor a patient and know what to look for.

So I think it's still a work in progress. And now 40,000 patients in the United States have gotten CAR T for their cancer, and that number is growing very rapidly. So they're trying to figure all of this out, including issues with payers and with support. But I would say that it's very much a work in progress, and they need to take into account the voice of everybody at the table, considering not just the needs of the pharmaceutical company to make money but also whether they are delivering a treatment that a patient can tolerate and managing side effects. So again, it's a multifaceted answer.

MS. EDWARDS: I agree with that, Laurie: It is. And I really do believe, if there's a company getting started and it wants to sponsor a clinical trial, it should start working with a patient advocacy group early. We are intimately involved with our patients and care partners. We know them, we do surveys, we have data to support things, we know the needs of the community, and we can engage our community to help the sponsor.

MS. SIMON: Thank you so much to our amazing panelists for joining us today. I know we're a few minutes over time, but there were so many good questions — and we didn't even get through all of them.

Closing Remarks

MS. SIMON: Thank you all so much, again, for sharing your experiences as patients and advocates and your personal stories today. I also want to thank our attendees. We appreciate you joining us today, all of your great feedback, and your great questions throughout the webinar. And thank you to everyone who helped plan today's great event: our colleagues at OTP, at CBER, and at FDA Patient Affairs. We truly appreciate your support. And of course, I want to thank our wonderful backstage, behind-the-scenes team.

Just a couple of reminders and notes to everyone: Please stay up to date with all of the latest happenings through our website, our listserv, and our social media channels. Again, we encourage you to use the hashtag #RegenMedEd on social media to share your thoughts on today's event and let us know what information and resources you're interested in seeing from OTP in the future.

Lastly, I'd like to note that CBER is hosting a patient listening meeting on December 4 to better understand patient and care partner perspectives on enrolling in gene therapy trials rare disease patients who are in the presymptomatic or early symptomatic stages of their disease. This listening meeting is for all patients, care partners, and advocates. You're welcome to attend. Registration is required. For those who are interested in speaking during the listening meeting, please make sure to register this week, as our deadline for speaker requests is quickly approaching.

As I mentioned earlier, we will be sharing a survey via email in the next few days to get your thoughts on today's webinar. The survey should take only a couple of minutes to complete, and we really appreciate your participation and feedback. So please be on the lookout.

With that, one final thank-you to our attendees and our wonderful panelists. Thank you all for tuning in. Have a great rest of your day. Thanks, everyone.