FOOD AND DRUG ADMINISTRATION (FDA)

RARE DISEASE DAY PUBLIC MEETING

Patient Perspectives on the Impact of Rare Diseases:
Bridging the Commonalities

DATE: Monday, April 29, 2019
TIME: 1:00 p.m.
LOCATION: FDA White Oak Campus
10903 New Hampshire Avenue
Building 31 (Room 1503-C)
Silver Spring, MD 20993
REPORTED BY: Samuel Honig, Notary Public
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I N D E X

PROCEEDINGS

DR. MAYNARD: Good afternoon, everyone. Thank you for being here today. Welcome to FDA's Public Meeting on Patient Perspectives on the Impact of Rare Diseases: Bridging the Commonalities. My name is Janet Maynard, and I'm the director of the Office of Orphan Products. I will provide introductory remarks for this meeting.

We are pleased to have this opportunity to engage directly with you. Patients and caregivers are experts on their diseases, and this meeting will allow us to learn about the impact of rare diseases on you, and to assess for commonalities in symptom management, treatment considerations and clinical trial and registry considerations.

FDA's mission is to promote and protect public health by helping safe and effective products reach the market in a timely manner. At today's meeting we will focus on rare diseases and the impact of these rare diseases on patients and caregivers.

There are over 7,000 rare diseases affecting an estimated 30 million people in the United States.

Rare diseases can be fatal and highly disabling with significant impacts on patients and families. Notably, it is estimated that about half of rare diseases affect children. We recognize that there are unmet needs for patients with rare diseases, as most rare diseases do not have approved therapies. The availability and access of safe and effective medical products for patients with rare diseases is critically important. With scientific advances, there are new opportunities for the development of therapies for rare diseases.

We at FDA are dedicated to supporting public health and rare disease product development. The Office of Orphan Products Development specifically advances the evaluation and development of products, including drugs, biologics, devices and medical foods that demonstrate promise for the diagnosis and treatment of rare diseases or conditions.

In fulfilling that task, the Office of Orphan Products Development evaluates scientific and clinical data submissions from sponsors to identify and designate products as promising for rare diseases and to further advance scientific development of such promising medical products.

In addition, the Office of Orphan Products Development provides incentives for sponsors to develop products for rare diseases. Our programs have successfully enabled the development and marketing of drugs, biologics and medical devices for rare diseases since 1983. To optimally support rare disease product development, FDA collaborates both internally and externally with of stakeholders.

Today's meeting is one example of FDA's dedication to rare disease product development and includes representatives from the medical product centers, CDER, CBER and CDRH, the Office of Pediatric Therapeutics, the Office of Orphan Products Development, and the Patient Affairs staff.

I would like to acknowledge and thank the cross-agency collaboration that supported the planning and organization of today's meeting. Each of us here today has a unique perspective and are committed to working together to achieve success. Developing a treatment for a rare disease can present unique challenges, such as the small number of individuals affected and heterogeneous etiologies and manifestations. While the differences between rare diseases are critically important, it is also important to assess commonalities to synergize product development in rare diseases.

We recognize that each patient's experience is unique. By sharing our experiences together, we will learn from each other. Further, we may find commonalities that are not as rare as one would think. The involvement of patients and caregivers and their input is critical in addressing the challenges of developing a treatment for rare diseases. FDA is committed to working with patients and caregivers to ensure products address patient needs.

The goal of this meeting is to obtain patient and caregivers' perspectives on the impacts of rare diseases on their daily life, and to identify common issues and symptoms in rare diseases to help advance medical product development. This may potentially support medical product development in consideration of novel endpoints or trial design that focuses on commonalities across a variety of rare diseases.

We are pleased to see so many patients, caregivers and advocates in the audience. We also have many more of you joining remotely from the web. Thank you for being part of this meeting and sharing your experiences.

Today's meeting builds on FDA's efforts to hear directly from patients and caregivers. Today we will hear from those affected with a variety of rare diseases and conditions rather than focusing on a specific disease. We appreciate this unique opportunity to hear directly from patients and caregivers, and to assess for commonalities across rare diseases.

After this meeting we will take what we learn and write a summary document. It will take us some time to produce this document. The document will consider the transcript and our notes from this meeting, and the docket comments. We leave open the docket after the meeting so we can get submissions of information from people on the webcast, or other things that may occur to people in the room or on the web after they hear this meeting. We will put together this information from the meeting and the docket to develop a summary document. We hope that the document will be extremely valuable to the various stakeholders in product development. We hope to capture as accurately as we can what we heard today and what we read in the docket. This will serve as a resource to the staff at FDA and sponsors who are developing products for rare diseases.

We hope this will be valuable to sponsors as they consider aspects of their development program, such as the outcome measures and the design of clinical studies and registries. We will be producing this document in the coming months after the meeting.

Today's meeting focuses on patients with rare diseases. Similarly, we have portraits on display that focus on rare disease patients from the "Beyond the Diagnosis" art exhibit. These portraits help us see and experience people who are living with these rare diseases and conditions. The portraits help us see beyond the diagnosis and instead see people who live with this day in and day out.

The goal of the "Beyond the Diagnosis" exhibit is to put a face to all known rare diseases through the medium of art. Artists from around the world have contributed their talents to this beautiful exhibit that is traveling to medical schools, research institutes and hospitals around the globe, encouraging the medical community to look beyond the diagnosis to the patient.

We are excited to have this opportunity to have so many portraits on display outside the meeting room today, and we encourage those attending in person to take time to look at the exhibit.

Thank you for your participation in today's meeting to support product development for rare diseases. We are encouraged to work together and energized to work together so that we can have stakeholder engagements to bridge the gaps for rare diseases. I will now turn it over to Andrea from the Patient Affairs staff. Thank you.

MS. FURIA-HELMS: Good afternoon and welcome to the public meeting, Patient Perspectives on the Impact of Rare Diseases: Bridging the Commonalities.

My name is Andrea Furia-Helms. I am the director of the Patient Affairs staff at FDA. Welcome to patients and family members who are here in the Great Room for this very important meeting. We know it can be a bit of an effort to get to the FDA campus, so we thank you for making it here. Thank you to those joining by webcast as well. We understand not everyone can be here in person, so we appreciate you taking the time to participate and contribute online.

We also have many participants in the room and online, such as patient advocacy organizations, healthcare professionals, academia, industry, and others in government, including many from FDA. We are glad you are here, and we hope that the input we hear from our patients and caregivers today will be valuable to you as well.

So, before we begin the meeting, I just want to make a few administrative announcements. Please silence any cellphones or other mobile devices, as they may interfere with the audio in the room today. If you haven't already, we ask that attendees sign in at the registration table outside the meeting room.

Restrooms are located in the lobby past the coffee area to the right and down the hallway. For media inquiries, our press officer, Sandy Walsh, is here today. Sandy? If any members of the media are here today, please sign in, and if you have any questions or are interested in speaking with FDA about this meeting, please contact Sandy Walsh. The meeting is intended to give the FDA an opportunity to hear from patients and caregivers, so the FDA panelists and other FDA employees will not be available to make statements to the media.

For the Wi-Fi in the Great Room, the network and password is displayed on the screen. A public docket, as Janet mentioned, is open until May 30th to submit comments. We highly encourage you to do so. The webcast recording of this meeting will be available approximately one week after the meeting. Copies of the transcript will be available approximately 30 days after this meeting. For urgent issues, please speak to the registration desk staff or any FDA staff you see in the room wearing a nametag. In case of an emergency, please exit the Great Room or overflow room you are in and follow the exit signs to leave the building.

Please let us know how the meeting has gone today. Evaluation forms were placed on your seats. If you do not have one, please stop by the registration table. Now, I'd like to take a moment to walk through the agenda for the afternoon.

As Janet mentioned, the goal of this meeting is to facilitate an open dialogue on personal experiences that will identify common issues and symptoms in rare diseases to help advance medical product development. To accomplish this goal, we will have two facilitated discussions led by Susan Chittooran, who is also with Patient Affairs. Susan? Just a disclaimer, our color coordination was by mishap.

The first session will focus on symptom management and treatment considerations, and the second session we'll explore clinical studies and registries. During each session we will be hearing from patients and caregivers on our panels, as well as from patients and caregivers joining in the room and on the webcast.

A little bit about how we selected the panel members. Panel participants were selected from those participants who expressed an interest at the time of registration and submitted summaries that addressed the discussion questions on the meeting webpage. We identified individuals with a range of experiences related to the discussion topics for today.

For those in the room, please raise your hand if you would like to speak. We will bring a hand-held microphone to you. You may remain anonymous or state your first name, and we encourage you to state the disease area you are representing. For transparency purposes, when you're sharing your comment, we acknowledges that you please disclose if you are affiliated with an organization or if your travel has been funded, or if you have a significant financial interest in rare disease medical product development.

For those of you in the overflow room, you can write your comment on a notecard on your seat and pass it to the end of the aisle, where someone will collect it. For those on the webcast, please type your comments into the chat feature in Adobe Connect. We will periodically be checking in to see what our remote attendees are sharing in the chat box. After session one concludes, we are delighted that the Principal Deputy Commissioner and Acting Chief Information Officer, Dr. Amy Abernathy, will provide remarks with us. We will have a break before we begin session 2, and conclude the afternoon with the open public comment period. So, some information about the open public comment period. Say that 10 times fast.

We have time set aside for the open public comment later this afternoon, and the session will give anyone in the audience the opportunity to make any comment. To participate in that, you would have needed to sign up at the time you registered or sign up today at the registration table. Participation is first-come, first-served, and has accommodated up to 10 commenters. We are excited that we have so many that were interested in the open public comment period that the slots have already been filled up. The time allowed for each speaker will be about two minutes each. After the open public comment period, Janet

Maynard will provide some closing remarks.

We want you to stay connected. Please know that once the meeting ends today, that doesn't mean that this is the last or only opportunity you can speak with FDA. The Patient Affairs staff and the Office of Orphan Products Development are here, and we want to stay connected with you. Whether it's helping you to stay connected with other activities at FDA or addressing any further questions you may have, please do keep in contact.

Here is our contact information and Twitter handle. Speaking of Twitter, if you choose to tweet about today's meeting, please use #rarediseasefda.

Now, just for some rules of engagement for today's discussion. Patients, caregivers and their advocates are encouraged to sit near the front of the room. FDA is here to listen to you and we -- it's not about us; it really is about you today, so we encourage you to contribute to the dialogue. Your stories and experiences are what can move medical progress forward. Because we really want to hear about your experiences, we ask that if you have any other FDA questions, please email Patient Affairs at patientaffairs@fda.gov.

The views expressed today are personal opinions. Please be respectful of others. Have the courtesy to allow participants to finish sharing their experiences without interrupting. FDA panel members will also have the opportunity to ask follow-up questions of the participants, and participants in the room use a microphone so that the webcast attendees can hear their remarks.

So, before we begin, I would ask my FDA colleagues on the panel to introduce themselves. We can start with Lucas.

MR. KEMP: Hi, I'm Lucas Kemp. I'm the acting associate director for the rare diseases program within the Office of New Drugs within the Center of Drug Research, CDER.

MS. SPENCER: Hi, I'm Caroline Spencer. I'm a patient with Friedreich's ataxia. I am from Cincinnati, Ohio. And for those of you who may not familiar, Friedreich's ataxia, or FA, is a progressive neurological disease. It's a degenerative neuromuscular disease that leads to progressive loss of ambulation or walking. It can also cause cardiac problems, scoliosis, diabetes and other comorbid difficulties.

MR. ROTBERG: Hi, everyone. Seth Rotberg here, a patient as well as advocate for the Huntington's disease community, rare disease community as a whole. I am a patient as well as I was a caregiver for my mom. Huntington's disease, also known as HD, is a rare neurological, genetic disease that slowly deteriorates a person's physical and cognitive abilities. It's like having ALS, Alzheimer's and Parkinson's all into one. I tested positive at the age of 20; I'm 28 now. And I also sit on the board for the Huntington's Disease Youth Organization supporting young people impacted by Huntington's disease worldwide, and really just excited to be here.

MS. SHAPIRO: I'm Adrienne Shapiro. I am fifth generation of mothers in my family to have a child born with sickle cell disease. Sickle cell disease is just that -- it's a disease where our red blood cells, rather than being round, disk-shaped, there's a large portion that become sickle-shaped, which cause problems as you try to circulate through the bone marrow, ending up in very painful episodes and damage to major organs of the body. There is a life expectancy here in the US of 45 years. Throughout the world, children live less than five years. And I have a nonprofit called Axis Advocacy, and we advocate for people living with sickle cell disease, particularly the adults.

MS. WITTEN: Hi. My name is Rachel Witten. I'm from CBER. I am from Office of Tissue and Advanced Therapies. One of our activities of work, we do regulate clinical gene therapy clinical trials for rare diseases.

DR. MAYNARD: Hi. I'm Janet Maynard. I'm the director of the Office of Orphan Products Development and the Office of Commissioner.

DR. SILVERSTEIN: I'm Doug Silverstein. I'm a pediatric nephrologist. Most of the diseases that we treat in our subspecialty are rare diseases, and I work in the Center for Devices and Radiological Health in the Renal Devices branch.

Dr. MCCUNE: Good afternoon. I'm Susan McCune. I'm the director in the Office of Pediatric Therapeutics in the Office of the Commissioner. My background is I'm a pediatrician, and my subspecialty is neonatology, or newborn intensive care, and I'm very interested in hearing what all of you have to say about the impact of rare disease on your lives, especially with respect to pediatrics.

MS. CHITTOORAN: Hi. I'm Susan Chittooran. I am a social worker by background and I work with Andrea on the Patient Affairs staff. I'll be facilitating the meeting this afternoon.

MS. FURIA-HELMS: Thank you so much. Just a few last things. The live webcast is being recorded, which will be archived on our website, along with the transcript. You may also notice a film crew around during the meeting. We are capturing the video footage of this meeting.

And in closing, I want to thank everyone, including our panelists, for participating today, and I look forward to a very productive meeting. I'm now going to turn it over to Susan Chittooran. Thank you.

MS. CHITTOORAN: Hi, everyone. As I mentioned earlier, my name is Susan Chittooran. I work with Andrea and the Patient Affairs staff. I am very excited to be here today with such a full room, where the patients and caregivers here on the panel, as well as here in the room in the front rows. We're very interested to hear what you have to say, and we're interested in listening and learning from you and your experiences.

So, as Andrea mentioned, we are going to be spending this first session here talking about your symptoms, the way you're managing your symptoms, and then any considerations in treatment. So, we recognize here that not everybody in the room may have the same disease; they may have different diseases, but we recognize your experiences may be different, even if you maybe treat diseases or conditions in different ways. So, we're very happy to learn from that.

So, we have designed this session as interactive, and what I mean by that is I will be posing questions first to our panel here, and then we will be asking some questions back-and-forth. My FDA colleagues here may have follow-up questions, and then we will turn to you all in the room. We have patients here, and we also have patients on the web as well. My colleague here, Wendy -- Wendy, if you'd raise your hand -- will be kind of filtering some of the stuff that we're hearing online. So, she'll help us kind of capture the patient and caregiver voice from online. And then after that we'll go back to the panel. So, we'll sort of take turns in terms of how we are doing the discussion.

So, in order to best accommodate the most number of speakers as we can, we just ask everybody to please be mindful of their time in responding. Also, if there are things you think about that you didn't get to say here today, we do have a docket, as we mentioned a couple of times, that's open until May 30th. So, we encourage you to utilize that if you're in the room and on the web.

So, yeah, and then finally, just please, as Andrea mentioned, please just be respectful of others when speaking. Just recognize that people are talking about personal experiences that may not be easy to share. So, with that, I'll get started. We've already done some introductions of our panel, so I will start off by asking questions to our panel. And, again, we may have some follow-up.

So, Adrienne, I will start with you. So, you mentioned that you are a caregiver to your daughter with sickle cell disease. So, in terms of your own experience as a caregiver, what would you say the two to three most burdensome symptoms that your daughter has sort of experienced, from your perspective?

MS. SHAPIRO: The disease, the nature of the disease basically prevents the flow of blood throughout the body. So, that, sort of, if you think of the terms if you were sort of gasping for air, right, or drowning, or that pain that you get, right? So, she experiences great, great pain within the bone marrow and as a result has been on opioids since she was two years old. So, I would say the pain. I think also being anemic and having the lack of oxygen, the fatigue. Fatigue is something that most researchers initially, because the pain was so intense and acute, it was a long time before the researchers realized that fatigue, of course, was a major, major burden, to the point where things like a remote feels very, very heavy.

And I think the -- for our population, the mental health problems that come. First of all, your foggy brain if you don't have enough energy, enough oxygen. There's silent infarcts, so that children who grow up to be adults have some cognitive problems which only until recently were documented. So, I would say those were the three major symptoms that we deal with.

MS. CHITTOORAN: Okay. And would you say that you've seen some of those symptoms change a little bit over time? I know you mentioned pain from being very young, but are there other ones?

MS. SHAPIRO: Well, the pain, when they're young, and we do have treatment protocols for when you're young, so the experience with the disease is very different as a young person. When they're young they can go to the hospital, we get immediate treatment, the pain is relieved; but as they get older, due to the effects, right? So, as these blood cells block in the capillary it forms scar tissue. They have, by the time they're 18 years old, vascular disease, they have lung disease, they have heart disease, they have kidney disease. On the outside at 18, they might look 13, but have the body of, you know, a 60-year-old. So, I guess it's the transition (a) from being a child to being an adult who is not really an adult, having to deal with advanced disease.

MS. CHITTOORAN: Thank you. And you mentioned a little bit about this in your response so far, but what types of things are you and she doing to help manage some of the symptoms that she's experiencing?

MS. SHAPIRO: Oh, well, there are all stages, right, as there are stages of the pain, so you do meditation, you do heat, you do massage. And then there's this step up on the pain scale that you go until you're actually -- when there is nothing that you can do other than opioids, and that just sort of masks it. We have a real problem, because as you do that, of course, year after year after year, her tolerance for the opioid has become higher and therefore she needs larger dosages of it.

We have -- this may be going ahead of things -- have at this point our first medicine. The disease is 100 years old and we've got our first medicine, and it's made a lot of difference. So, we have hope that in the near future, you know, there will be something we can do to prevent this. But as far as all the damage that's done up to this point, there's nothing that can be done for that.

MS. CHITTOORAN: Would anybody on the FDA panel have any questions or anything to clarify?

DR. MCCUNE: Thank you so much for your description. Having taken care of numerous patients with sickle cell anemia, it's very hard to see how much pain they go through. Can you comment a little bit about how this has affected your daughter's school and friends, and kind of just the activities that you would expect for a normal child?

MS. SHAPIRO: What I want to say is this about all of us, I think, sitting here. A diagnosis of a rare disease is really a lifestyle, and becomes a lifestyle start and stop. If you look at any of our calendars, if you could, I'm sure you'll see where even we'll plan out something and you never know what you're going to be able to do from moment-to-moment what known -- I'm going on vacation in three weeks.

So, with the school, it was very challenging. She would be okay and then she would say I'm not okay, and they'd be looking at her, because she looked perfectly healthy. And the next thing I'd know, I'd be running to the school and then we would be taking her to the hospital, and then there would be a hospitalization. I think that that really, really, if we had a category for that, that inability to have that prediction or that safety or that continuity in life is a major, major problem throughout all of our community.

So, I think it is the weight of the disease causes mental stress that is prominent and something that until now has not really been addressed.

DR. MCCUNE: And I just wanted to rescind the use of the word normal, because none of us are normal.

What I would like to say is how you differentiate from a child who does not have a chronic disease or your particular daughter's chronic disease, so just for the record.

MS. SHAPIRO: Yeah, yeah. And by that I think that's exactly what it meant. By normal, meaning you could have a fairly predictable schedule.

MS. CHITTOORAN: Yeah?

DR. SILVERSTEIN: Yeah. I echo Susan's comments about the appreciation about how difficult it is to get in front of a group like this. Without identification of where your daughter gets her care, or anything like that, do you feel that the healthcare team where you are, or maybe you've been to more than one place. Has a full knowledge of the various aspects of the disease that affects your daughter, more than just the medical effects of it, but also all the psychosocial and cognitive and mental health aspects of the disease -- do you feel that they are adequately trained, and what can be done to enhance that in general, not necessarily at the center where your daughter's getting her care?

MS. SHAPIRO: My daughter gets care at one of the most excellent facilities in -- where we live, and my answer to you is absolutely not. I do not feel that they're prepared. I do not feel that there are any protocols or protections in place to ensure that she gets quality care. And it's not only her; I do what we call at point of advocacy for other adults in our area. That means when someone has no one and they have to go to the ER, or are having problems, I go out, and we have a team of people who go out, and anyone can change our care. So, if a hematologist prescribes a pain regimen, or the pain doctor or whatever the treatment is, anyone can say I'm not comfortable with that and change it. So, I don't think any of us living with sickle cell disease are safe anywhere.

MS. WITTEN: I have a question. Have you ever considered to participate in any clinical trials, natural history or clinical trials for drugs or gene therapies? If it's not, why?

MS. SHAPIRO: Yes, actually, we're very active. I actually got into advocacy when gene therapy became a possibility. We -- bone marrow transplants were the only curative for us, but getting a match for us is very rare, so gene therapy was it for us. So, yes, we are very much involved in clinical trials and gene therapy, and it is truly our community's belief that gene therapy will lead to a cure for us. Of course, until we get to the point where we can do reconstructive therapies, the damage to our bodies at whatever point won't be cured -- I mean, won't be corrected. But we are very, very interested and very involved in educating people and getting them into research. But that's not going to help us, yeah, at this point.

MS. WITTEN: Thank you.

MS. CHITTOORAN: Thank you, Adrienne. Okay, Seth, just wanted to move on to you next. So, you recently learned that you had a genetic marker for Huntington's disease after caring for your mom, who also had the disease. And from what I understand you are asymptomatic right now; is that correct? Okay. So, given that, when you're thinking about the two or three symptoms that you're most concerned about in the future, what would you say that those are?

MR. ROTBERG: So, with Huntington's disease, it's a cognitive, psychiatric and movement disorder, and some of those main symptoms include involuntary movements, which is known as chorea. So, with my mom she had poor balance and wobbly movements, where we had neighbors who thought that she might have been drinking or had just like these drunk movements. The other big symptom was mood swings. So, that behavior of having a perfect conversation and then, I don't know if she was angry or upset or just simply depressed. And then I think the last one would be like that cognitive decline. So, being able to make decisions on her own, short-term memory loss, among other things.

And for me personally, what's challenging is that kind of touching upon potential treatments and how to manage it. My mom did try to take an FDA-approved drug for Huntington's disease that helped with the movement aspect of it. The challenge is that the side effects of that impacted her -- increased, I guess, her depression and suicidal thoughts.

So, what I've noticed with Huntington's disease as well as other central nervous system conditions, like ALS, MS, Parkinson's, is that there's a big focus on that, you know, the movement disorder biomarkers and not looking at the cognitive or psychiatric aspect. And so for me, like, yes, I'm not symptomatic yet, but unless there's a cure in 10 or 15 years, I will end up just like my mom one day, and she battled it for 17 years before passing away.

So, for me, it's thinking about, well, can researchers now try to figure out biomarkers for these cognitive and psychiatric symptoms that don't just impact Huntington's disease, but a lot of these rare diseases, and that mental health ability of trying to improve that overall quality of life.

For me, it was touched on before, was the point about, you know, living a normal life, and I think for young people like myself, it's how do you live that new normal life? How do you not just transition in the child care, or from child care to adult care, but transitioning into that future planning? So, a lot of these things I have to think about now is how do I build a romantic relationship, family planning, career choices, and these are always things that are on my mind and a lot of other young people's minds of how to live that new lifestyle, but also how do you plan your life for the future?

MS. CHITTOORAN: Thank you. And so what would you say, and you alluded to this a little bit already in your response so far, but just sort of seeing her experiences, what kind of -- what were you sort of thinking about when you decided to get tested? Is it something that you sort of knew that you were going to do sort of sooner rather than later, or how did you -- how did that impact your decision on testing?

MR. ROTBERG: My mom was misdiagnosed with major depression and bipolar, which, again, the mood swings and depression were just symptoms of Huntington's disease, so probably misdiagnosed for about seven years. She was officially diagnosed when I was 15, and so five years later I tested, but I was definitely in denial because I felt like I lost out on that normal childhood. And no one truly understood what I was going through. I felt the isolation of not really having anyone, especially my age, to be, like, oh, yeah, I get what you're going through. And I kept thinking about it, again, my future of how to plan for what those next steps are, and that's kind of what brought me to the decision of testing. But it was definitely a very personal decision. Genetic testing is very, you know, a very big decision in anyone's life.

I mean, the other challenge was that it took me about, actually, three years to tell my dad and my sister to try and protect my mom, not wanting her to feel guilty, not wanting to be another burden to the family. And so for me it was eventually opening up more about that and realizing is my story and this is how I'm going to make a difference. But it's always about, you know, well, when am I going to start showing symptoms, and even there's days where, if I forget something or I can't multitask, which I know is huge challenges for anyone, I'm always thinking right away, is that Huntington's disease or is that just me being just a 28-year-old kid?

MS. CHITTOORAN: Okay, thank you. Is there anything that you are doing now to delay the onset of your symptoms?

MR. ROTBERG: There is not anything in particular that's like shown, or I guess proven to help. A lot of people say exercise, and I actually -- even though I don't -- or I can't participate in any clinical trials because of the criteria and it being so tight, tight-niched, I am able to participate in some observational trials. So, I did participate in an exercise study, waiting to see the results. And I try to exercise three to four times a week. But besides that, it's tough, because you see in a lot of these online communities about different remedies, like off-label drug use or trying all these different supplements, and for me it's like that could help, but I'm trying to focus on today and not worry too much about what's going to happen in the future.

MS. CHITTOORAN: Okay, thank you. Is there anybody from the FDA panel that has any follow-up questions? Sure.

MR. KEMP: Hi. You mentioned the online

community. Sort of wondering how much of a role does that actually play in your sort of day-to-day life or decision-making, or just general support?

MR. ROTBERG: Personally speaking, it's definitely challenging because a lot of times I tend to see a lot of misinformation or information that's not, I guess, medically backed by people who just happen to Google something and they just post it in these groups. But it is challenging to see some of this stuff. Because for me I'm always trying to -- I really want to help others and help them realize they're not alone. And when I see people struggling, it hurts me, because I wish I could do more, just like I wanted to do more for my mom but I couldn't.

So, I think with the online platforms it's really trying to figure out the best way to understand what those needs are, especially with -- depending on if it's a young adult versus an older adult versus a child, and really just getting their perspective, especially when it comes to, I guess, clinical trials and potential treatments and cures for any rare disease.

MR. KEMP: Thank you. I helped set up schizophrenia.com when I was probably around your age, and many of the same things we had in the common disease issues are exactly what you just said -- a lot of misinformation, needed medical curation to make sure that the information was accurate, people weren't preying on the patients, like trying to sell some snake oil cures to the population. But it was also the large benefits that people who were in these isolated communities. Because we did surveys to see who was actually using it and what they're using it for.

MR. ROTBERG: Yeah, I mean, I definitely think it's valuable, online platforms, especially with some of these rare diseases where your closest connection could be someone from across the pond. And so being able to connect with people, whether it's the same condition or a different condition and seeing a lot of familiar faces here, it's great to see, like, okay, I've connected with them through some type of online platform or through some social media channel. And just knowing that, you know, I really think being able to connect with one another helps improve that overall quality of life.

MS. CHITTOORAN: Thank you. So, Caroline, just moving on to you. So, what would you say the top two or three symptoms are that you find most burdensome?

MS. SPENCER: So, for me, mobility issues are definitely number one. It leads to progressive loss of balance, walking. So, right now I use a service dog, my dog Clark, to help me get around. And then second-most impactful symptom is fatigue, for me, and fatigue really ends up being a moderator for a lot of the other symptoms. You know, when I'm fatigued my speech is less precise, my voice is quieter. I'm tired, I can't balance as well, I can't walk as far. In addition, too, I just maybe need to take a nap before I respond to an email or something. It could mean that I don't make it through a whole school day.

And to touch on what Adrienne mentioned, it really -- it takes a lot of planning to deal with both the mobility issues and fatigue issues, to be able to anticipate challenges and figure out how to get around that, or to still do what I need to do in spite of that.

MS. CHITTOORAN: Okay, thank you. How would you say your symptoms might have changed over time?

MS. SPENCER: So, up until about three and a half years ago, I walked independently. I did use a walker for a few months. So, there are gradual changes in my mobility, but once they become more apparent, they're pretty significant. A really tangible example, so I'm working on my doctorate at the University of Cincinnati right now, and 10 years ago I was an undergrad student. At that point I didn't have a diagnosis. I did have slight noticeable balance problems, but getting around the campus then compared to now is so different. So different.

MS. CHITTOORAN: Okay. So, you mentioned, in terms of managing your symptoms, you mentioned Clark, you were mentioning taking naps and just sort of the planning that you have to go through. Just wondering if there are other things beyond what you've already mentioned that you're doing to help manage some of those symptoms?

MS. SPENCER: Exercise, staying active. I do focused intensive balancing gait training twice a week, and I've done that for years. So, really keeping up on that. Keeping up with walking, even if I can only walk a quarter of a mile, that is better than nothing. And I really focus on not doing too much so that I can't do it again the next day, and that helps me balance the -- trying to do too much but sometimes I want to do nothing at all.

MS. CHITTOORAN: Thank you. So, I want to turn to the audience. I just wanted to see if there's any quick questions the FDA panel has for Caroline? No, okay.

MS. SHAPIRO: I just wanted to clarify that when you asked about treatment, pediatric treatment for children with sickle cell tends to be really, really good. So, my comment about there being none, no place for sickle patients to be completely safe or looked after was with adults. I just wanted to clarify that.

MS. CHITTOORAN: Thank you.

MR. KEMP: I just had a quick question for

Caroline. As your disease progressed and you need more and more help, very similarly, how did your physicians and medical team help you with that? Or do you think they were identifying the issues in sort of a timely manner and got you the things that you needed, or was it sort of one-off learning experience?

MS. SPENCER: So, I think my doctor definitely sensed a change in balance and walking and probably would have recommended using a mobility aid sooner than I accepted that. So, part of it, my diagnosis came, like, as a culmination of multiple symptoms. My diagnosis happened because things got so bad, whereas, maybe with Huntington's, like you kind of know and you can forecast out and see ahead a little bit. Mine, it seemed more like retrospective.

MS. CHITTOORAN: Thank you.

DR. MAYNARD: This is Janet Maynard. Maybe just one housekeeping thing as we transition to the audience. If folks can just remember to identify themselves before speaking just for the transcriptionist, just so we know who is speaking. So, if people don't mind on the panel and the audience as they transition, just to say your name before speaking. Okay, thank you.

MS. CHITTOORAN: So, now I just want to turn over to the audience, and let me pose the same questions, some of the same questions I've asked the panel here already. And then I'm going to go to Wendy, who can also capture what was being said on the web as well.

So, so far in terms of the two to three symptoms that our panel has mentioned, I've heard pain, I've heard fatigue, I've heard difficulty with movement. Just out of -- by a show of hands, who here, patients and caregivers, who is experiencing or has experienced pain as part of their rare disease? Okay. Okay, so about a third or so. What about fatigue? Okay, a little bit more hands, maybe about half. What about challenging with movement, getting around? Okay, most people. And then one of the things that we heard a lot through the panel is that just the challenge of going through the day-to-day parts of life -- school and work. What about that? Have the people been -- okay, so about half.

Okay, so I want to hear just from a couple people in the audience. Who would like to share about some of those symptoms that you're experiencing? We do -- you know, if you feel comfortable, you don't have to use your first name, but, again, as Dr. Maynard said, if you would just identify the name of your disease or condition? Yes.

MS. HARTMAN: Hi, thank you. I'm Christina Hartman and my daughter, Charlotte, has a rare genetic disorder called NAA10. It's also known as Ogden's in boys. And one of the things I wanted to add to the list of difficulties is speech. So, one of the challenges for a lot of folks with rare conditions is being able to communicate. And my daughter Charlotte, like many of the NAA10 girls, had a very difficult time learning to walk. In fact, most of the girls are still in wheelchairs, but I think in large part due to really early and intense intervention, physical therapy twice a week for a year, Charlotte started walking at 2-1/2. However, we have not had the same intervention in terms of speech, and so she really struggles to communicate. You know, she can make a few sounds and says "Da-da." She says "Mom" when she's mad and has started saying, "Head, head," but she'll be 3 this summer and that's about it. And so I would say that that's a pretty big concern as well, you know, for the future.

MS. CHITTOORAN: Okay, thank you. Yes?

LORIE: Hi. My first name is Lorie. My sister had Lennox-Gastaut disease, and I have two grandchildren, 1 and 3, with a rare genetic disorder called MECP2 duplication syndrome. I've noticed from having been a caretaker for my sister with Lennox-Gastaut, and also from my grandchildren, a few commonalities just in those two syndromes, and some of the things that were already said with the fatigue. One of the things that is a real big concern, I think, for a lot is the blow to the system in terms of immunity, because it makes the body so susceptible to comorbid problems. I see Adrienne shaking her head. And I think, Seth, you also mentioned having trouble sometimes telling the differences, is it the disease or is it a normal going through at your age. And that's something that parents have problems with whenever my grandchildren catches a cold. Some of the kids with MECP2, they can't -- they have asthma, they have lung conditions, they end up on, you know, with a lot of breathing difficulties. And so every time one of the kids gets a cold, we wonder is this a precursor of something worse or is it just a normal cold?

And another common thing that a lot of rare diseases in children is seizures. And one of the doctors, I believe, asked about how well the medical community understands. And a tremendous problem that I had in taking care of my sister was that the medical community did not even recognize when my sister was having a seizure because there are so many different kinds of seizures, that just a staring spell or a fall could be seizure activity.

So, I don't want to hog up everything, but those are some of the things that I noticed in relation to what other people said as well.

MS. CHITTOORAN: Thank you so much for sharing. Is there anybody else in the room? We'll go to this side.

MS. WELT: Hi. This is for Adrienne. My kids -- my name is Patricia Welt, and my kids have Ehlers-Danlos syndrome, which is an invisible illness. And you spoke a little bit about that, and when we go to the emergency room, oftentimes because my children look fine, their symptoms are dismissed, especially since they're young women. And my concerns are dismissed because I'm a woman, and I'm wondering if you run into -- you know, even if they're in severe pain, that it's something that -- it's kind of a fine line.

MS. CHITTOORAN: Just a reminder, we can address that in a little bit. I just want to make sure I'm hearing from other symptoms first before we go back to the panel. Thank you. Does by anybody else, maybe one more, and then I'll go to the web. Sure.

MS. STONE: Hi. I'm Geneva Stone, and this is my son Robert. Robert has dystonia 16, and he also has -- it's a genetic -- we used sequencing to get that diagnosis, and it's a very rare form of dystonia. And he also has the clinical symptoms of biotin-thiamin-responsive basal ganglia disorder. And he experiences all of the common symptoms that were brought up here, and one thing that the FDA and doctors might think more about is Robert can't swallow due to his gastric symptoms. He has severe GERD, and he currently uses a G-tube and a J-tube for medication adjustment, and it can sometimes be extremely difficult to get liquid forms of medications. And we spent much of Robert's early years trying to compound medications ourselves until Robert had Medicaid waiver and we've been able to get pure vitamins, thiamin and biotin compound by our pharmacy. But those patients who are using vitamin therapies face significant hurdles because over-the-counter vitamins are typically, like, chock a lot with fillers and many people cannot tolerate fillers at that level. So, just wanted to talk about method of administration briefly.

MS. CHITTOORAN: Okay, thank you. Wendy, what are we seeing on the web? Do people have -- are people talking about some of the symptoms they're having and how are those maybe similar to the ones that we've heard already?

MS. SLAVIT: So, I'd like to address a few of the symptoms that have been mentioned online and then there is a question for Caroline. So, people have been talking about shortness of breath, lack of oxygen, feeling breathless. We also had someone online talk about inability to speak and swallow, and how difficult that is.

We also had a few people talk about pain and fatigue and pain management. And so the question for Caroline is, actually, how has your mobility dog affected your ability to get around and interact with society?

MS. SPENCER: So, I get way more attention now than I used to. It's very, like -- "Oh, there's Clark," and I'm like, "I'm here, too." So, and actually, like, being a quiet person and being more private about wanting to share with stranger about my -- why I walk like that or talk like that, that was an adjustment at first. But now -- so, I meet friends everywhere I go. He's a great conversation-starter, and really it's opened the door for me to be comfortable and relate to people who may not have heard about Friedreich's ataxia before, and so it gives me a chance to educate, to help educate others. So, it really helps me relate to other people.

MS. CHITTOORAN: Thank you, Wendy.

MS. SLAVIT: No, not at this point.

MS. CHITTOORAN: Okay, thank you. So, we talked a little bit and heard a little bit about symptoms you're experiencing that are similar. I'm curious, are there others in the room that are experiencing symptoms that you feel are burdensome that we haven't already heard about or talked about? Yes?

MS. GILAZZO: Hi. I'm Elizabeth Gilazzo (ph), and my 4-year-old daughter has a rare neurogenetic syndrome called Angelman syndrome. So, as we think about our kind of two to three most burdensome symptoms, I'll echo two that have been talked about and bring up a third that we haven't mentioned.

So, children with Angelman syndrome, or individuals with Angelman syndrome are completely nonverbal, so I'll absolutely echo the impact on daily life of having a child who can't communicate any of her basic needs and the frustration that comes from the lack of appropriate services and coverage of services for children with complex communication disorders.

The second is epilepsy, and access to appropriate care of people who recognize what is a seizure and how seizures might best be treated in individual syndromes. And then the third is sleep disturbances. So, I'm also a pediatrician. That's the other hat that I wear, and I care for lots of kids with pervasive developmental disorders, and this is a huge problem across the community. And if you want to talk about something that impacts caregivers' lives, is sleep disorder. So, kids in the Angelman community might sleep two to three hours a night, which really means that they need 24-hour-a-day supervision, and this -- the impact that has on caregivers and families is really quite huge and not unique only to the Angelman community.

MS. CHITTOORAN: Thank you. Anybody else? Yes?

MS. MAUGHAN: I'm going to stand up because I don't stand out enough in the hat. My name is Annette Maughan, and I am the CEO of KGB Foundation. It's a rare genetic disorder caused by mutation of the ANKRD11 gene. For our patient population, the number one complaint that they have is behavioral or impulse control. Those prevent the majority of our patients to go to school, especially when you have, you know, they're typical in every other sense, but you have this behavioral issue because of, probably, a lack of communication skills, because that is the second most impactful thing is delayed speech, delayed milestone walking. But it's always amazing to me to hear patients and their caregivers talk about that impulse control changes everything in a social setting, right? Because, I mean, we've all been there where you're out and somebody has an outburst and then everybody else in the room is kind of, "Oh," they're whispering, "it must be autism." Well, sometimes it's not autism; sometimes it's just something else. So, that for us is number one. Seizures are also up there, but I think that's about it for me. Just wanted to get that out there. Thanks.

MS. CHITTOORAN: Thank you. And let me just go to the web. Is there anybody on the web, Wendy, that has anything different than what has already been mentioned?

MS. SLAVIT: No. I just wanted to say, actually, there was someone on line who was speaking on behalf of Angelman syndrome, also, and they also talked about difficulty sleeping.

MS. CHITTOORAN: Okay, thank you. I want to ask the panel, do you have anything, any questions for anybody you've heard from today? Otherwise, we can move on to the next question. Yes?

DR. MCCUNE: I just wanted to ask Seth a question, if I might?

MS. CHITTOORAN: Sure.

DR. MCCUNE: You had mentioned sort of three different domains -- the cognition, the movement and the mood swings, and that I believe your mother was treated for one, but it made -- the movement, but it made the mood swings oh, so much worse. Do you have a feeling for which one of them -- so, clearly, there's kind of a risk-benefit discussion there. Is there one that you would have rather treated and taken the side effects? And would you answer that question differently?

MR. ROTBERG: I know we'll be discussing that in the next question, but I'll try to sum it up. Personally, I mean, unfortunately, I can't speak -- I can try to speak on what I would think she would want. The biggest thing is because you can actually visibly see the physical movements. That's, I think, why obviously they wanted to treat that aspect, but I definitely, you know, in my mind, I feel like I would personally rather deal with that mental aspect of it, the cognitive and psychiatric symptoms because, one, you can't see it and, two, those are just as important, if not more important. But I think it was tough, because, again, as we'll talk about in the next question, that was the only option.

So, what other options does she have? Yes, she took medication, like, for anxiety and depression, but there's only so much that that can do to offset the other medication. And, again, it did work for a good amount of Huntington's disease patients, it just didn't work for her and there's, again, unfortunately no -- there wasn't an ideal drug or alternative for her to take.

DR. MCCUNE: Thank you.

MS. CHITTOORAN: Thank you. Okay, so I want to talk a little bit about how some of the symptoms you're experiencing, how you're managing them. We've heard the panel mention several things already -- medication, opioids, Clark. We heard a little bit about supplements and vitamins. So, want to hear from a couple people in the audience. How are you managing your symptoms?

BONITA: Hi. Good afternoon. I am a patient living with Ehlers-Danlos syndrome, hypermobile type. For me, I've had so many different things, but the number one gold standard for treatment for Ehlers-Danlos is physical therapy. Now, the problem with that is insurance companies provide barriers, such as copays and the deductibles and caps on visits. I've tried medications. I've tried naproxen, I've tried Robaxin, I've tried heat. I've tried all kinds of different things, but the number one most effective thing, from my second round in PT I've gone from at least 80% of pain down to about 60% of pain. So, that's like the number one thing, but, like I said, there are barriers.

MS. CHITTOORAN: Thank you. Anyone else like to share? Hi.

AUDIENCE MEMBER: I just wanted to add to Bonita's comment about physical therapy. So, with my daughter, the reason she's walking is that early intense intervention in terms of physical therapy. One of the challenges, at least in the state of Maryland, and I'm sure this is common across-the-board, the insurers are not required to cover physical therapy until you have a diagnosis. It took me a year of fighting to get a diagnosis. It's impossible to get insurance coverage for genomic sequencing most of the time, and I had a platinum Aetna Insurance plan at the time. So, I would just add that it all ties together.

MARIA: Hi. My name is Maria and I have a 6-year-old daughter with Prader-Willi syndrome, and the hallmark symptoms of PWS are hyperphagia, which is a chronic insatiable hunger, and obesity. But for my daughter, the most burdensome symptoms are disordered sleep and slow processing speed. And what I love about this conversation is that she was just recently diagnosed with narcolepsy, and so we're actually managing her symptoms right now using natural stimulants and behavior modification. Because we now know that what the problem is, we're helping her get back to sleep, get better sleep at night, and we're exploring medications to treat the symptoms now of narcolepsy. And to your point about insurance, because we have a diagnosis now, it's easier for us to get medications covered.

MS. CHITTOORAN: Thank you. Yes?

AUDIENCE MEMBER: As far as physical therapy you mentioned, I will say we're managing for my daughter, but it's a double-edged sword because the children need physical therapy, occupational therapy, speech therapy, and they also need pediatric gastroenterologist, an ophthalmologist, you name it, they need the specialist. And my daughter ended up having to quit her job just to care for the children, and so that's what I mean it's a double-edged sword, because so much isn't covered on insurance and it takes so much attention. And the sleep issues are sleep issues for my daughter, for mental health and psychiatric needs, my daughter needs to go for counseling. It's -- we can't neglect the family members. As a sister growing up, my parents tried to give them a normal life but, you know, the identified patient takes so much attention. And about speech, when you've got cognitive decline, that paired with the lack of speech makes it doubly scary and difficult.

MS. CHITTOORAN: Thank you. Yes?

MS. WELDON: Hi. Monica Weldon, and my son has a neurologic disorder called SYNGAP1, and I wanted to add this symptom because it's something that's kind of a hidden symptom. But I know that several of my rare disease leaders who are in our gut cohort that we've put together is constipation. And I will have to say that for us, we have to help my son go twice, twice a week because of a low muscle tone. And you can -- it seems very simple, but with some of our kids that have the gut issues between, of course, the brain and the gut and the muscles and the peristalsis not working correctly, I mean, that could be maybe why they lack sleep. That could be why they're acting out. What are those things? And so, of course, us together as a group in the rare disease community looking at the autism component, I think it's very important. Because some of our kids have been hospitalized because they just simply cannot go. And so I wanted to kind of throw that out there as a symptom, and I know the moms and parents out here that live with that know that that's a big issue around that, and having to treat it, because it's something you can't not let go on a weekly basis.

MS. CHITTOORAN: Thank you. Okay, Wendy, I just want to hear if there is anything on the web that people are mentioning in terms of how they're managing their symptoms?

MS. SLAVIT: We also have someone mention speech therapy, which was already mentioned earlier. So, I just wanted to reiterate that as one of the comments people have made.

MS. CHITTOORAN: Okay, thank you. Okay, so know that I didn't get to everybody so far, but I just want to remind people that we do have a docket open. It's open until the 30th of May, so just, please, make sure if you have comments that you didn't get to make, or if there is something you said and you missed out on adding something, please do so in the docket.

I just want to turn back over to our panel for about the last 30 minutes or so. I have a couple more questions for you and then we'll turn back to the audience and have sort of another discussion.

So, we'll start again with you, Adrienne. So, and this question is sort of related to the benefits of treatment and how you weigh those against -- how you and she might weigh those against potential side effects. So, when you're thinking about managing her disease, what potential benefits would you and her consider most important in your sort of decision-making process?

MS. SHAPIRO: Well, again, it depends if she's in the chronic phase or the acute phase. So, the acute phase is when the pain is really, really awful. And so when she's in acute phase, of course, there is nothing for us to do but to go to the hospital and get more opioids, or whatever combination. It's funny, many of the warriors think of it as the decision to go to the hospital is a decision to -- between their mental wellbeing and their physical wellbeing. I mean, they really struggle to go for that.

So, I think for us it is really kind of -- we manage as much as we can before we have to go to that high level of meds. The meds in themselves, when you're on painkillers or opioids, and those kind of things, they cause a lot of these problems we've been talking about. There's constipation, there's foggy brain, there's more fatigue. There is this itching from -- if you can imagine itching from inside of your bones, you know, and then they need Benadryl, and then that becomes a struggle to get that. And so, really, pretty much it's always against am I so bad that I have to do these things? I mean, that's really what it is for us. And many times we end up with some real complications because we put off going to the hospital for so long because of that.

I guess for us, when you talk about potential benefits, we have, like all communities, we have some really brave young people who are into doing trials, going and having bone marrow transplants, even though they know there's a percentage that it won't work, that they might end up with graft-versus-host, that particularly the girls will end up being infertile. And so that's kind of the thing is, I want this treatment. I want to help the community.

There's also a sense of others saying I'm too sick to get into trials, which is an interesting discussion to have. I had to have that one with my daughter, because her fear is that she was so sick that if anything went wrong, it might affect the outcome of the trial.

So, I think for us, because it's kind of a different than -- we have a diagnosis, it's part of newborn screening, so pretty much we're told from the beginning what the kids have. We have a protocol that pretty much -- 95% of our children live, where sickle cell is sickle cell any other place in the world and it's the opposite -- 95% of the children die. And so I guess we're always kind of trying to weigh what -- you know, what's the loss? What's the gain, what's the loss, and in many ways we're much more fortunate than many of the other people in this room. But it is a daily struggle, and in that daily struggle I think we're all united.

MS. CHITTOORAN: Okay, thank you. So, I think what we'll do is, just to make sure we're maximizing our time, I'll just go down the panel and then I'll turn to the FDA table and just see if you have any follow-up questions for any of the individual panelists. So, okay, so thank you. Thank you very much, Adrienne. So, Seth, if there was a treatment available for Huntington's disease, what benefits do you think -- would you think about when you're comparing, thinking about potential risks and side effects?

MR. ROTBERG: So, for me, I'm very fortunate enough that with Huntington's disease there's a lot of upcoming, I guess, trials in the pipeline, whether it's -- we have one in Phase 3, we have some that are starting Phase 1. I think the biggest thing that I'm trying to teach myself is learning about the ins and outs of clinical trial development and getting the patient perspective from the beginning. Because when you think about it, there could be, as mentioned, an oral medication, but is it the liquid form or is it the pill form? There's gene therapy, there's a spinal injection, and try and understand what the needs are and interests of those patients. Can they take it once a week, once a month, once a year, once in a lifetime, and really try to understand and be patient with knowing what's in the horizon. So, am I going to take something that's now or am I going to wait for this next drug that could help me even more, three to five years down the road, or even 10 to 15 years down the road?

So, that's kind of something I really want to emphasize is, like, what are the options? What are the alternatives? And then for me it's kind of like let's see the data on the animal models and then the preclinical discovery stage, but let's get the young adults' perspective, the older adults, the caregivers, all of them involved from the beginning versus once we're going through it. Because what I've learned is that once a patient is in a trial, you know, a lot of people see it as, hey, I need to get in this, I need to get in this, but it's a big commitment, and if you drop out, it's not like the next person can just come in. And that can really impact enrollment as well as if it eventually gets FDA approval.

MS. CHITTOORAN: Okay, thank you. If you were taking a medication that delayed the sort of development of the symptoms that you're experiencing, what kind of risks would you sort of be willing to tolerate, the side effects you would be willing to tolerate?

MR. ROTBERG: I mean, anything that's really going to slow it down, I definitely would be interested in. The challenge is, as mentioned before, because of the criteria, I can't even get involved or even get my perspective involved currently in any trials, whether it's preclinical or it's in a Phase 3.

So, for me it's trying to understand the ins and outs about trials, that opportunity, and then trying to go from there. I mean, personally, if I had to choose between those three different aspects of it, I'd probably rather have the movement disorders, only because, you know, that cognitive and psychiatric, I think I'd rather try to manage that first, if I had to pick, based off what I saw in my mom of being depressed, wanting to sleep all the time, you know, having these mood swings. And then knowing that there's a higher risk of suicide is very scary, especially already dealing with a rare diseases and then having those thoughts on top of that can be challenging.

MS. CHITTOORAN: Thank you. Caroline, so I'm going to pose the same question to you. So, when you're thinking about managing your disease, what potential benefits you consider most in your decision-making process?

MS. SPENCER: Well, you know, based on the symptoms that affect me most, I would say better mobility, better balance, increased ability to walk on my own. You know, I have a cart, but I can't take two steps without some kind of assistance. So, if I was able to take five steps without assistance, that would be an improvement. And improving my ability to keep up with friends, keep up with schoolwork, being engaged in daily life activities, that would be kind of the most benefit to me.

MS. CHITTOORAN: Okay. And how about when you consider that when you're thinking about the side effects, whether they're serious, very serious, or not very common, or maybe more common side effects?

MS. SPENCER: So, kind of the biggest thing that I weigh as far as side effects is my ability to do my job, to go to school. I feel it's really important to me to be able to have a life aside from FA, to do the things I would have done anyway. So, you know, there currently are no treatments, FDA-approved treatments for FA, but if there were, I think I would most weigh the impact on me still being able to go to school and do my job and, you know, have a normal life, so-to-speak. Yeah.

MS. CHITTOORAN: Okay, thank you. Does anybody, yes, I see a question.

DR. SILVERSTEIN: So, here at the FDA, I can speak for my center, but I think it probably goes across all of our centers. I'm in the Center for Devices. We consider patient preferences, patient perspectives, and patient-related outcomes as something that we must think about when we're looking at clinical trials that companies, investigators are interested in doing.

And with that as a background, I'm curious to know what's happening on -- as all of you have either yourself or your child comes to -- is introduced into a new therapy, and how much is that being considered what your preferences are? How much risk, exactly what Susan was trying to get at -- how much is risk considered related to benefit, but also what you might want to happen in a trial in terms of what you're willing to risk for a certain benefit? How much is that considered by your physicians or by trial specialists who are conducting a trial? Is that part of the equation or is it simply not part of the equation?

MS. CHITTOORAN: Sure. Adrienne?

MS. SHAPIRO: Well, I think I can -- and I can only speak for the ones that we've been involved with in the last, I guess, five years. It is very much part of the conversation. I think that for a long time it wasn't. I think for a long time that the patient voice or the patient experience was not a part of clinical trial development, and that through PCORI and other organizations, patients' perspectives have now been put front and center. I know the stem cell trials, even from the beginning the actual design of the trial has a patient or patient advocate there, and I think that they're changing now to even encompass in their trials that looking at the patient as a whole patient and the caregiver and family and what the effects of not only the trial, the medicine, whatever they're testing, but the experience of going through that will be.

So, I think it's a sea change in research, and I think it has to do with the fact that medicine at this point, medical research, doing stem cells and using your own tissue is so much -- I mean, it's much more personal than it's ever been before. And I think, also, that we've learned some stuff, I mean, from software development, right? In the beginning with software they would create something somebody said be cool to be able to do that, but they didn't have the end user in the room. And now we've got the end user in the room, and I think it's going to help, or is helping to escalate and to streamline the process.

MS. CHITTOORAN: Anybody else on the panel have anything to add?

MS. WITTEN: Hi. It's Rachel Witten from CBER. I have a couple of questions for the audience. I know pediatric patient with rare diseases is very commonly presented with lack of sleep. They do sleep two, three hours, and my question to you, do you have any help from insurances, from the community? Because lack of sleep in our kids can affect our life, and how you as a parent, how you can go through the day if you don't sleep? What do you do?

MS. CHITTOORAN: Do we have a mic?

MS. WITTEN: And I'll explain why I'm asking.

MS. RASKIN: I'm Julie Raskin, and I have a

22-year-old son with congenital hyperinsulinism, and I'm also the executive director of Congenital Hyperinsulinism International and the Rare Action Network ambassador for New Jersey. And we have a campaign at CHI, which we call HI, which is hyperinsulinism for short. HI never sleeps, and so I don't have a solution, but this is such an enormous problem. With us, it's not about our kids not being able to sleep, it's about us needing to be up all night taking care of them and checking their blood sugars and making sure that they eat when they might not want to eat. We might have to trick them into sleeping in order to feed, and when you are dealing with something that's metabolic, it goes on and on and on, and it doesn't understand the normal biorhythms of day and night. And in the community of other rare diseases that I know, people living with the diseases in their parents, this is so much the case, that one part of it is a sleep disorder. But so much of it is just the weird rhythm of our lives and, yes, this affects our lives in so many ways -- ability to work, our ability to make money, our ability to care for our other children, our ability to go to school, and so on and so forth. So, it's an enormous problem that needs a tremendous amount of focus.

MS. CHITTOORAN: Thank you. I think this is a great opportunity to hear more from the audience here in the room and then on the web. I'm just going to pose the same question to those of you in the audience. So, when you're thinking about managing your disease or condition, what potential benefits factor in most?

AUDIENCE MEMBER: I'm actually here representing two communities, because I have a newly diagnosed son, so I have two with Duchenne muscular dystrophy and an 11-year-old with primary immune deficiency. And you might think that the Duchenne is what I want to talk about, but I'm actually really interested in talking about our treatment of immune deficiencies today. My son was 11 when he was diagnosed in November, and the symptom was major infections that were causing hospitalization, so it's chronic antibiotic use followed by allergic reactions to antibiotics and immunities to the ones that he could still take. And so now he's on a plasma treatment once a week, which comes with a lot of the same symptoms that he was getting because he was sick all the time -- chronic headaches, fatigue, rashes, unexplained vomiting, nausea. And so it's becoming a really pertinent discussion right now. He's not getting sick as often, but he's really sick from his medication, and so I think as we start to -- the physician and clinician environment was such that they said, hey, great, this kid has a treatment. Your other boys, you know, we didn't have much we could do for Duchenne muscular dystrophy, but there's a treatment for immune deficiency. Unfortunately, there's not a lot of research going on into new treatments because there is one, but it's a really horrible treatment.

And I now infuse my son once a week by myself because there isn't insurance coverage for nursing in a subcutaneous infusion at home. And then we have horrible side effects for half the week until it's time for his next infusion. So, really wanted to put that into the hopper, that just because it's a treated disease doesn't mean that the treatment is sufficient.

MS. CHITTOORAN: Thank you. Anyone else?

MS. CISCO: Hi. Jill Cisco from acromegaly community. In our disease state we also have some approved medicines that treat our condition, but if they were perfect, I wouldn't be here today. Most of our injectables are long-acting injectable, and they're supposed to last 28 days, and patients start to have symptoms again typically at about day 21. And when you do the math, seven days every 28 days, that's more than three months a year that patients are suffering. And I would love to find something that could give patients a continuous amount of medicine every single day so that they weren't symptomatic.

Acromegaly, I don't know how many of you know about acromegaly, but it affects every single symptom in your body, because it's hormonal. It affects your appearance, it affects -- growth hormone makes you aggressive. It affects your moods; it affects your joints. It affects every little aspect of your life. And so, in my opinion, patients suffering seven days every single month because they're on a long-acting medicine, we need to do better.

MS. CHITTOORAN: Thank you. Yes?

MS. O'BOYLE: Hi. This is Megan O'Boyle from Phelan-McDermid Syndrome Foundation, and Phelan-McDermid syndrome is on the terminal end of the 22nd chromosome shank, 3 is one of the guilty genes. And like countless syndromes, we look a lot like many of them -- autism, intellectual disability, epilepsy, sleep issues, GI issues, and I think the panel is probably going, okay, we're up to about 30 different syndromes that all look the same without seeing the genetic report.

Although my daughter suffers from a lot of the comorbidities, epilepsy is hideous, and I know families with PMS that have tried all 18 anti-seizure drugs. They all have side effects. They get given as cocktails, and it's really difficult, especially with a nonspeaking community, to really know the extent of the side effects, until you get the bloodwork done. And let me just tell you, getting bloodwork from this population is not a walk in the park.

So, I think to these other points that just because there's an anti-seizure med doesn't mean it's working, especially for the genetic causes of these syndromes that also crossover into autism, GI issues. I mean, we could probably do a show of hands of who has these comorbidities. And so I just wanted to point to that, that just because there's, you know, seizure treatments, it doesn't mean the seizure treatments are working on this population, because for our families, they don't.

MS. CHITTOORAN: Thank you. I want to ask my FDA colleagues here, do you have any questions for the audience about anything that you've heard or any other questions?

MS. WITTEN: I have a comment. I'm from CBER. We do evaluate gene therapy trials, and what we start doing in trying to have some trial for a specific indication, we try to invite the community and talk to them about the endpoints. Because sometimes, you know, when you receive this clinical trial, the endpoint is kind of meaningless, and I'd like to hear from the community what would be this reason, you know, what we think and what condition you will enroll your child in the clinical trial. And two different communities have told me, you know, the sleep disorder, we would like to treat sleep disorder, but we're not sure if it's reasonable or possible, I can tell honestly.

And what we're also started, we try for specific indications for clinical trial to have maybe one, if it's available, to have special government employee, somebody who knows the disease, or somebody has a child with the disease, to look at our clinical trial and kind of thinking, would they enroll myself or my child in this clinical trial when you have to go back every month, spend four or five hours for evaluation, or you will stay away from this clinical trial? And receive and we'll try to receive some comments from the parents or patient caregiver, what is your opinion on this design? Again, it's usable or friendly or whether the endpoints, and this is where we need your help.

MS. CHITTOORAN: Okay. Just take one more comment and then I'll go to the web because we're getting short on time.

MS. FOSS: My name is Beth Foss. I'm with the Choroideremia Research Foundation, and we have clinical trials happening now. We have two, and we have a third that's coming, so I appreciate your question and, sir, you asked that, too. I have a son -- actually, I have two sons. I'm really glad they sleep. At least we sleep, so I'm really appreciative of that. So, my older son, who is 26 now, was treated with a gene therapy up at Mass Eye and Ear, and so we are starting year three post, and it's been challenging in the sense that we go up -- as you say, we go up every six months and we spend a good day or day and a half. Any little aversion or change in his vision is -- it weighs heavily on them. Is it worth it? I would say yes. As a mother, it is worth it to undergo that. What we have a challenge with, and I'm with my colleague and friend, Eric Hartman, who has choroideremia, I'm a carrier mother, my father is blind, I have two sons, as I say, who have been diagnosed with it and are starting to see the blindness. It starts peripherally, and we lose about 7%, 8%, 10% a year. And so one of the things, one of the things that we are having -- the indicators is they measure the central vision, and much of our central vision is still perfect, 20/20, but we're losing peripheral vision. So, we have older patients that are in the trial, and if we could start with younger, when they're kids, we can preserve so much more of their vision. So, the endpoints is something that we're really trying hard to work with our researchers and with the FDA.

One other thing real quickly, I will say, as many of you are mothers and parents of children, that's one thing. I was looking at how do you weigh potential benefits versus less common risks? I think some of the younger in the Choroideremia Research Foundation, we have a robust organization. It's 1 in 60,000, 50,000 people get this disease, and there's a lot of talk about sex selection studies. Do we have children? Do we not? And a lot of our members deal with guilt as a parent, and that's something that's really hard on them. Not sure how we tackle that one, but being a parent with kids that are hurting, I don't think there's anything quite worse than that.

MS. CHITTOORAN: Thank you. Wendy, just for the next 20, 30 seconds, is there anything you're hearing on the web in terms of this question?

MS. SLAVIT: Two people that have diseases that are quickly progressing, they say anything to slow down the progression until they're able to get a cure. One parent of a child mentioned that his career is impacted by not being able to sleep due to caring for his child in the evenings. And then also another parent mentioned that IV medication can be really difficult to administer to children.

MS. CHITTOORAN: Thank you so much. Okay. Well, I know we are sort of running out of time here, but I just want to reiterate that if you didn't get a chance to share it today, either in the room or through the web, please submit comments to the docket. Again, it's open until May 30th. We'd love to hear more about you, your symptoms your experiencing and the things that you're considering in terms of treatment.

So, now I just want to introduce a special speaker we have here, Dr. Amy Abernathy. Dr. Amy

Abernathy has a dual role here at FDA as principal deputy commissioner and acting chief information officer. As principal deputy commissioner, she helps oversee the agency's day-to-day functioning and directs special and high priority initiatives that cut across offices overseeing FDA's regulation of drugs, medical devices, tobacco and food. As acting chief information officer, she leads our data software and computer hardware efforts to help us to continue to advance public health agenda. Dr. Abernathy is a hematologist and oncologist and palliative medicine physician. Before coming to FDA, she was a professor of medicine at Duke, and most recently worked in the health technology industry at a cancer-focused software and data company. She is an internationally-recognized clinical data expert and a clinical researcher, and one of the early pioneers in bioinformatics. We are very proud that Dr. Abernathy has joined us in February to continue to advance our mission in patient-centered care and public health. She has been a longstanding patient advocate and is well known across the patient community for her commitment to ensuring that the voices of patients are heard. So, please welcome Dr. Abernathy.

MS. ABERNATHY: Thank you. Thank you very much. So, first of all a hearty and appreciative thank you and welcome to all of you here. We greatly appreciate your being here, contributing your voice to this meeting, to the docket. We also appreciate all the folks who are on the web. We know you're there, so also continue to participate.

So, as you just heard, I'm new to the FDA, and I've been here about two months, both as principal deputy commissioner as well as the chief information officer. And I thought I would take just a few minutes to tell you a little bit about myself, how I got here, and then bring that to the conversation we're having here today about the patient perspective in rare diseases.

As you just heard, I'm an oncologist. So, I spent a fair part of my career taking care of patients with melanoma, and particularly patients who had a family history of melanoma and who had advanced disease. And, really, to this day, one of those patients, who actually in some ways represented all of the different patients coming through my clinic, but she had a way of sort of sitting on my shoulder and talking to me for the rest of my life. And her name is Janet, and Janet and I got to know each other in the mid-2000s. And I remember her coming into my clinic. She's got this really curly red hair. She had freckles on her nose. She was about 35. She always wore scrubs because she was an ER nurse, happened to be an ER nurse from not far across town, and had this bounding energy. And I have this little couch thing in my office. She never sat in any of the patient spaces; she insisted she was going to sit on the couch when we had these conversations in clinic. And one of the first things I noticed here in my melanoma clinic was that a woman with a fairly advanced cancer at that time was on prenatal vitamins. And as we were trying to figure out how to take care of her, one of the issues was that she was asking me about the impact of the treatments that we were talking about and what was going to happen to her fertility. And, in fact, I couldn't answer any of those questions. And we would talk about whether or not her mother's melanoma and her sister's melanoma had any impact on how her personal illness was going to go. I wouldn't have any answers to that, either, although I was pretty confident that this was, indeed, a genetically derived and motivated illness.

I remember sitting in clinic as we were talking and she's like, "You're typing it all into that machine over there, gosh forbid, just go over there and do some queries and you'll be able to answer all these questions for me." And I couldn't do that. And, in fact, I was so frustrated with not being able to do that, and she was so frustrated with me for not being able to do that, that we really worked through that period of time in trying to figure out ways to unlock the patient personal story from the computer systems and turn that into reliable underlying information that we could use to figure out how to take care of Janet, and so that Janet's story could be reinvested in her legacy in the future.

In fact, all of the work I did of the subsequent 10 to 15 years, and how I landed at FDA was really to figure out how could Janet's story be informed by all the people who came before her who had similar problems and questions -- what does this mean for my fertility, and how her story could live on as we continue in the future. And we worked on this at Duke at the time through building computer systems and patient reported outcome systems. Ultimately, I discovered that any one organization in one place just sort of hit the boundaries of what's possible, so I jumped the line and took a right-hand turn and ended up in a tech company, in a startup, thinking maybe if I motivate the tech industry we can do it from that direction. Actually, we got a long way, but then one of the things I realized was that in order to continue to motivate the story going forward, one of the places that's got as much bloody pulpit as anywhere in the world was to come to FDA, and that's why I came to FDA, and in a lot of the ways, the same reason that you're here today at FDA as well.

Interestingly, in December of 2016, Congress passed a piece of legislation called the 21st Century Cures Act. That piece of legislation asks us to modernize our process of drug development, a medical product development overall so that ultimately we can figure out what works as efficiently as possible and right size those treatments for the patients who need them. And I have been very encouraged by 21st Century Cures and all the other legislation that goes along with it, but it's only a starting point. It asks us to do things, like learn how to use data better to modernize our clinical trials, to include the patient voice and patient report outcomes, to include the patient race in developing our evidence development programs. It asks us to do that, it doesn't specify how. And ultimately going from the motivation of, please, let's move this process forward and setting the guideposts to now moving to the how do we do this? How do we get the patient perspective, the caregiver perspective, the advocate perspective into this process is one of the things that this meeting is intended to be a part of and the work going forward.

Here at FDA, my core responsibility as a principal deputy commissioner is a series of trans-FDA policy responsibilities and commitments. So, including, for example, rare orphan diseases in pediatrics, where, really, what we're trying to think about is how do we advance the work in these critical areas? And also includes the Patient Affairs staff, who also sits right next to Rare Diseases and Pediatrics, so we can make sure that we incorporate the patient voice, and we also have as many two-way communication channels as possible.

But you're probably wondering how in the world did a person who is the principal deputy commissioner also end up as the acting chief information officer? That's because ultimately if we're going to do this work, if we're going to scale to the many, many diseases that affect you, and the continuous learning processes it's going to take to get this done, we've got to scale our capabilities inside of FDA, and that includes using data and technology to do so. And we have to build the handshake points so that we're able to handshake as efficiently as possible to all of the other different parts of the biomedical community so they can scale their processes as well. So, that's why these two pieces are together.

A bit about incorporating the patient perspective for rare diseases into the work that we do, and I just want to kind of hint on a couple of things. You know this better than me. You are the experts in your conditions. You're the experts in the lives that you're living and what this feels like to you every day. There are as many commonalities are there are differences. Part of our goal today is to identify those commonalities, but also to be very respectful of the fact that there are differences.

As I was just sitting here listening even for just the last half hour, I was thinking about some of the commonalities that come through, for example, the conversation about sleep. The end user, the fact that ultimately you want to go to school and do the other things that are important in your life, right? And many of these aspects we can share across our stories, but I also think about what's unique about our disease and how do we have to understand and deal with those capabilities as well? At FDA, we need to understand the full totality of the story so that when we think of clinical trials and also the understanding of how a medical product works, we're able to do so in putting into the context of the experiences that you have. To develop endpoints and outcomes that align with the experiences that you have, and to be able to communicate across the overall biomedical spectrum within the context of the experiences that you have, including into the payer space.

Somebody asked me a little earlier today if I had any advice for the patients communities, what that might be. And the first piece of advice is use your voice. You're here today because you're using your voice. You're on the web today because you're using your voice. But continue to stand up and to tell your stories, because there is no other way to do this besides to break those stories, come together in totality as a whole.

My second piece of advice, though, is actually almost exactly the opposite. As an oncologist, I always had to remind myself our jobs are always to have compassion. As a patient and as a daughter and as a mother, I also need to have compassion. So, one of the things that can be really hard when we've had too much pent-up energy to use your voice is also to want it to move really fast, and so have compassion that we're listening, but also we're going to need to figure this out together, and it may not move always as fast as we all want it to, but that making sure that we don't give up in continuing to put our voice to the story.

Use the docket. Put your information into the docket, encourage your compadres to do so as well, because that is truly a mechanism where we call and create a robust totality of the story to be able to use for our internal work and process making.

And I think my last point is that as we think about the patient community, think about our caregiver community as well. Often, we talk about patients because we're thinking about developing medical products individually for diseases and for patients, but as we have compassion for each other, we also have to have compassion for caregivers, because it is also a huge part of the story. So, with that, I just wanted to say thank you. I'm here to answer questions, and thank you for all that you do. So, I'm going to do this or should do questions?

MS. CHITTOORAN: Any questions? Yes, sir. Do we have the microphone?

MR. HARTMAN: Thank you, Dr. Abernathy. My name is Eric Hartman. I told you I'd get chocked up. And if I get choked up, it's fine with Eye Foundation. (inaudible) and I can go right though it without getting choked up. Weird reaction. But I wanted to talk to you about your idea of a commonality of data. Eye foundation is incredibly fortunate. We've been at it for almost 20 years, and we have two gene therapy trials underway. Here we go with British, sorry about that -- and a third about to start. The biggest problem we are having, and I see it as a commonality with all our rare and ultra-rare diseases, is fighting the fatigue of those patients who are available to be in natural history studies or any of the other medical device studies, anything along like that. Because our natural history study, our personal health information is locked. I'm a prime example.

I was in a two-and-a-half-year study, natural history study quarterly. I had to fly all the way to Portland, Oregon to be in that study. After two and a half years, as it turns out, my progression, I only have one degree left in my central eye, it's too advanced for me to have -- or it's too risky to have a subretinal injection. So, there's another potential therapy or even other, like, cell replacement therapy. My two and a half years of data is locked. I can't get to it because they say the study is still ongoing. And there should be something for the rare disease community and the ultra-rare disease community where we can at least get our natural history study stuff that is observational, not therapeutic, to get an electronic copy of that so we as a patient community can move forward. The duplicity and the expense of all of that is huge. And if there is some way that the FDA can get together where we as a patient community or as the ultra-rare community can gain access to this natural history data, it will advance the science quicker and reduce the costs involved in these multiple therapies that are now available, or soon to be available.

MS. ABERNATHY: (Off mic.) Because the information, the natural history data, is critical to essentially setting the baseline for which different new treatments are compared. It also helps you predict what's going to happen, and helps you understand how to compare your story against others. So, it's important for all those reasons. Solving this problem from a technical perspective is different in the rare disease community than it is for an illness like type 2 diabetes, and so the technical solve needs to be available for situations where there's only a few hundred or a few thousand patients.

So, my advice is that we need to put this on our list, our working list of things to continue to think about. It actually is a problem that has to be solved from multiple sides, across government, across tech, across the patient community, but as a patient community, continue to agitate for it, because you've got the most powerful voice in the story.

I think we have time for one more question and then we'll need to --

KRISTEN: Hi. I'm Kristin, and I represent a community of PTEN hamartoma tumor syndrome patients, a rare genetic heredity cancer syndrome with a whole neurocognitive component. This is more just a comment to what he said and what you said. The importance for sharing data and being able to collect that data for patients is critical. And what we're seeing more and more in the rare disease community is patient organizations are becoming wise to that in starting patient-driven registries, which we have recently done. But the purpose is not to hold the data for ourselves; it's to be able to open it up to all researchers and also share snapshots of that data with our patient community, which we're doing. So, it's possible; you just have to have motivated patient organizations.

MS. ABERNATHY: I 100% agree. I'll tell you that Janet, my patient, this was exactly what she ultimately pushed to do, and I do see it as a part of how all of us in this room can solve the problem together.

I am going to stop and switch gears for a moment, because we have a special announcement. So, you've already heard earlier about the Beyond the Diagnosis exhibit, which is really intending to provide a face to all 7,000 and more rare disease. This whole exhibit is traveling across the country. It's going to medical schools and research institutes and hospitals around the globe, even, so even beyond United States, to look beyond the diagnosis of the patient. And so today the founder of the Beyond the Diagnosis exhibit -- oh, she's right next to me, there you go -- is Patricia Welton, and she's joined us to unveil the newest piece.

MS. WELTON: Do you mind if I just say something about the girls? Before I unveil this, these girls have Ehlers-Danlos syndrome, like my kids. They both had several brain surgeries. One is tube fed. They cannot attend school because they're too sick. And I want to say that in rare diseases, things are not always the way they seem, and this is -- I think this is a perfect example of that. Are you ready?

MS. CHITTOORAN: Yes.

MS. WELTON: You guys are the first to see this. [Applause.]

MS. CHITTOORAN: Okay, everyone. Thank you so much as we just wrapped up the beautiful unveiling here. I know we're a couple of minutes behind, but I just wanted to thank the panel so much for sharing your perspective with us, as well as those in the audience and on the web. It is -- I want to make sure we have a 15-minute break. So, it's like 3:01. Let's try to be back here about 3:15 or so, to get started. Thank you so much.

[Break.]

MS. CHITTOORAN: Okay. Hi, everyone. We're going to get started, just because I want to maximize the use of our time here. So, we are getting ready to start Session 2. This will be another facilitated discussion between our panel here and our audience in the room and on the web. This session will be focused on commonalities in clinical studies and registry considerations.

So, just some reminders before we get started. If you don't get to provide feedback today, please do so on our docket, and the just so everybody knows, we do have a large audience on the web as well. There's almost -- about 500 people or so on the web as well, so in addition to what we have in the room, so that's very exciting.

So, what I will do is, we will go do some introductions here for our panel, and then I will pose the questions to them, and then we will then turn back to you. So, if we would just start with Julie here, and we'll just work our way down. Just, if you would, please introduce yourself, your name, your role, if you're a patient or caregiver, and a little bit about the disease or condition that you're representing here today. And then just because people may not be familiar with it, please just provide like a couple sentences, a little bit about what that is. So, thank you. Julie?

MS. RASKIN: My name is Julie Raskin and I live and work in New Jersey with my husband, and we have two children, Hannah and Ben. They're both young adults. And Ben, who is the younger one, was born 22 years ago, almost 23, with congenital hyperinsulinism. And congenital hyperinsulinism is a disease that causes the overproduction of insulin, and that causes severe hypoglycemia, or low blood sugar. And the brain and the body need blood sugar to grow and develop, so if it's not controlled early on, it could cause brain damage or death. And a lot of what you all talked about this morning really, really resonated with me. And we sort of think of hyperinsulinism, a lot of us it can be like a global insult to the family, not necessarily just the brain, but to the family, for all the reasons that you all spoke about. And I think that in and of itself is a commonality among so many of the rare diseases. So, thank you for giving an opportunity to meet you all.

MS. CHITTOORAN: Thank you, Julie. Michael?

MR. BUSBY: Good afternoon, everyone. My name is Michael Busby. My wife Kristin and I have three children, Alexandra, 8 years old; Michael, 6; and Joseph, 3. Alexandra and Joseph were both born with progressive familial intrahepatic cholestasis, or PFIC2. We are -- anyhow, sorry. We are -- I'm happy to be here to talk about rare disease. Like Julie just said, a lot of what you all said this morning certainly resonated with us. One of the topics was, you know, sleep disorder, or patient care due to lack of sleep, so that definitely hit home. I also sit on the board of directors for the American Liver Foundation in Greater New York. Thank you.

MS. CHITTOORAN: Thank you, Michael. Monica?

MS. WELDON: I'm Monica Weldon, and I am the mother of five children. I'm married to my husband Chris. My children, I should start, I guess, with my oldest three: Hailey, Taylor and Sawyer. They are my three adult children. Started over and I have twins, 11-year-old twins next week, and one of my twins, Beckett, has a condition called SYNGAP1, and this is a neurological disorder, developmental disorder that causes intellectual disability. It is also an epilepsy gene or condition, where he has absence seizures and it is also an autism gene, where we struggle, of course, with the behaviors, sleep issues, a lot of sensory processing issues, muscle coordination problems. And, of course, now, as we move through to learning more about this disorder, because it's newly -- pretty much newly discovered, a lot of immune system problems, a lot of digestive problems. And I am also the president and CEO of the Bridge the Gap SYNGAP Education Research Foundation, who is focused on research for this disorder, and I appreciate the opportunity to come and share.

MS. CHITTOORAN: Thank you so much. Okay. So, I'm going to move into some of the questions. And I will address you by name, and then like before, my colleagues here at the FDA table may have some additional follow-up questions for you, so we'll make sure that we pause and have that opportunity, and after that we'll move to the audience.

So, Julie, we'll start with you. So, I understand that you have some experience with both clinical trials and registries. I was wondering if you could tell us a little bit about both your experiences with those things?

MS. RASKIN: Sure. So, I have those experiences personally with my son, and also as the executive director of Congenital Hyperinsulinism International. And in terms of clinical trials, we -- when my son was born, there weren't any FDA clinical trials, but there were some -- well, they might have been FDA, but they were smaller, investigator-led trials. And we very much benefited from some activities like that that were at one of the leading centers in the world, the Children's Hospital Philadelphia, for treating congenital hyperinsulinism. My son basically could not get home from the hospital and start his life without clinical experimental protocol that included using two off-label medications in an off-label device. And so after some surgeries, we were able to go home on that kind of regime. So, that was an absolute godsend.

And through the years, through the work with CHI, for short, Congenital Hyperinsulinism International, I've had the opportunity to work with investigators, researchers and some biotech companies starting early in preclinical phases where we have an opportunity as a patient organization to share our experiences. And then moving forward with some work on the clinical trials themselves and developing protocols. So, that's clinical study. Did you want me to talk about registries?

MS. CHITTOORAN: Sure.

MS. RASKIN: Okay, great. So, as a community, our congenital hyperinsulinism community started a -- just an Excel spreadsheet, where we collected some information, natural history information about the condition, and that was done by a lovely colleague of mine, Isabel Calderon. And it was really a backbone, very important to our community in understanding how the condition affected others in our community and that helped us to benchmark sort of where we are and what was happening to our children. And that was our sort of launching pad. And then we wanted to go farther and develop a really -- a real patient registry with an institutional review board and with steering community members, professional scientists and researchers, and patient advocates from around the world to really guide this work. And so we did that and it took us years and years and years. We're the opposite of Monica. Very slow in our development, but with a very focused purpose to try and be as comprehensive as we could in creating it, and we went live in October. And then I've had the experience with Benjamin, my son, being part of that. And so that was extremely interesting, and to see the effect on him of sharing his data and what it meant to him to be part of that was very meaningful and compelling for him.

MS. CHITTOORAN: Thank you. So, what -- when you're going back to the clinical studies, so what factors did you consider when deciding to participate in that?

MS. RASKIN: Well, as I said, this disease was such a global insult to the family. My son was always just a love, just delightful, and we adored him. And he brought us so much happiness even in the depths of our depression and grief over the disease. But we were really desperate, and there was no way to go home without participating. And we, you know, in terms of -- we were already in a hospital. We were already cycling through potential different treatment possibilities, and so it wasn't even in our mind that this was somewhat experimental, because everything seemed kind of experimental. There was no treatment. So, our biggest consideration really was listening to the professionals, and we were so lucky that CHOP had been studying and caring for patients with this disease for already a pretty long time, even though it was so rare. And so we really trusted in them in terms of deciding to do this, but over time, fast-forward to know, and my son was in -- he traded his rare disease for a common disease, because his pancreas was removed. So, he went from having hyperinsulinism to being diabetic. And so he had an opportunity to participate in a trial that was a pilot study also at CHOP, and for the artificial pancreas. And it was an incredible experience for him to be able to give back to science and to be part of something that could really be life-changing for him in the future.

He had some disabilities because of the hyperinsulinism, and so one thing that I think is important to think about in clinical studies is how disability affects the ability to participate. Even if it's -- it's not about inclusion-exclusion, but just accessing the basics of being in a trial, and that's something maybe people want to get into later.

MS. CHITTOORAN: Thank you. Does anybody on the FDA panel have any questions they'd like to ask Julie? And I just want to remind you that when you're speaking, just make sure that the mic is close to your mouth so that everybody on the web, especially, can hear. Anybody from the FDA table? Any questions? Okay, we answered them all.

Okay, Michael, we'll move on to you. So, if you would tell us a little bit about your caregiver. So, will you talk a little bit about your daughter's experience with clinical studies?

MR. BUSBY: Sure. So, for us at two months old, we knew something wasn't right with our daughter. She was consistently scratching herself, you know, pretty regularly. There wasn't a minute that went by, and no matter how hard we tried to cover her hands, she would get out of it. It was pretty incredible, actually. But she would tear her nose and tear her ears and tear her eyes up, and it was really baffling to us, because most people that would come over or talk to us family members, they would say, "Oh, she's probably colicky or gassy," or, "She's going to grow out of it."

At two months old we first went to the pediatrician and the pediatrician really, you know, he didn't have anything. And from there we saw every specialist you probably could imagine and not one person could tell us that there was something wrong with our daughter. It was actually pretty incredible. We didn't sleep. She scratched herself all night long. We couldn't put her in a bed. People talk about co-sleeping; that didn't work. It was pretty incredible to watch a baby scratch herself legitimately 24 hours a day. She wasn't jaundiced, she wasn't anything that you would think of. She just scratched.

So, fast-forward, we saw numerous doctors at about 13 or 14 months old. It kind of just went away on its own. It was very strange. And she slept, and it was very new, and we were waiting for something else to happen, because something just didn't seem right. And so we said maybe everybody is right; maybe she just is colicky.

Twenty-four months old, it was incredible that it came back and even worse than it was before. At that point, we had already seen about 12 different specialists and nobody could really understand what it was. We went back to a pediatric dermatologist, and this is kind of -- and I talk about this and it really was that aha moment that was a complete accident. And the dermatologist said this is not derm-related, but I want to give you some type of medicine that will help her sleep. He prescribed her a drug, and on Thursday night we started giving that drug to her. On Saturday night I was in a wedding and I came back on late Saturday night, Sunday morning, and my daughter was as bright yellow as she could possibly be. It was actually incredible.

Thinking back to it, you know, we knew something wasn't right. To see where it wound up putting us, you know, it was almost satisfying that we found out that there's something not right. By the time we got to the doctor, they rushed us to Mount Sinai in Manhattan and we were told our daughter was in acute liver failure.

So, it's a lot. That's a lot to handle. She was just about two and a half years old at that point.

When we got through Mount Sinai and the doctors there, who had seen a lot of pediatric liver stuff or disease, they informed us that she had PFIC2. I didn't touch on this before, but PFIC2 is a genetic mutation within the liver that prevents the excretion of bile out of the liver. The bile winds up building up and thus gets into your bloodstream and body.

So, when we found out that there was something legitimately diagnosed here, it was kind of -- it was a relief and an "Oh, my God" moment at the same time. I read a lot. I recall that I read probably 20, 30 hours a day. And one of the things that I read was on clinicaltrials.gov, and there was nothing at that point available. You know, there was no trials, you know, drugs that just kind of limit the pruritus, but she was itchy just all the time. At the worst she had a 23 bilirubin. That is pretty yellow for being jaundiced. And her INR was extremely elevated, which her liver function was pretty bad.

You know, about a year after that we kept reading and reading, and ultimately on clinicaltrials.gov found a trial that was starting and in Phase 2 that basically offered a solution to getting bile through the system so that the itchiness or the pruritus would go down. And fortunately she has been in that trial since, I think it's been about four years now, and her bile acids are within range and she is functioning at a normal 8-year-old life. It's a pretty amazing experience, for sure.

MS. CHITTOORAN: Thank you. Thank you so much for sharing that. When you -- so, when you mentioned that you initially saw the trial on clinicaltrials.gov, where there things that you considered in terms of whether or not to join that clinical trial?

MR. BUSBY: So, for my family, when you're faced with the -- and much like everybody. You know, when you're faced with the decision of the end result is a transplant, you kind of look at every solution before you have to get to that decision. For us, it just seemed -- to me it seemed unreasonable that there was not some type of medication that could help this, or at least prolong it to get to me not making a decision at two years old or three years old to have my daughter liver transplanted. And just to kind of going back to how far we would have gone, I would have gone all the way to that point of transplant to try something. You know, and we were told very specifically that there was no guarantees and side effects, and so forth. And fortunately for us, the side effects are minimal and she's doing really well.

MS. CHITTOORAN: So, if you're sort of searching for clinical trials in general, including the one that you already were doing, was there anything, or is there anything that you might see that might make you less willing to consider being a part of a clinical trial, whether that's time commitment or distance from your home? Is there anything that you could identify that might make you less willing to consider?

MR. BUSBY: No. And I'll back that up by saying that we currently, much like Julie, travel from Long Island, New York to Children's Hospital in Philadelphia on a regular basis for that treatment. And I would have gone to California. Oh, yeah, I would have gone anywhere. It would not have stopped us, and fortunately Philadelphia is a three-hour trip, you know. And I look at that, to me there is nothing I would stop doing or say, oh, that's just too far or too much. I wouldn't.

MS. CHITTOORAN: Thank you. And the panel, I see, questions?

DR. MCCUNE: So, it sounds to me like the most critical thing for you at the time was really the itching. For the clinical trial, do you know what the endpoints are for the clinical trial?

MR. BUSBY: I do not. I do know what they are; I cannot recall right at this point. And I do know that without going into too much detail, I see that there's a lot of secondary endpoints that have been met, but not the primary.

DR. MCCUNE: And I wasn't -- was itching a primary endpoint? I guess because we see a lot of endpoints that -- and itching, we hear a lot about this, but not necessarily that it's a primary endpoint. That's all I was getting at.

MR. BUSBY: Yes. The itching for this

specific one was the primary endpoint.

DR. SILVERSTEIN: I wanted to follow up on Dr. McCune's comment, and I think it's really important. This is more of a statement as opposed to a question. But I get from all three of you who are up here and those who were here before that you're very, very intelligent, well-informed persons. But not everybody out there in the world is as informative as I think many of you. You may be more of a selected group. If you come to this meeting you're very engaged in all the aspects of your children's care and the care of other children who have similar diseases. But I think it's important when you're considering putting your child in a clinical trial, is to consider exactly what Dr. McCune is saying, what are the endpoints? So, basically, what are they trying to show? What are they trying to assess as an outcome of the study? And so if your child, as in your child's situation, the itching was the most problematic part of her disease at that time, you would want to find something where they're addressing that particular outcome. That doesn't mean that they don't -- if the outcome of that endpoint is not achieved in the trial that your child may not benefit from that, because the outcome is a general result. But it's important to know when you look on clinicaltrials.gov, and I think also when you talk to your child's physician is, what problems are being addressed in the trial, and is that appropriate for your child's problem? Because disease may have various symptoms and it depends what you're trying to achieve with that trial.

So, being in a clinical trial is only useful if it is appropriate for your child. We talked about the preferences of the family and of the child especially, if the child is the one with the disease, and to try to match it together. Because there's a desperation to try and get yourself or a child into a clinical trial, which I can only understand through patients I've had and friends I've had who have had children who have diseases. But at the same time you want to make sure it matches well so that you're giving your child the best chance to have the symptom relieved that needs to be relieved. And is that how you guys approached it, you all approached it? I'm sorry, I'm from New York; we say guys. Is that how you all approached it? How did you figure out which trial? What got you to that point where you can say this is the right trial for my child, or --

MS. RASKIN: So, with congenital hyperinsulinism, we deal with a lot of the issues that are common to many rare diseases, but for us the main thing is to be able to live in the world without being hooked up to sugar 24 hours a day. So, the main -- the main thinking that goes around that, yeah, it's definitely considering the endpoint, which can be a variety of different things to get you to that goal, which is to live in, really, the least restrictive environment, hopefully home, and to have a life that is not tethered to being connected to a pump that gives you sugar. Also, to preserve your organs, you know, to keep your -- to keep your pancreas so that you can lead as normal a life and not develop another disease. So, that's, you know, kind of dicey as an endpoint, but it's a goal. So, it's really looking at the very central issue. That's where we are, yeah.

MS. CHITTOORAN: Thank you.

MR. BUSBY: And just to add to what Julie had said there, for PFIC2 patients, pruritus is an all-day event, and so failure to thrive, you know, the open wounds become an issue. So, when we were considering trials, fortunately/unfortunately, depending on how you look at it, there was only one. So, fortunately, it was specific to pruritus, and if you can take away the major symptom, right, then you can prolong the disease until there is a better, you know, genetic advancement.

MS. CHITTOORAN: Thank you. Okay, let's move to Monica. You've been waiting patiently, so thank you. So, you started your own registry. So, can you tell us a little bit about that and sort of why -- like, how and why you got involved with that?

MS. WELDON: Well, I started out, I'll give you a brief synopsis of my son's story. It kind of was similar to yours. And you notice when they're young infants and they're not progressing the way they need, and we knew that Beckett was not progressing the way he should at four months -- not sitting up in comparison to his twin sister Piper, and noticed different things along with him. And, of course, after having five children, I knew that there was something wrong with him not being able to walk within the normal range and meet his milestones.

So, we had -- you know, fast-forward into a year later, where I thought he was having seizures and, of course, went through -- I think we went through about 19 different specialists -- four neurologists, two pediatricians, geneticist, psychs, you name it, we've seen, I think, everyone, everybody at Texas Children's Hospital knows me, I think, now.

But fast-forward, we finally ended up getting the genetics and he was diagnosed at the age of 4. And so when we had gone to the genetics doctor and he handed me one paper that had been written on this -- you know, written about this disorder, SYNGAP1, saying it just caused intellectual disability. We didn't even know at the time it was an epilepsy gene, or a gene that caused a multitude of different types of epilepsy. And so I knew then that -- I remember looking at my geneticist and said, "Is this it?" And he goes, "That's all we have." And I said, "Well, are there any others?" And he said, "Well, we only know of about five others in literature, and he's No. 6." And I said, "Oh, wow, okay," just kind of sitting there in shock and feeling probably the most alone I've ever felt. Drove home. I think it took me about two days to process and realized I couldn't live -- I could not allow my child to continue living the quality of life he was living with the sensory processing -- we didn't know at the time he was having seizures with the behavior problems and things like that. I had to do something.

And so I started the organization and we found, of course, a group of people in between by the time I started on Facebook, started out with three families on Facebook. And that grew into the organization, and within the first year, after getting involved with the rare diseases community, I realized everything is revolving around data, and I had to educate myself on the drug development process. And so I took a shot at writing my very first grant. I taught school for 23 years and my background was science, so I knew there was something there. Ended up winning one of the FDA pilot program registries through the National Organization of Rare Disorders, which has been up and running for two and a half years now, and it was a lifesaver for our organization. Launched at Christmas Day. That as the best Christmas present anybody could ever have, because with that registry we ended up finding trends. We found that SYNGAP1 is the gene, that mechanism that controls sensory processing in our patient community, possibly overlapping into other autism communities as well. And I just realized that watching my own son and the symptoms that he had at home, and reading through the trends, of course, on our social media, that we needed to start asking these questions under an IRB-approved, organized way of collecting this data.

And that brought us to our new finding with the scientist who used our data to find our very first biomarker that was just published on Friday this last week. And it has just been phenomenal, and those types of things has motivated our community, those results, to showing them how the data and how these -- and we're not in a clinical trial right now. I'm shooting for that. I'm going to get there with our group, I'm bound and determined. But on a side, the clinical studies that we are involved in, that we have set up with our researchers, and gathering all those scientists together, basically pleading and begging. I think I begged Dr. Jimmy Holder, which I love him to death. He's at Texas Children's, and he goes, "Okay, I'll study." No, he was excited to come and study with us, but he was our first clinician ever to study SYNGAP1. And being a part -- involving these scientists and these clinician researchers in on our disorder changed the game for us. And so now we're in these clinical studies to help find more biomarkers and more clinical endpoints, because you made a really good point that I didn't think about is, what is going to be primary for us? And we're only going to get that from the patient community, which we have to prioritize. What symptom do we want to treat? And, of course, seizures is probably our primary. But then we have behavior, then we have sleep, then we have all these different things. And how are we going to incorporate and measure those endpoints and get those biomarkers? And the only way to do it is through data and through our registry. And I hope I didn't talk too long and I hope I answered your question.

MS. CHITTOORAN: No, you did. Are there any other factors -- you mentioned you are working on trying to get the clinical trials started. So, are there other factors that you are considering when doing so?

MS. WELDON: Well, I think right now, the biggest thing that -- time is everything, right? And we have to accelerate, and we have to accelerate in a fashion that makes sense and that's strategic. And, of course, educating your community is one on the drug development process. I think the biggest thing for us is we're spread out everywhere. We're all over the world. I think that organizations like our organization and the other patient community organizations that are out there, I think it's important to help your families eliminate some of the challenges, like travel, and offering -- you know, we're going to start raising money for travel stipends. We've already provided some for some of our

European families to get to clinical study in Europe. And I truly believe that all that tied together, and it's not just about policy, driving policy and legislation. It's not just about advocacy and spread awareness, but you also -- in parallel with all of that, you've got all these gears that you need to focus on, and I think that as an organization, you need to try to help create protocols, like with our gait study that we're doing at Texas Children's right now. All of those are to look for these endpoints, and we want as many families to be involved with those pilot programs as possible so that we know exactly how to design this clinical trial. Because, like most of you know, 95% of all clinical trials fail. Why? Why? Because, well, participation, retaining your patients, but also some of the clinical designs suck. I mean, I don't mean to be blunt, but, you know, I'm from Texas, I'm blunt, so I just speak my mind. And that's because the patient voice wasn't included on that. And I believe that real world data, along with the clinical data and all of the -- all of that has to tie in together, and if you're not designing a trial to make sure it is waterproof, you're setting yourself up for failure. And I'd rather have a 50/50 chance than a 5% of it succeeding.

And so I think all of these things, it's going to be a complicated mess trying to get through all those challenges. I personally believe that if you strategically plan it out right, it can be done, and I think that we can change that number of 95% failure right to at least a 50/50. And call me, like, out of the world like crazy, but I think it can be done, but I think people have to be onboard to do it, and I think educating your patient population is critical in that. Because I would, I'd fly. I would move hell, high water, snow, sleet, wherever. Like I said, if I can't get it done and I die, somebody's going to get haunted until it does get done, because I would do anything for -- and all of you would -- for yourself and for the love of your children. You don't want to see them suffer. You don't want to see your loved ones suffer. And I think that is the motivation; we just have to help remove some of those -- some of the most obvious barriers, like travel.

And then also educating on side effects and -- because it is scary. You know, I pray we have gene therapy, but then I'm scared to death that day comes and I'm sitting there with my child in a chair ready to take an injection, or go through a surgery, where the only way it can be administered is through intracranial, you know, gene therapy, and then it maybe not working.

So, I think we have to put realistic expectations out there, because I know the desperation. These families are desperate. But also you have to not necessarily take the emotion out of it, but just be a little bit more realistic about educating them on these things, because they're lost. They don't understand, and that's one of my goals personally as an organization leader is to try to educate these families on why it's important to take every little bitty step, because you can't eat an elephant all at once; you've got to eat an elephant a bite at a time and you've got to do it right.

MS. CHITTOORAN: Well, thank you very much. So, before I move into the audience and expand this conversation to you all, I just want to check. Does anybody on the FDA table have any questions before we move on?

MS. WITTEN: I have a question.

MS. CHITTOORAN: Sure.

MS. WITTEN: Thank you so much for this story. It's just -- it definitely was you and your journey. I have a question. You started, your child was diagnosed with this disease, well, just practically you were No. 4, right? Oh, No. 6, and it's a very difficult diagnosis to make. How did you put this community together? How did you find these people? And do they have the same mutation, or they have the same symptoms?

MS. WELDON: Well, it all started, I guess, if you've ever been to Houston, just like in DC, traffic is horrible. So, I'm stuck in traffic on my way home and I realized I was alone in the world, but I knew, I knew that he wasn't the only one. There had to be more. I mean, you've got 8 billion people on this planet; what are the chances of him being the only one? And I've heard of more even ultra-rare disorders, but I had to -- how I processed is I started to blog. And I started to actually track my own natural history of my son's symptoms and his and own lives dealing with this. And I started putting, you know, the hashtag thing was the -- I don't know what people did before social media and hashtags. But that's how, you know, finding -- actually, I didn't go out finding anyone; they found me. They put in, I guess, in search SYNGAP1, and then all of a sudden, I guess six months later, after I was blogging and just praying that something had to change, she reached out. And I think we stayed on the phone until 2:00 or 3:00 -- it was 3 a.m., I know, Eastern. It was 2 a.m. Central, but we stayed on the phone for about two or three hours talking about our kids, and we were, like, I think I've found my child's you know, boyfriend/girlfriend, because, you know, she was a little girl and my son was, you know, my son. And we're like, "We're not alone anymore." "Oh, you don't sleep, either?" "Yeah, okay." You know, it was crazy. And she goes, "Well, you know I know of one other person," and I was like, "Can you contact her?" And then we said, okay, well, let's do the Facebook group thing. Well, there's only three of us. I said, "Well, let's do it anyway."

And then I started a page an open page, and I started researching all of the papers I could find. I also found a lot of mouse model data, but no human data. But I posted it anyway, because then people started going, oh, well, you know, and it snowballed. And so not all of the -- we have two -- I know that there are right now in one of the databases here in the United States -- I can't remember all of the acronyms, but it's -- I think we have 262 different SYNGAP1 variants. I know that we currently have about 209 registrants in our database. I know that we have close to about 350 families within our Facebook group. Not all of them participate in the research, and I'm trying to coerce them to do that because we're such a small population. And that's when I just took a leap of faith and quit my job teaching and went into this full time and started just telling my story. Anybody who would listen. And the people out in the audience who know me, know I never shut up. You can probably tell right now.

MS. CHITTOORAN: Thank you very much to our panel. So, I want to hear from those of you in the audience who are patients and caregivers, and maybe hear from somebody who didn't get to speak last time. I see one hand here, if you would like to start. So, just curious, just in general, just before we get to you, just a show of hands who has participated in a clinical trial before, clinical study? Okay. Okay, so let's start with you, if you wouldn't mind sharing your experience and what sort of factors you considers in deciding to do so?

MR. LACEY: Sure. My name is Patrick Lacey. I'm with Beat Nb, a nonprofit in Boston. My son was diagnosed with neuroblastoma -- it's a pediatric cancer -- as a child, and he enrolled in probably nine or 10 different clinical trials, Phase 1s and Phase 2s. I founded the nonprofit and we've funded probably 18 clinical trials at this point. And what I've discovered first as a father searching for clinical trial options, hoping to save my child, I discovered a lot of things about study design that I would change if I had the power to do so. And one of those is the patient voice, as many people have mentioned.

Some of these trials are designed in a perfect way that isn't necessarily what patients would want to enroll on. It doesn't necessarily take into account, if you're looking at the preclinical data or the Phase 1 or Phase 2 adult data, safety data, a Phase 1 dose escalation 3 by 3 design study starts at a much lower dose than was effective in adults. So, why am I going to put my kid in that first cohort? It makes no sense -- single agent, low-dose drug. So, those types of studies.

The idea of randomizing versus maybe using historical control in the disease is fairly well understood. That's something that's very strong to me in a belief that maybe randomizing isn't the best choice.

Looking at travel considerations, cost. You know, everyone in this room is here for a reason -- they're passionate, they have the desire to help, and we have the ability. And as you alluded to earlier, not everyone has that same capacity to either attend these meetings or to search for those clinical trial options. So, having clinical trial options that are available close to home, that travel and losing a job and doing all these other commitments makes it challenging for families to access clinical trials. So, having them available in regional locations is really important as well so that families, if they want to make that choice and they think it's a good study, they're not precluded from doing so because they have to travel halfway across the country and make sacrifices that would be impossible for some families to do.

So, those are the things that I've seen in terms of clinical trial and decision-making for our own choices that kind of influenced the clinical trials that we enrolled my son on, and also our involvement in a research consortium, and having a voice from the patient side on how those studies are designed. Because at the end of the day, for me, I think enrollment tells the story.

When you see a clinical trial consortium that's enrolling patients, patients are traveling from other countries and all over the globe to get on those studies, that's because of great trial design. And that's because of trials that are putting the patient and their outcome, both of those things, and the questions that are asked in the study, those all-important considerations, and melding all those together in such a manner that you address all of those needs, is something that I find to be critically important going forward in helping all these patients.

And before I give the microphone up, I just want to thank you to the panel and the earlier panel for sharing your stories.

MS. CHITTOORAN: Thank you. Anyone else? I see a hand here.

MS. SHELTON: Thank you. So, my name is Deborah Shelton, and I'm here on behalf of the ACPMP Research Foundation, which is a research foundation for patients and their caregivers with appendix cancer and pseudomyxoma peritonei, which is a very rare and lethal form of cancer, effects about one to two people per million.

So, thank you very much. This meeting has been just really informative for me. I'm new to the patient advocacy world. My spouse was diagnosed with ACPMP about six months ago. I'm an FDA regulatory lawyer by day, by training, and so now I'm trying to kind of use my skills to do some patient advocacy work.

This question kind of channeling our patient constituents that I work with. We have a Facebook group of about 3,200 patients, and the first thing that comes to my mind when I see this question is how many of our patients would love the luxury of being able to talk about these factors. Right now, unfortunately, they don't, and I just kind of have a quick list that I was brainstorming on, kind of channeling patients and caregivers that I talk to on a regular basis, what would they say? What are the reasons for that?

And so one of the reasons is eligibility criteria, which I've heard a lot of discussion about, is very, very narrow. And when we're talking about randomized clinical trials, that has its own set of issues. Some of the eligibility criteria, just for example, a big one is to do with the dosage form. So, a lot of our patients have small bowel obstruction as a result of the appendix cancer, which essentially produces mucinous tumors throughout the abdomen and just compresses the digestive system, compresses the lungs. But with a small bowel obstruction, so many of these trials are for immunotherapies and are capsules, and so that's an exclusion criteria. Even if the patient wanted to, could not participate because they just can't swallow and have bioavailability issues.

A huge issue there with eligibility criteria is that for appendix cancer, the trials, most of these are not focused on appendix cancer specifically, but rather the tumor agnostic clinical trials with all the fantastic immunotherapies coming down the pike. The problem there is you have to have genomic sequencing, and we've got patients who are having real issues getting insurance to cover that genomic sequencing, which is quite, quite expensive. And often the clinical trials are designed that you have to come in the door with those sequencing results in hand. So, that's a real problem.

Very quickly, just a couple of the other big problems. The distance, the frequency. Would love to have more remote monitoring, more regional. You know, I have to tell you that when my spouse was diagnosed, and I knew it at the time, but, boy, do I know it now more than ever, we are so privileged that we could go and search and talk to specialists all across the country and pick and choose who we wanted to treat my spouse. But the reality of it is, most patients do not have that luxury. Boy, they have the passion. They'd travel to the ends of the earth for their loved ones, but they can't. They have to work, they have financial constraints. I'm working with a Medicaid patient now whose daughter is dying. Probably within the next couple of months she'll be gone if she can't get into a clinical trial. But she's on Medicaid, and so she's really bootstrapped and it's heartbreaking.

MS. CHITTOORAN: Thank you.

MS. SHELTON: It gets me emotional. Just last but not least, the real shocker of the reason for why our patients are having problems with clinical trial is they have no knowledge of them. Their doctors are not talking to them about them unless they're clinical trials at their own institution, and even then it's a longshot. And, you know, I sat in with a patient and they were told, "Just go to clinicaltrials.gov." I'm a lawyer. I helped with the legislation that created clinicaltrials.gov. It's difficult for me to navigate, and so to tell some of these patients, just go do that, especially when you're searching for biomarkers and whatnot, it's just a real challenge. Thanks for listening.

MS. CHITTOORAN: Thank you. Thank you. Wendy, I just want to go to you. Are there folks on the web that have participated in clinical trials, and what factors were they considering when deciding to do so?

MS. SLAVIT: Yeah, so we've actually heard a lot of the same things that people have been talking about in the room. The difficulty of the time commitment, that it can be disruptive. There are also concerns about the treatment being conflicting with what the treatment regimen they are currently on. Also not knowing maybe what some of the side effects of some of the medications will be. A few people are concerned about being on the placebo and not getting the drug that's being tested. As a lot of people have mentioned, the location of the trial, and so just the cost of getting there. People have talked about the endpoints and really looking at the endpoints as a decision of whether they're going to participate or not.

Someone talked about remote support, which was just actually mentioned, so if you're involved in a trial that's not in your area, when you're not actually there for the trial and you're back home, being able to access information that you need for the trial.

People have also talked about wanting to see the data kind of in real time whenever they can. They also want to see an impact. And a few people also talked about gene therapy trials can be invasive, so that's a barrier to potentially participating.

MS. CHITTOORAN: Okay, thank you. So, just a show of hands. Has anybody here who is a patient or caregiver wanted to participate in a clinical trial and wasn't able to? Okay. So, I'd like to hear from a couple folks about that, if you wouldn't mind sharing. Do we have a mic coming up?

MARIE: Hi. Marie again. So, my daughter is 6, she has Prader-Willi syndrome. And I didn't mention before, I do also have a for-profit company called TREND Community. But all the clinical trials that are currently recruiting, the primary endpoint is hyperphagia, and though I think she might benefit with regards to some of the secondary endpoints, she's not in hyperphagia, so she doesn't qualify for any of the clinical trials.

MS. CHITTOORAN: Okay. I think the gentleman across -- do you want to share?

MR. HARTMAN: Hi. Eric Hartman again with the Choroideremia Research Foundation. I was in a natural history study for the selection for a Phase 3 for my eye disease, and the surgery involves a subretinal injection and you need to have a certain amount of elasticity in the retina to take the injection of the vector. And both the original principal investigator from England and the surgeon out in at the other institution here in the United

States, they both said they would do it, but they had serious concerns. And would I be willing to risk my one degree of central vision? I mean, I see you, I don't see you guys. But to risk what little I have became incredibly difficult for me, especially knowing there's a potential intravitreal delivery that may be in the offing. So, I chose not to risk it because of that, but I would have traveled anywhere for it.

MS. CHITTOORAN: Thank you. Anyone else? I saw a couple other hands. Hi. Go ahead.

LENNIE WOODS: Hi. My name is Lennie Woods. I'm with Sarascure.org. We are a patient advocacy group, but I'm also the mother of Sarah, and I feel like I've got a sister in Monica, because we were told my daughter was the only living one with clear cell sarcoma at the time. An interesting fact, there was another patient in the same hospital being seen by another doctor with a different pathologist. He found us, God bless social media and Facebook. And when we -- we didn't confront, but when we brought it to the attention of the hospital, Memorial Sloan Kettering, there were some very upset people. But there were papers being written on him and studies being done on my daughter, and no one was communicating. And we've since -- I mean, that's hurtful. We've since found 25 patients living and about 10 years of natural history data on a Facebook page, yes. It was a secret page, so it wasn't infiltrated by others, and I want to talk to you.

But we have problems with trials in that we're considered soft tissue sarcoma, and clear cell is extremely different. We're almost hurt by being called that. So, they want to throw us into trials for soft tissue sarcomas and they're never successful. And on papers, when you read papers and you try to out clear cell sarcoma patients, they're thrown in with other soft tissue sarcomas. And this is also a problem. We support other small groups, like epithelioid sarcoma, who are parents doing the same thing we are. So, there's a whole bunch of us out here with a lot of good information. But I will tell you, the people from the FDA should know, when we try to share information and talk to our doctors, we get the eye-roll, we get -- I mean, we are shut down. I call them the gatekeepers. They will not let us patients get beyond to make the change. So, I say I had to jump over them, but thank you.

MS. CHITTOORAN: Okay. So, I know we are very short on time here, but, Wendy, do you have anything from the web that you'd like to share with the group here in the room?

MS. SLAVIT: Nothing additional at this point.

MS. CHITTOORAN: Okay. Does our FDA table have any other questions for anybody in the audience at all? Sure.

DR. SILVERSTEIN: Yeah, I'm sorry to hear about your experience. As a physician, that's disappointing, obviously, but it's disappointing for all of us. Just the one comment, and the question, I think, focused on two different, very different aspects of getting patient data, clinical study and registry, and I think it's appropriate to put it in the same question. But I would also say that registry data is what we consider real world evidence, or real world data. Five years ago I don't think we put much stock into the value of registry data. I think nowadays at the FDA, especially for children, where data is very, very hard to generate under the best of circumstances, we really do take seriously registered data. As a reviewer myself, on several applications I've accepted registry data as the proof either as a control group or whatever. So, I would encourage everybody, especially those that are here and on the phone, to consider entering your child or your own data into registries. And if you need to, I'm sure Monica would be able to show you how to basically just Google "registry" and put in -- and I'll bet you'll find somebody who will get you some information about how to do it. Because that data, even if it's just as a control group, can be very, very useful to help assess whether an intervention, a device or a drug is beneficial.

So, I'm just curious, how many of you here either entered your own or your child's data into a registry over the last 10 years? That's great. For those who didn't raise your hand, try every way you possibly can to connect with people on social media. I'm not a social media person myself, but connect with people. I'll bet if I had a situation like yours and I needed to, I would become a social media person tomorrow. But try to use that, because it's extremely important. And I'm speaking from the device world -- we do look at registry data very differently than we did a few years ago. We see the value in it, especially for rare diseases, which includes a lot of pediatric diseases. So, it's a small pitch, but I'm glad a lot of you are doing it.

MS. CHITTOORAN: Thank you so much. And I just want to thank our panel for sharing so much, such personal experiences and personal stories, and to the audience as well. Thank you so much for doing so, and the folks on the web. Recognize it's not always easy to talk about things that hit so close to our heart. But thank you so much for that, and if you didn't get to finish your thoughts or share, we, again, I know I sound like a broken record, but I encourage you to please submit those comments to the docket so we can capture your perspective that way.

So, I just want to turn over to Andrea, who is going to be moving to the next portion of the meeting, which is the open public hearing. Thank you so much.

MS. FURIA-HELMS: Okay. Thank you all so much. I think it is so important to hear your stories and experiences, and I think it's been a really, really helpful meeting today, to hear those situations. We are now going into the open public comment portion of the meeting. So, today we have registered speakers, and each of them will have two minutes to speak. If a speaker finishes early, we intend to move on to the next speaker. We will call each speaker by name. When it is your turn and if you are able, please approach the microphone at the middle of the room for your comments, right here at the front in the middle aisle. Otherwise, raise your hand when your name is called and someone will bring the hand-held microphone to you for your comments.

For transparency purposes, again, we ask, please disclose if you are affiliated with an organization or if your travel has been funded, or if you have significant financial interest in rare disease medical product development. As you are speaking, you will notice that there will be a timer and lights to guide you. The light will indicate you can begin speaking, when it is green. It will turn yellow when you have 30 seconds left in your time, and the timer will turn red when your time has come to an end. If you have not concluded your remarks at the end of the allotted time, I will ask you to do so, gently. As a reminder, you also have the option to submit comments to the docket, which will remain open until May 30th. You can find additional information about this in the federal registered notice. So, with that, let's get started with the first speaker. And I'm calling up the first speaker, who is Kristin Moro (ph).

MS. MORO: Hi. I'm very happy to be here today. My name is Kristin Moro, and our daughter Anna is 13 years old and was diagnosed with Friedreich's ataxia, the same disorder as Caroline on panel 1. She -- I'm going to speak today about her participation in clinical trials and how it's affected our family.

I guess four years ago, when she was diagnosed at age 9, we were noticing that her symptoms of fatigue were minimal at that point, but upon her diagnosis realizing that she would lose mobility, there was risk of speech and vision loss, scoliosis, cardiomyopathy, potential diabetes. We were very eager to participate in any clinical trial.

On her 10th birthday I was on the phone, and the only place that was open to her was Iowa or UCLA, and we were in Baltimore and California sounded more fun. So, we got on a plan, but we were aware from the beginning that it would be nine trips within the year. And I have to say we were taken care of so well there. Our travel was paid for, hotel stay was paid for, car while we were there. So -- and we had a great time. But the biomarkers at the end, you know, she does experience -- you know, her handwriting has decreased, so looking at the clinical trials and what the endpoints were was a concern just with what we -- with what was the end result and whether that was a good determination of what was successful.

MS. FURIA-HELMS: Thank you so much. Our next speaker is Daniel Campian.

MR. CAMPIAN: Good afternoon. Thank you. My name is Dan Campian. I am an account management director with IQVIA, a human data science company, and for the past 10 years I've worked with patient advocates and medical societies to build patient registries. The registry collects real world information about patient symptoms and treatments and care experience, either directly from patients and/or with their doctors. My colleagues and I submitted comments to the FDA a couple weeks ago about this meeting, and based on those comments I have one plea and a couple of questions.

The plea is for cooperation. It is spelled out in our recent whitepaper that we submitted, Registries for Rare Diseases, a foundation for multi-arm, multi-company trials. By working together, rare disease stakeholders have an opportunity to create broad-based registries that share common technology platform and collect data to address all their needs. The toughest challenge for these partnerships is not finding a multi-tenant technology platform, but getting people to cooperate, to agree on common data definitions and to use a common data hub rather than setting up separate registries for their natural history studies, quality improvement projects, post-market studies, or other projects.

The Cystic Fibrosis Foundation and the Muscular Dystrophy Association are outstanding examples of nonprofit groups that are successfully bringing together their communities around these multi-stakeholder registries.

So, in terms of today's discussion, thank you all for your comments. The two questions to keep focused on are, if you're going to invest your time to push -- to submit data for yourself or a loved one to a registry, what kinds of information or analyses do you want to get back from those registries in order to keep feeding that and to encourage others to do so? And, second, would you be willing to submit scientifically validated questionnaires regarding your experience of care? So, those are the two things that we're thinking about when we're designing registries. Thank you.

MS. FURIA-HELMS: Thank you so much. The next speaker is Rachel Sher.

MS. SHER: Good afternoon. I'm Rachel Sher, Vice President for Policy and Regulatory Affairs at NORD, the National Organization for Rare Disorders. For those of you who don't know, NORD was founded in 1983, and we represent more than 290 individual rare disease patient groups. We have been focused this whole time on the identification, treatment and cure of rare disorders through programs of education, advocacy, research and patient services. We really today just want to thank FDA for holding this meeting and for its leadership on these issues.

As many of you know, this meeting is coming on the heels of several other meetings that FDA has held in which it's really put the patient voice front and center in the drug development process, and in FDA's own thinking about the regulatory process, and we just fully agree with that approach.

We also thank FDA for its continued flexibility with respect to its oversight of medical products in the rare disease space, including looking at alternative sources of data, like registry data, like we've been talking about.

As you may know, NORD has started a registry program for rare diseases. It's called the IAMRARE, natural history patient registry program. It is a very easy to use program for patients and providers and patient organizations to create quality data. More information is on NORD's website, the rarediseases.org, and we encourage you to check it out. We have several programs already up and running for various disease sates, and are always happy to work with more programs.

I also want to just give a shout out to the Patient Affairs staff here at FDA, who has been doing an incredible job. They made the plea to be in touch with them and in our experience they've had an open door and we would just encourage everyone to continue to work with them closely, too.

In short, I won't take the full two minutes, just want to say we stand ready to continue to be a partner to FDA and just thank you for holding this meeting and for your leadership. Thank you.

MS. FURIA-HELMS: Thank you so much. And I apologize if I mess up people's names. So, don't take it personally; I'm doing my best. Next speaker is Robyn Himick.

MS. HIMICK: Hi. My name is Robyn Himick, and I am here to speak on behalf of the Amyloidosis Consortium, also known as ARC. ARC is a patient-led organization with the vision of accelerating the development of and the access to new treatment through the collaboration and innovation. For those of you who may not know, amyloidosis is a term of a group of rare diseases in which the abnormal proteins deposit its amyloid into tissue and organs. It is progressive and fatal disease with currently no approved cure. Amyloidosis can develop as part of a genetic mutation that's passed on within families, or can develop during a person's lifetime for unknown reasons.

The diagnosis of amyloidosis is often delayed because the symptoms are so varied and the delays in diagnosis are uncommon. It can also be very challenging to find a specialist with the appropriate expertise, and seldomly are these conveniently located, which only adds to the additional stress and burden to the patients and their families.

In the past several months, the landscape of amyloidosis treatments have dramatically changed, and for the first time we've seen two new approved treatments for ATTR amyloidosis. While these treatments were recently approved, the struggle for accessibility and affordability has proven to be just as problematic, particularly for patients and families affected by the hereditary nature of the disease, since multiple members of a single family can be affected with the same disease complications and financial burdens.

Considering the new available treatments, ARC recently developed an online survey designed to obtain the perspective from patients and caregivers to understand the burden of the disease, the impact of quality of life, and the treatment perception. From the survey we learned that patients diagnosed more than five years ago struggled with the most burdensome symptoms of numbness and pain, dizziness and fatigue. These symptoms only left patients unable to engage in the basic activities of their daily lives with significantly impaired independence.

Amyloidosis, like many rare diseases, causes a high burden on patients and families, impacting all aspects of their life. In our surveys, patients reported that he greatest impact of the disease was in their work and professional life and financial wellbeing, whereas, caregivers reported their emotional wellbeing and relationships were most greatly impacted. The complex nature of amyloidosis coupled with the limited access to treatment and services means that caregivers are often the primary source of support and care for their loved ones, often leaving them to balance all of life's priorities and manage the wellbeing of their entire family. Thank you.

MS. FURIA-HELMS: Thank you very much. The next speaker is Jill Cisco.

MS. CISCO: Hi there. Jill Cisco with Acromegaly Community. I wanted to discuss just for a couple moments, you know, we have an online community, and although it sounds like some of the things that happen online, that they're open. We have a closed group that we interview every single person before we allow them in. We only allow medically approved documents to be posted. They have to be from accredited sites. You know, we try to educate our patients. Our last conference that we did, we held in concession with the Pituitary Society, because we try to put the correct information out to our patients.

One of the biggest complaints that we see worldwide with our patients is the fact of symptom control. And there's a couple clinical trials that are going on right now, and the main complaint that I hear from the patients is I've worked so hard to get my numbers within the normal range; I don't even want to take the chance of being a placebo patient. And I hope that you all will understand that. When you have a disease that dramatically affects your quality of life, in every aspect of your life, you don't want to have to take the chance of taking a placebo. And I think that is a huge dramatic thought process. It's not the travel, it's not anything else; it's the placebo that stops patients from going into these clinical trials.

MS. FURIA-HELMS: Thank you very much. The next speaker is Christina Hartman.

MS. HARTMAN: Hi. My name is Christina Hartman and I'm with the EveryLife Foundation for Rare Diseases. I have been in Washington for the past 20 years. I was hired to run policy and advocacy for the foundation following their move to Washington DC. I came to the foundation because my youngest daughter was recently diagnosed with a rare genetic disorder, NAA10, also known as Ogden in boys. The boys typically die in infancy and early childhood. Because it's an X-linked disorder, the girls live, of course with lots of health issues. We, too, have a Facebook group and the parents post their daughters' mutations on the group. We have a researcher, thankful, many organizations or disease groups don't, and he is currently looking for funding from the NIH to run the phenotypes of these girls. There's less than 100 of them that we know of in the world. We are currently seeking money from NIH. He got a good score on his NIH R35 recently, so fingers crossed.

But one of the challenges that I've seen -- you know, I've worked for HHS for the first third of my career in the Office of the Secretary, and there doesn't seem to be a ton of collaboration between NIH and FDA. And I would really like to see more of that. The other challenge that many folks in the rare disease community have, my daughter's group in addition, is we don't have any treatments. There are no clinical trials. Now, my daughter is not dying, so I'm very thankful for that, but many of the families and the children that I work with are. So, almost 95% of the rare disease community does not currently have an FDA-approved treatment. Some people have nothing; some are taking conditions -- taking medications off-label so they don't have the proper dosage, safety or efficacy information, and they often don't get insurance coverage for their drug. So, this is a major issue. The other major issue that we've seen is the lack of diagnosis, and without diagnosis, of course, you can have no treatment.

So, one of the things that EveryLife is doing is we are asking Congress for $1.5 million to do a burden study to demonstrate the true public health crisis of rare disease in the United States. And so this would be a comprehensive study that the National Academy of Medicine would do, and it would look not only at direct medical costs of rare diseases, but it would also look at the cost to caregivers and families, the comprehensive societal burden. And I hope that that would provide the justification necessary to put the resources behind this and to justify the collaboration across the Department of Health and Human Services, including FDA.

MS. FURIA-HELMS: Thank you very much. The next speaker is Shazia Ahmad.

MS. AHMAD: Hi. I'm Shazia Ahmad. I want to disclose I'm with UBC. UBC is a service provider, and my role there is providing -- working with sponsors and patient and stakeholder engagements specifically in the rare disease area. But I'm more here as a patient advocate. My daughter was diagnosed with Kawasaki disease at the age of 3. Thankfully, she recovered because she got the treatment in time. My question or really more statement is there really is more of a need for early education and awareness of rare diseases, especially in the medical community.

We were in a small area in Chattanooga, Tennessee when she was diagnosed, but we were very lucky because she was near a teaching hospital. My husband was a physician at the time doing his training. But, really, my statement is more what we can do more professionally, the CLOs, service providers, sponsors in raising education awareness and working with patient advocacy groups. Thank you.

MS. FURIA-HELMS: Thank you very much. And our next speaker is James Valentine.

MR. VALENTINE: Hi. Good afternoon and thank you, Andrea, and thank you FDA for putting on this fabulous meeting, and really tremendous gratitude for all of our patients and caregivers here today sharing their experiences and truly being brave. My name is James Valentine, and I'm an associate at Hyman, Phelps & McNamara. Prior to joining the firm I worked at FDA, actually as a patient liaison, and among other things helped implement the patient-focused drug development program.

In the past several years I've had the pleasure and opportunity to help plan and moderate 16 externally led patient-focused drug development meetings, four rare disease patient communities. Of those 16 meetings I was involved with, my colleague, Larry Bauer, and I, looked at the 11 published Voice of the Patient documents that summarize the findings of those meetings, and we want to share some of what we found for the theme of this meeting today.

So, some meetings identified issues common to most of the diseases, and others were unique to specific diseases. One of the overarching themes from all of the patient communities and consistent with what we have heard here today is the willingness of patients and caregivers with rare diseases to share their experiences and provide invaluable input into how their diseases impact their lives. Patients are the experts and can articulate what symptoms have the most impact, what kind of treatments are helping, and what amount of risk they are willing to tolerate in a new treatment.

All the rare diseases except one that we looked at shared the commonality affecting multiple body systems; however, every community was still able to identify one or two symptoms that most patients had that caused the most severe impact. Every disease has phenotypic variability with different symptom clusters and different levels of disease severity, and every rare disease has unmet medical need, and 8 out of 11 diseases cause premature death.

All the patients talked about impact on activities of daily living, including impact on school and work; all were progressive; all had mental health consequences, and all cause fatigue.

For future treatments, every community identified the desire to improve quality of life and to slow disease progression, and patients say that they're willing to tolerate some risk as there are potential life-impacting benefits.

What was unique to some meetings was the specific body symptoms and types of symptoms that were experienced. Some still had challenges related to early diagnosis; some communities identified challenges through the route of administration; and others stated that they were willing to participate in research to help others in the future.

So, in the near future we plan to provide a more detailed analysis of our observations from these 16 externally led meetings, including looking to themes that we heard today -- things like pain, speech impairment, sleep disorder, caregiver burden and more, and we will be sure to provide those to the docket. Thank you.

MS. FURIA-HELMS: Thank you very much. We have two additional slots open, so we are opening it up to anyone who would like to provide a two-minute comment at this time.

MS. YOUNG: Thank you. My name is Ni Young. My name is Ni Young. I congratulate FDA at this time, allow people to speak their own voices, but I have my own consideration. One is this type of disease, I need some professional to tell me is it preventable and how many from here are allowed to speak, but how many lost their loved ones? I suppose the statistics should be variable, and this is maybe the result of many call malpractice, and how are we going to train the physician to do a better job, or the government to have a better responsibility to supervise them, in a sense? Otherwise, the people's complaint should be documented. So, to count on physicians should be avoided.

And also I'm thinking the financial burden is a big, huge issue, and environmental -- the environment, people are adversely impacted, so should we ask the government to do a better job in this direction? Because currently other people are forced to be homeless, and if I'm in financial trouble, that should be very much the number one issue. The priority of our government is to protect people's life and protect people's properties, businesses, their home, their car. Currently, the government is part of the problem, because they rob people's home and life and the car and everything. So, we've got to ask FDA to do a better job, too. Thank you.

MS. FURIA-HELMS: Thank you very much. Any other takers? Okay, we have one more.

MR. FELDMAN: Hello. I'm David Feldman at the National Kidney Foundation. I want to thank FDA and especially the panelists for this wonderful meeting. I've had the opportunity to work with James

Valentine on two externally led, patient-focused drug development meetings, and one of the things that I've struggled with, and I believe that probably everybody in this room who is trying to improve clinical trial design has struggled with this. How do you get to the issue of risk-benefit? What do patients really think about this? And my problem is what question to ask to get that information? Because it's a very difficult issue to probe. So, I would like to suggest that the FDA have a meeting like this with patients specifically focused on the question, how do we get this information? How can we get it and use it better to design clinical trials. Thank you.

MS. FURIA-HELMS: Thank you very much. This concludes the open public comment period, and we appreciate and thank everyone for participating today, not only in the OPC, but also today in the audience, especially our panel members, the FDA panelists, the folks online. Thank you so much for participating today. And I just want to briefly thank the Patient Affairs staff for all your hard work, along with the Office of Orphan Products staff that has been really working really hard to get this meeting to be successful today, that I think we might have done a good job there. So, thank you all.

DR. MAYNARD: Thank you. So, I'm Janet Maynard. And on behalf of FDA, I'd like to thank all the speakers and everyone who attended today, both in the audience and on the web, for your participation. We greatly appreciate all that has been contributed to this meeting today.

This has been a very important meeting both for us at FDA, but for all of the stakeholders in drug development. I think for the patient advocacy groups, industry, for our research partners, I think we can all learn from what we have heard today.

So, recognizing that we do have differences, today I think we heard many commonalities, and I think where the commonalities that resonated most with me was the importance of using our voice. Also, something that resonated with me was something that Julie said about the global insult to the family, and really the significant impact that each rare disease has on both the patient and the family.

When we talked about some commonalities and symptoms, some of the commonalities I heard were related to fatigue, pain, communication impairment, difficulty with movement, sleep disorders, and seizures. These were some of the commonalities I heard. I also heard that life can be unpredictable and that it can be very difficult to plan when you have a rare disease and that that adds a lot of complexity to life in terms of thinking about how to get things done on a day-to-day basis, and saying true to the important things that you were trying to accomplish relating to school or work or family time.

Some commonalities I heard in terms of symptom management, I heard difficulties related to not having a treatment, when there's no treatment available at all for a rare disease, but I think we also heard the important balance that sometimes when there is a treatment available, that might not necessarily be the answer, either. That there may be significant side effects associated with that treatment that cause difficulties for patients and families.

For clinical trials, I really appreciated hearing about the complex decisions that these raise for patients and families. Also about the importance of data. I'm thinking about how we can use data to synergize rare disease product development.

This was a very informative meeting for all of us. I think we've heard today that the impact of rare diseases is enormous. The need for better products is really huge, also, and we look forward to incorporating what we have heard today as we continue to move forward with rare disease product development.

I wanted you to know that even though the meeting is over, that there is still opportunity to connect with FDA. So, you can see on the screen here that you can connect either with the Patient Affairs staff, or you can connect with the Office of Orphan Products Development, if you have any questions in follow-up from this meeting.

And as you have heard, we really encourage you to submit comments to the docket, which will remain open until May 30th. We appreciate all the feedback that we receive into the docket, especially as follow-up today, as you maybe think about additional issues or considerations that we didn't have time to address today.

So, I think your voices were definitely heard today and the need for therapeutic options is very clear. And we look forward to all working together to improve medical product development for rare diseases.

A few housekeeping items. So, you should have had on your seat when you came in a survey. We want to continue to improve our public meetings, so if you could please complete that survey, we would be greatly appreciative. If for some reason a survey has gotten misplaced, no fears; we should have additional surveys at the registration table. So, if you don't mind taking some time to fill out the survey to give us feedback. You can give it back to any of the FDA staff who has one of the badges, or you can drop it off at the registration table. And for folks who are attending via the web, you will be emailed the same survey that's being completed in the room.

A transcript of this meeting should be available within 30 days. And as I mentioned at the beginning, we will work on a meeting summary document, but we'll need to incorporate information from the docket, which will remain open until the end of May.

So, on that note, thank you again for everyone's participation today. We sincerely appreciate it, and we wish you safe travels. And on that note, I will close the meeting. Thank you.

[Applause.]

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