

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

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

JOB No.: 3156041

Job No. PA3156041

1	I N D E X	
2		Page
3	Opening Remarks (Janet Maynard)	3
4	Meeting Overview (Andrea Furia-Helms)	10
5	First Session	23
6	Susan Chittooran, Facilitator, Patient Affairs	
7	Andrea Furia-Helms, Patient Affairs	
8	Lucas Kemp, Office of New Drugs, CDER	
9	Susan McCune, Office of Pediatric Therapeutics	
10	Janet Maynard, Office of Orphan Products	
11	Douglas Silverstein, Renal Devices, CDRH	
12	Rachel Witten, Office of Tissue and Advanced	
13	Therapies, CBER	
14	Adrienne Shapiro (Sickle cell)	
15	Caroline Spencer (Friedreich's ataxia)	
16	Seth Rothberg (Huntington's disease)	
17	Remarks by Principal Deputy Commissioner and Acting	
18	Chief Information Officer, Dr. Amy Abernathy	81
19	Second Session	96
20	Andrea Furia-Helms, Facilitator, Patient Affairs	
21	Susan McCune, Office of Pediatric Therapeutics	
22	Janet Maynard, Office of Orphan Products	

1 Second Session (continued)

2 Douglas Silverstein, CDRH

3 Rachel Witten, Office of Tissue Advanced Therapies

4 Monica Weldon (SYNGAP1)

5 Julie Raskin (Congenital hyperinsulinism)

6 Michael Busby (PFIC)

7 Also Present:

8 Wendy Slavitt (Web facilitator)

9 Open Public Comment 142

10 Closing Remarks (Janet Maynard) 160

11

12

13

14

15

16

17

18

19

20

21

22

1 P R O C E E D I N G S

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

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

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

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

1 Rare diseases can be fatal and highly disabling with
2 significant impacts on patients and families.

3 Notably, it is estimated that about half of rare
4 diseases affect children. We recognize that there are
5 unmet needs for patients with rare diseases, as most
6 rare diseases do not have approved therapies. The
7 availability and access of safe and effective medical
8 products for patients with rare diseases is critically
9 important. With scientific advances, there are new
10 opportunities for the development of therapies for
11 rare diseases.

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

19 In fulfilling that task, the Office of Orphan
20 Products Development evaluates scientific and clinical
21 data submissions from sponsors to identify and
22 designate products as promising for rare diseases and

1 to further advance scientific development of such
2 promising medical products.

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

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

17 I would like to acknowledge and thank the
18 cross-agency collaboration that supported the planning
19 and organization of today's meeting. Each of us here
20 today has a unique perspective and are committed to
21 working together to achieve success. Developing a
22 treatment for a rare disease can present unique

1 challenges, such as the small number of individuals
2 affected and heterogeneous etiologies and
3 manifestations. While the differences between rare
4 diseases are critically important, it is also
5 important to assess commonalities to synergize product
6 development in rare diseases.

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

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

1 commonalities across a variety of rare diseases.

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

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

15 After this meeting we will take what we learn
16 and write a summary document. It will take us some
17 time to produce this document. The document will
18 consider the transcript and our notes from this
19 meeting, and the docket comments. We leave open the
20 docket after the meeting so we can get submissions of
21 information from people on the webcast, or other
22 things that may occur to people in the room or on the

1 web after they hear this meeting. We will put
2 together this information from the meeting and the
3 docket to develop a summary document. We hope that
4 the document will be extremely valuable to the various
5 stakeholders in product development. We hope to
6 capture as accurately as we can what we heard today
7 and what we read in the docket. This will serve as a
8 resource to the staff at FDA and sponsors who are
9 developing products for rare diseases.

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

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

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

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

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

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

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

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

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

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

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

1 overflow room you are in and follow the exit signs to
2 leave the building.

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

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

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

1 on the webcast.

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

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

19 For those of you in the overflow room, you
20 can write your comment on a notecard on your seat and
21 pass it to the end of the aisle, where someone will
22 collect it. For those on the webcast, please type

1 your comments into the chat feature in Adobe Connect.
2 We will periodically be checking in to see what our
3 remote attendees are sharing in the chat box. After
4 session one concludes, we are delighted that the
5 Principal Deputy Commissioner and Acting Chief
6 Information Officer, Dr. Amy Abernathy, will provide
7 remarks with us. We will have a break before we begin
8 session 2, and conclude the afternoon with the open
9 public comment period. So, some information about the
10 open public comment period. Say that 10 times fast.

11 We have time set aside for the open public
12 comment later this afternoon, and the session will
13 give anyone in the audience the opportunity to make
14 any comment. To participate in that, you would have
15 needed to sign up at the time you registered or sign
16 up today at the registration table. Participation is
17 first-come, first-served, and has accommodated up to
18 10 commenters. We are excited that we have so many
19 that were interested in the open public comment period
20 that the slots have already been filled up. The time
21 allowed for each speaker will be about two minutes
22 each. After the open public comment period, Janet

1 Maynard will provide some closing remarks.

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

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

14 Now, just for some rules of engagement for
15 today's discussion. Patients, caregivers and their
16 advocates are encouraged to sit near the front of the
17 room. FDA is here to listen to you and we -- it's not
18 about us; it really is about you today, so we
19 encourage you to contribute to the dialogue. Your
20 stories and experiences are what can move medical
21 progress forward. Because we really want to hear
22 about your experiences, we ask that if you have any

1 other FDA questions, please email Patient Affairs at
2 patientaffairs@fda.gov.

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

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

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

18 MS. SPENCER: Hi, I'm Caroline Spencer. I'm
19 a patient with Friedreich's ataxia. I am from
20 Cincinnati, Ohio. And for those of you who may not
21 familiar, Friedreich's ataxia, or FA, is a progressive
22 neurological disease. It's a degenerative

1 neuromuscular disease that leads to progressive loss
2 of ambulation or walking. It can also cause cardiac
3 problems, scoliosis, diabetes and other comorbid
4 difficulties.

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

19 MS. SHAPIRO: I'm Adrienne Shapiro. I am
20 fifth generation of mothers in my family to have a
21 child born with sickle cell disease. Sickle cell
22 disease is just that -- it's a disease where our red

1 blood cells, rather than being round, disk-shaped,
2 there's a large portion that become sickle-shaped,
3 which cause problems as you try to circulate through
4 the bone marrow, ending up in very painful episodes
5 and damage to major organs of the body. There is a
6 life expectancy here in the US of 45 years.
7 Throughout the world, children live less than five
8 years. And I have a nonprofit called Axis Advocacy,
9 and we advocate for people living with sickle cell
10 disease, particularly the adults.

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

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

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

1 in the Renal Devices branch.

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

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

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

20 And in closing, I want to thank everyone,
21 including our panelists, for participating today, and
22 I look forward to a very productive meeting. I'm now

1 going to turn it over to Susan Chittooran. Thank you.

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

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

21 So, we have designed this session as
22 interactive, and what I mean by that is I will be

1 posing questions first to our panel here, and then we
2 will be asking some questions back-and-forth. My FDA
3 colleagues here may have follow-up questions, and then
4 we will turn to you all in the room. We have patients
5 here, and we also have patients on the web as well.
6 My colleague here, Wendy -- Wendy, if you'd raise your
7 hand -- will be kind of filtering some of the stuff
8 that we're hearing online. So, she'll help us kind of
9 capture the patient and caregiver voice from online.
10 And then after that we'll go back to the panel. So,
11 we'll sort of take turns in terms of how we are doing
12 the discussion.

13 So, in order to best accommodate the most
14 number of speakers as we can, we just ask everybody to
15 please be mindful of their time in responding. Also,
16 if there are things you think about that you didn't
17 get to say here today, we do have a docket, as we
18 mentioned a couple of times, that's open until May
19 30th. So, we encourage you to utilize that if you're
20 in the room and on the web.

21 So, yeah, and then finally, just please, as
22 Andrea mentioned, please just be respectful of others

1 when speaking. Just recognize that people are talking
2 about personal experiences that may not be easy to
3 share. So, with that, I'll get started. We've
4 already done some introductions of our panel, so I
5 will start off by asking questions to our panel. And,
6 again, we may have some follow-up.

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

13 MS. SHAPIRO: The disease, the nature of the
14 disease basically prevents the flow of blood
15 throughout the body. So, that, sort of, if you think
16 of the terms if you were sort of gasping for air,
17 right, or drowning, or that pain that you get, right?
18 So, she experiences great, great pain within the bone
19 marrow and as a result has been on opioids since she
20 was two years old. So, I would say the pain. I think
21 also being anemic and having the lack of oxygen, the
22 fatigue. Fatigue is something that most researchers

1 initially, because the pain was so intense and acute,
2 it was a long time before the researchers realized
3 that fatigue, of course, was a major, major burden, to
4 the point where things like a remote feels very, very
5 heavy.

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

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

18 MS. SHAPIRO: Well, the pain, when they're
19 young, and we do have treatment protocols for when
20 you're young, so the experience with the disease is
21 very different as a young person. When they're young
22 they can go to the hospital, we get immediate

1 treatment, the pain is relieved; but as they get
2 older, due to the effects, right? So, as these blood
3 cells block in the capillary it forms scar tissue.
4 They have, by the time they're 18 years old, vascular
5 disease, they have lung disease, they have heart
6 disease, they have kidney disease. On the outside at
7 18, they might look 13, but have the body of, you
8 know, a 60-year-old. So, I guess it's the transition
9 (a) from being a child to being an adult who is not
10 really an adult, having to deal with advanced disease.

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

16 MS. SHAPIRO: Oh, well, there are all stages,
17 right, as there are stages of the pain, so you do
18 meditation, you do heat, you do massage. And then
19 there's this step up on the pain scale that you go
20 until you're actually -- when there is nothing that
21 you can do other than opioids, and that just sort of
22 masks it. We have a real problem, because as you do

1 that, of course, year after year after year, her
2 tolerance for the opioid has become higher and
3 therefore she needs larger dosages of it.

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

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

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

21 MS. SHAPIRO: What I want to say is this
22 about all of us, I think, sitting here. A diagnosis

1 of a rare disease is really a lifestyle, and becomes a
2 lifestyle start and stop. If you look at any of our
3 calendars, if you could, I'm sure you'll see where
4 even we'll plan out something and you never know what
5 you're going to be able to do from moment-to-moment
6 what known -- I'm going on vacation in three weeks.

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

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

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

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

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

8 MS. CHITTOORAN: Yeah?

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

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

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

21 MS. SHAPIRO: Yes, actually, we're very
22 active. I actually got into advocacy when gene

1 therapy became a possibility. We -- bone marrow
2 transplants were the only curative for us, but getting
3 a match for us is very rare, so gene therapy was it
4 for us. So, yes, we are very much involved in
5 clinical trials and gene therapy, and it is truly our
6 community's belief that gene therapy will lead to a
7 cure for us. Of course, until we get to the point
8 where we can do reconstructive therapies, the damage
9 to our bodies at whatever point won't be cured -- I
10 mean, won't be corrected. But we are very, very
11 interested and very involved in educating people and
12 getting them into research. But that's not going to
13 help us, yeah, at this point.

14 MS. WITTEN: Thank you.

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

1 future, what would you say that those are?

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

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

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

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

16 For me, it was touched on before, was the
17 point about, you know, living a normal life, and I
18 think for young people like myself, it's how do you
19 live that new normal life? How do you not just
20 transition in the child care, or from child care to
21 adult care, but transitioning into that future
22 planning? So, a lot of these things I have to think

1 about now is how do I build a romantic relationship,
2 family planning, career choices, and these are always
3 things that are on my mind and a lot of other young
4 people's minds of how to live that new lifestyle, but
5 also how do you plan your life for the future?

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

15 MR. ROTBERG: My mom was misdiagnosed with
16 major depression and bipolar, which, again, the mood
17 swings and depression were just symptoms of
18 Huntington's disease, so probably misdiagnosed for
19 about seven years. She was officially diagnosed when
20 I was 15, and so five years later I tested, but I was
21 definitely in denial because I felt like I lost out on
22 that normal childhood. And no one truly understood

1 what I was going through. I felt the isolation of not
2 really having anyone, especially my age, to be, like,
3 oh, yeah, I get what you're going through. And I kept
4 thinking about it, again, my future of how to plan for
5 what those next steps are, and that's kind of what
6 brought me to the decision of testing. But it was
7 definitely a very personal decision. Genetic testing
8 is very, you know, a very big decision in anyone's
9 life.

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

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

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

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

22 MR. KEMP: Hi. You mentioned the online

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

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

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

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

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

1 able to connect with one another helps improve that
2 overall quality of life.

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

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

19 And to touch on what Adrienne mentioned, it
20 really -- it takes a lot of planning to deal with both
21 the mobility issues and fatigue issues, to be able to
22 anticipate challenges and figure out how to get around

1 that, or to still do what I need to do in spite of
2 that.

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

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

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

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

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

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

21 MS. CHITTOORAN: Thank you.

22 MR. KEMP: I just had a quick question for

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

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

16 MS. CHITTOORAN: Thank you.

17 DR. MAYNARD: This is Janet Maynard. Maybe
18 just one housekeeping thing as we transition to the
19 audience. If folks can just remember to identify
20 themselves before speaking just for the
21 transcriptionist, just so we know who is speaking.
22 So, if people don't mind on the panel and the audience

1 as they transition, just to say your name before
2 speaking. Okay, thank you.

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

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

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

8 MS. HARTMAN: Hi, thank you. I'm Christina
9 Hartman and my daughter, Charlotte, has a rare genetic
10 disorder called NAA10. It's also known as Ogden's in
11 boys. And one of the things I wanted to add to the
12 list of difficulties is speech. So, one of the
13 challenges for a lot of folks with rare conditions is
14 being able to communicate. And my daughter Charlotte,
15 like many of the NAA10 girls, had a very difficult
16 time learning to walk. In fact, most of the girls are
17 still in wheelchairs, but I think in large part due to
18 really early and intense intervention, physical
19 therapy twice a week for a year, Charlotte started
20 walking at 2-1/2. However, we have not had the same
21 intervention in terms of speech, and so she really
22 struggles to communicate. You know, she can make a

1 few sounds and says "Da-da." She says "Mom" when
2 she's mad and has started saying, "Head, head," but
3 she'll be 3 this summer and that's about it. And so I
4 would say that that's a pretty big concern as well,
5 you know, for the future.

6 MS. CHITTOORAN: Okay, thank you. Yes?

7 LORIE: Hi. My first name is Lorie. My
8 sister had Lennox-Gastaut disease, and I have two
9 grandchildren, 1 and 3, with a rare genetic disorder
10 called MECP2 duplication syndrome. I've noticed from
11 having been a caretaker for my sister with Lennox-
12 Gastaut, and also from my grandchildren, a few
13 commonalities just in those two syndromes, and some of
14 the things that were already said with the fatigue.
15 One of the things that is a real big concern, I think,
16 for a lot is the blow to the system in terms of
17 immunity, because it makes the body so susceptible to
18 comorbid problems. I see Adrienne shaking her head.
19 And I think, Seth, you also mentioned having trouble
20 sometimes telling the differences, is it the disease
21 or is it a normal going through at your age. And
22 that's something that parents have problems with

1 whenever my grandchildren catches a cold. Some of the
2 kids with MECP2, they can't -- they have asthma, they
3 have lung conditions, they end up on, you know, with a
4 lot of breathing difficulties. And so every time one
5 of the kids gets a cold, we wonder is this a precursor
6 of something worse or is it just a normal cold?

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

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

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

22 MS. WELT: Hi. This is for Adrienne. My

1 kids -- my name is Patricia Welt, and my kids have
2 Ehlers-Danlos syndrome, which is an invisible illness.
3 And you spoke a little bit about that, and when we go
4 to the emergency room, oftentimes because my children
5 look fine, their symptoms are dismissed, especially
6 since they're young women. And my concerns are
7 dismissed because I'm a woman, and I'm wondering if
8 you run into -- you know, even if they're in severe
9 pain, that it's something that -- it's kind of a fine
10 line.

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

17 MS. STONE: Hi. I'm Geneva Stone, and this
18 is my son Robert. Robert has dystonia 16, and he also
19 has -- it's a genetic -- we used sequencing to get
20 that diagnosis, and it's a very rare form of dystonia.
21 And he also has the clinical symptoms of biotin-
22 thiamin-responsive basal ganglia disorder. And he

1 experiences all of the common symptoms that were
2 brought up here, and one thing that the FDA and
3 doctors might think more about is Robert can't swallow
4 due to his gastric symptoms. He has severe GERD, and
5 he currently uses a G-tube and a J-tube for medication
6 adjustment, and it can sometimes be extremely
7 difficult to get liquid forms of medications. And we
8 spent much of Robert's early years trying to compound
9 medications ourselves until Robert had Medicaid waiver
10 and we've been able to get pure vitamins, thiamin and
11 biotin compound by our pharmacy. But those patients
12 who are using vitamin therapies face significant
13 hurdles because over-the-counter vitamins are
14 typically, like, chock a lot with fillers and many
15 people cannot tolerate fillers at that level. So,
16 just wanted to talk about method of administration
17 briefly.

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

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

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

13 MS. SPENCER: So, I get way more attention
14 now than I used to. It's very, like -- "Oh, there's
15 Clark," and I'm like, "I'm here, too." So, and
16 actually, like, being a quiet person and being more
17 private about wanting to share with stranger about my
18 -- why I walk like that or talk like that, that was an
19 adjustment at first. But now -- so, I meet friends
20 everywhere I go. He's a great conversation-starter,
21 and really it's opened the door for me to be
22 comfortable and relate to people who may not have

1 heard about Friedreich's ataxia before, and so it
2 gives me a chance to educate, to help educate others.
3 So, it really helps me relate to other people.

4 MS. CHITTOORAN: Thank you, Wendy.

5 MS. SLAVIT: No, not at this point.

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

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

20 So, children with Angelman syndrome, or
21 individuals with Angelman syndrome are completely
22 nonverbal, so I'll absolutely echo the impact on daily

1 life of having a child who can't communicate any of
2 her basic needs and the frustration that comes from
3 the lack of appropriate services and coverage of
4 services for children with complex communication
5 disorders.

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

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

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

1 out there. Thanks.

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

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

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

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

16 MS. CHITTOORAN: Sure.

17 DR. MCCUNE: You had mentioned sort of three
18 different domains -- the cognition, the movement and
19 the mood swings, and that I believe your mother was
20 treated for one, but it made -- the movement, but it
21 made the mood swings oh, so much worse. Do you have a
22 feeling for which one of them -- so, clearly, there's

1 kind of a risk-benefit discussion there. Is there one
2 that you would have rather treated and taken the side
3 effects? And would you answer that question
4 differently?

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

19 So, what other options does she have? Yes,
20 she took medication, like, for anxiety and depression,
21 but there's only so much that that can do to offset
22 the other medication. And, again, it did work for a

1 good amount of Huntington's disease patients, it just
2 didn't work for her and there's, again, unfortunately
3 no -- there wasn't an ideal drug or alternative for
4 her to take.

5 DR. MCCUNE: Thank you.

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

14 BONITA: Hi. Good afternoon. I am a patient
15 living with Ehlers-Danlos syndrome, hypermobile type.
16 For me, I've had so many different things, but the
17 number one gold standard for treatment for Ehlers-
18 Danlos is physical therapy. Now, the problem with
19 that is insurance companies provide barriers, such as
20 copays and the deductibles and caps on visits. I've
21 tried medications. I've tried naproxen, I've tried
22 Robaxin, I've tried heat. I've tried all kinds of

1 different things, but the number one most effective
2 thing, from my second round in PT I've gone from at
3 least 80% of pain down to about 60% of pain. So,
4 that's like the number one thing, but, like I said,
5 there are barriers.

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

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

21 MARIA: Hi. My name is Maria and I have a 6-
22 year-old daughter with Prader-Willi syndrome, and the

1 hallmark symptoms of PWS are hyperphagia, which is a
2 chronic insatiable hunger, and obesity. But for my
3 daughter, the most burdensome symptoms are disordered
4 sleep and slow processing speed. And what I love
5 about this conversation is that she was just recently
6 diagnosed with narcolepsy, and so we're actually
7 managing her symptoms right now using natural
8 stimulants and behavior modification. Because we now
9 know that what the problem is, we're helping her get
10 back to sleep, get better sleep at night, and we're
11 exploring medications to treat the symptoms now of
12 narcolepsy. And to your point about insurance,
13 because we have a diagnosis now, it's easier for us to
14 get medications covered.

15 MS. CHITTOORAN: Thank you. Yes?

16 AUDIENCE MEMBER: As far as physical therapy
17 you mentioned, I will say we're managing for my
18 daughter, but it's a double-edged sword because the
19 children need physical therapy, occupational therapy,
20 speech therapy, and they also need pediatric
21 gastroenterologist, an ophthalmologist, you name it,
22 they need the specialist. And my daughter ended up

1 having to quit her job just to care for the children,
2 and so that's what I mean it's a double-edged sword,
3 because so much isn't covered on insurance and it
4 takes so much attention. And the sleep issues are
5 sleep issues for my daughter, for mental health and
6 psychiatric needs, my daughter needs to go for
7 counseling. It's -- we can't neglect the family
8 members. As a sister growing up, my parents tried to
9 give them a normal life but, you know, the identified
10 patient takes so much attention. And about speech,
11 when you've got cognitive decline, that paired with
12 the lack of speech makes it doubly scary and
13 difficult.

14 MS. CHITTOORAN: Thank you. Yes?

15 MS. WELDON: Hi. Monica Weldon, and my son
16 has a neurologic disorder called SYNGAP1, and I wanted
17 to add this symptom because it's something that's kind
18 of a hidden symptom. But I know that several of my
19 rare disease leaders who are in our gut cohort that
20 we've put together is constipation. And I will have
21 to say that for us, we have to help my son go twice,
22 twice a week because of a low muscle tone. And you

1 can -- it seems very simple, but with some of our kids
2 that have the gut issues between, of course, the brain
3 and the gut and the muscles and the peristalsis not
4 working correctly, I mean, that could be maybe why
5 they lack sleep. That could be why they're acting
6 out. What are those things? And so, of course, us
7 together as a group in the rare disease community
8 looking at the autism component, I think it's very
9 important. Because some of our kids have been
10 hospitalized because they just simply cannot go. And
11 so I wanted to kind of throw that out there as a
12 symptom, and I know the moms and parents out here that
13 live with that know that that's a big issue around
14 that, and having to treat it, because it's something
15 you can't not let go on a weekly basis.

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

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

1 comments people have made.

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

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

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

21 MS. SHAPIRO: Well, again, it depends if
22 she's in the chronic phase or the acute phase. So,

1 the acute phase is when the pain is really, really
2 awful. And so when she's in acute phase, of course,
3 there is nothing for us to do but to go to the
4 hospital and get more opioids, or whatever
5 combination. It's funny, many of the warriors think
6 of it as the decision to go to the hospital is a
7 decision to -- between their mental wellbeing and
8 their physical wellbeing. I mean, they really
9 struggle to go for that.

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

1 complications because we put off going to the hospital
2 for so long because of that.

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

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

18 So, I think for us, because it's kind of a
19 different than -- we have a diagnosis, it's part of
20 newborn screening, so pretty much we're told from the
21 beginning what the kids have. We have a protocol that
22 pretty much -- 95% of our children live, where sickle

1 cell is sickle cell any other place in the world and
2 it's the opposite -- 95% of the children die. And so
3 I guess we're always kind of trying to weigh what --
4 you know, what's the loss? What's the gain, what's
5 the loss, and in many ways we're much more fortunate
6 than many of the other people in this room. But it is
7 a daily struggle, and in that daily struggle I think
8 we're all united.

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

20 MR. ROTBERG: So, for me, I'm very fortunate
21 enough that with Huntington's disease there's a lot of
22 upcoming, I guess, trials in the pipeline, whether

1 it's -- we have one in Phase 3, we have some that are
2 starting Phase 1. I think the biggest thing that I'm
3 trying to teach myself is learning about the ins and
4 outs of clinical trial development and getting the
5 patient perspective from the beginning. Because when
6 you think about it, there could be, as mentioned, an
7 oral medication, but is it the liquid form or is it
8 the pill form? There's gene therapy, there's a spinal
9 injection, and try and understand what the needs are
10 and interests of those patients. Can they take it
11 once a week, once a month, once a year, once in a
12 lifetime, and really try to understand and be patient
13 with knowing what's in the horizon. So, am I going to
14 take something that's now or am I going to wait for
15 this next drug that could help me even more, three to
16 five years down the road, or even 10 to 15 years down
17 the road?

18 So, that's kind of something I really want to
19 emphasize is, like, what are the options? What are
20 the alternatives? And then for me it's kind of like
21 let's see the data on the animal models and then the
22 preclinical discovery stage, but let's get the young

1 adults' perspective, the older adults, the caregivers,
2 all of them involved from the beginning versus once
3 we're going through it. Because what I've learned is
4 that once a patient is in a trial, you know, a lot of
5 people see it as, hey, I need to get in this, I need
6 to get in this, but it's a big commitment, and if you
7 drop out, it's not like the next person can just come
8 in. And that can really impact enrollment as well as
9 if it eventually gets FDA approval.

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

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

22 So, for me it's trying to understand the ins

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

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

19 MS. SPENCER: Well, you know, based on the
20 symptoms that affect me most, I would say better
21 mobility, better balance, increased ability to walk on
22 my own. You know, I have a cart, but I can't take two

1 steps without some kind of assistance. So, if I was
2 able to take five steps without assistance, that would
3 be an improvement. And improving my ability to keep
4 up with friends, keep up with schoolwork, being
5 engaged in daily life activities, that would be kind
6 of the most benefit to me.

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

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

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

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

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

22 MS. CHITTOORAN: Sure. Adrienne?

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

18 So, I think it's a sea change in research,
19 and I think it has to do with the fact that medicine
20 at this point, medical research, doing stem cells and
21 using your own tissue is so much -- I mean, it's much
22 more personal than it's ever been before. And I

1 think, also, that we've learned some stuff, I mean,
2 from software development, right? In the beginning
3 with software they would create something somebody
4 said be cool to be able to do that, but they didn't
5 have the end user in the room. And now we've got the
6 end user in the room, and I think it's going to help,
7 or is helping to escalate and to streamline the
8 process.

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

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

20 MS. CHITTOORAN: Do we have a mic?

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

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

1 22-year-old son with congenital hyperinsulinism, and
2 I'm also the executive director of Congenital
3 Hyperinsulinism International and the Rare Action
4 Network ambassador for New Jersey. And we have a
5 campaign at CHI, which we call HI, which is
6 hyperinsulinism for short. HI never sleeps, and so I
7 don't have a solution, but this is such an enormous
8 problem. With us, it's not about our kids not being
9 able to sleep, it's about us needing to be up all
10 night taking care of them and checking their blood
11 sugars and making sure that they eat when they might
12 not want to eat. We might have to trick them into
13 sleeping in order to feed, and when you are dealing
14 with something that's metabolic, it goes on and on and
15 on, and it doesn't understand the normal biorhythms of
16 day and night. And in the community of other rare
17 diseases that I know, people living with the diseases
18 in their parents, this is so much the case, that one
19 part of it is a sleep disorder. But so much of it is
20 just the weird rhythm of our lives and, yes, this
21 affects our lives in so many ways -- ability to work,
22 our ability to make money, our ability to care for our

1 other children, our ability to go to school, and so on
2 and so forth. So, it's an enormous problem that needs
3 a tremendous amount of focus.

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

11 AUDIENCE MEMBER: I'm actually here
12 representing two communities, because I have a newly
13 diagnosed son, so I have two with Duchenne muscular
14 dystrophy and an 11-year-old with primary immune
15 deficiency. And you might think that the Duchenne is
16 what I want to talk about, but I'm actually really
17 interested in talking about our treatment of immune
18 deficiencies today. My son was 11 when he was
19 diagnosed in November, and the symptom was major
20 infections that were causing hospitalization, so it's
21 chronic antibiotic use followed by allergic reactions
22 to antibiotics and immunities to the ones that he

1 could still take. And so now he's on a plasma
2 treatment once a week, which comes with a lot of the
3 same symptoms that he was getting because he was sick
4 all the time -- chronic headaches, fatigue, rashes,
5 unexplained vomiting, nausea. And so it's becoming a
6 really pertinent discussion right now. He's not
7 getting sick as often, but he's really sick from his
8 medication, and so I think as we start to -- the
9 physician and clinician environment was such that they
10 said, hey, great, this kid has a treatment. Your
11 other boys, you know, we didn't have much we could do
12 for Duchenne muscular dystrophy, but there's a
13 treatment for immune deficiency. Unfortunately,
14 there's not a lot of research going on into new
15 treatments because there is one, but it's a really
16 horrible treatment.

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

1 disease doesn't mean that the treatment is sufficient.

2 MS. CHITTOORAN: Thank you. Anyone else?

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

15 Acromegaly, I don't know how many of you know
16 about acromegaly, but it affects every single symptom
17 in your body, because it's hormonal. It affects your
18 appearance, it affects -- growth hormone makes you
19 aggressive. It affects your moods; it affects your
20 joints. It affects every little aspect of your life.
21 And so, in my opinion, patients suffering seven days
22 every single month because they're on a long-acting

1 medicine, we need to do better.

2 MS. CHITTOORAN: Thank you. Yes?

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

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

22 So, I think to these other points that just

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

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

14 MS. WITTEN: I have a comment. I'm from
15 CBER. We do evaluate gene therapy trials, and what we
16 start doing in trying to have some trial for a
17 specific indication, we try to invite the community
18 and talk to them about the endpoints. Because
19 sometimes, you know, when you receive this clinical
20 trial, the endpoint is kind of meaningless, and I'd
21 like to hear from the community what would be this
22 reason, you know, what we think and what condition you

1 will enroll your child in the clinical trial. And two
2 different communities have told me, you know, the
3 sleep disorder, we would like to treat sleep disorder,
4 but we're not sure if it's reasonable or possible, I
5 can tell honestly.

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

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

1 MS. FOSS: My name is Beth Foss. I'm with
2 the Choroideremia Research Foundation, and we have
3 clinical trials happening now. We have two, and we
4 have a third that's coming, so I appreciate your
5 question and, sir, you asked that, too. I have a son
6 -- actually, I have two sons. I'm really glad they
7 sleep. At least we sleep, so I'm really appreciative
8 of that. So, my older son, who is 26 now, was treated
9 with a gene therapy up at Mass Eye and Ear, and so we
10 are starting year three post, and it's been
11 challenging in the sense that we go up -- as you say,
12 we go up every six months and we spend a good day or
13 day and a half. Any little aversion or change in his
14 vision is -- it weighs heavily on them. Is it worth
15 it? I would say yes. As a mother, it is worth it to
16 undergo that. What we have a challenge with, and I'm
17 with my colleague and friend, Eric Hartman, who has
18 choroideremia, I'm a carrier mother, my father is
19 blind, I have two sons, as I say, who have been
20 diagnosed with it and are starting to see the
21 blindness. It starts peripherally, and we lose about
22 7%, 8%, 10% a year. And so one of the things, one of

1 the things that we are having -- the indicators is
2 they measure the central vision, and much of our
3 central vision is still perfect, 20/20, but we're
4 losing peripheral vision. So, we have older patients
5 that are in the trial, and if we could start with
6 younger, when they're kids, we can preserve so much
7 more of their vision. So, the endpoints is something
8 that we're really trying hard to work with our
9 researchers and with the FDA.

10 One other thing real quickly, I will say, as
11 many of you are mothers and parents of children,
12 that's one thing. I was looking at how do you weigh
13 potential benefits versus less common risks? I think
14 some of the younger in the Choroideremia Research
15 Foundation, we have a robust organization. It's 1 in
16 60,000, 50,000 people get this disease, and there's a
17 lot of talk about sex selection studies. Do we have
18 children? Do we not? And a lot of our members deal
19 with guilt as a parent, and that's something that's
20 really hard on them. Not sure how we tackle that one,
21 but being a parent with kids that are hurting, I don't
22 think there's anything quite worse than that.

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

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

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

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

1 Abernathy has a dual role here at FDA as principal
2 deputy commissioner and acting chief information
3 officer. As principal deputy commissioner, she helps
4 oversee the agency's day-to-day functioning and
5 directs special and high priority initiatives that cut
6 across offices overseeing FDA's regulation of drugs,
7 medical devices, tobacco and food. As acting chief
8 information officer, she leads our data software and
9 computer hardware efforts to help us to continue to
10 advance public health agenda. Dr. Abernathy is a
11 hematologist and oncologist and palliative medicine
12 physician. Before coming to FDA, she was a professor
13 of medicine at Duke, and most recently worked in the
14 health technology industry at a cancer-focused
15 software and data company. She is an internationally-
16 recognized clinical data expert and a clinical
17 researcher, and one of the early pioneers in
18 bioinformatics. We are very proud that Dr. Abernathy
19 has joined us in February to continue to advance our
20 mission in patient-centered care and public health.
21 She has been a longstanding patient advocate and is
22 well known across the patient community for her

1 commitment to ensuring that the voices of patients are
2 heard. So, please welcome Dr. Abernathy.

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

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

18 As you just heard, I'm an oncologist. So, I
19 spent a fair part of my career taking care of patients
20 with melanoma, and particularly patients who had a
21 family history of melanoma and who had advanced
22 disease. And, really, to this day, one of those

1 patients, who actually in some ways represented all of
2 the different patients coming through my clinic, but
3 she had a way of sort of sitting on my shoulder and
4 talking to me for the rest of my life. And her name
5 is Janet, and Janet and I got to know each other in
6 the mid-2000s. And I remember her coming into my
7 clinic. She's got this really curly red hair. She
8 had freckles on her nose. She was about 35. She
9 always wore scrubs because she was an ER nurse,
10 happened to be an ER nurse from not far across town,
11 and had this bounding energy. And I have this little
12 couch thing in my office. She never sat in any of the
13 patient spaces; she insisted she was going to sit on
14 the couch when we had these conversations in clinic.
15 And one of the first things I noticed here in my
16 melanoma clinic was that a woman with a fairly
17 advanced cancer at that time was on prenatal vitamins.
18 And as we were trying to figure out how to take care
19 of her, one of the issues was that she was asking me
20 about the impact of the treatments that we were
21 talking about and what was going to happen to her
22 fertility. And, in fact, I couldn't answer any of

1 those questions. And we would talk about whether or
2 not her mother's melanoma and her sister's melanoma
3 had any impact on how her personal illness was going
4 to go. I wouldn't have any answers to that, either,
5 although I was pretty confident that this was, indeed,
6 a genetically derived and motivated illness.

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

21 In fact, all of the work I did of the
22 subsequent 10 to 15 years, and how I landed at FDA was

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

20 Interestingly, in December of 2016, Congress
21 passed a piece of legislation called the 21st Century
22 Cures Act. That piece of legislation asks us to

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

20 Here at FDA, my core responsibility as a
21 principal deputy commissioner is a series of trans-FDA
22 policy responsibilities and commitments. So,

1 including, for example, rare orphan diseases in
2 pediatrics, where, really, what we're trying to think
3 about is how do we advance the work in these critical
4 areas? And also includes the Patient Affairs staff,
5 who also sits right next to Rare Diseases and
6 Pediatrics, so we can make sure that we incorporate
7 the patient voice, and we also have as many two-way
8 communication channels as possible.

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

1 pieces are together.

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

12 As I was just sitting here listening even for
13 just the last half hour, I was thinking about some of
14 the commonalities that come through, for example, the
15 conversation about sleep. The end user, the fact that
16 ultimately you want to go to school and do the other
17 things that are important in your life, right? And
18 many of these aspects we can share across our stories,
19 but I also think about what's unique about our disease
20 and how do we have to understand and deal with those
21 capabilities as well? At FDA, we need to understand
22 the full totality of the story so that when we think

1 of clinical trials and also the understanding of how a
2 medical product works, we're able to do so in putting
3 into the context of the experiences that you have. To
4 develop endpoints and outcomes that align with the
5 experiences that you have, and to be able to
6 communicate across the overall biomedical spectrum
7 within the context of the experiences that you have,
8 including into the payer space.

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

18 My second piece of advice, though, is
19 actually almost exactly the opposite. As an
20 oncologist, I always had to remind myself our jobs are
21 always to have compassion. As a patient and as a
22 daughter and as a mother, I also need to have

1 compassion. So, one of the things that can be really
2 hard when we've had too much pent-up energy to use
3 your voice is also to want it to move really fast, and
4 so have compassion that we're listening, but also
5 we're going to need to figure this out together, and
6 it may not move always as fast as we all want it to,
7 but that making sure that we don't give up in
8 continuing to put our voice to the story.

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

14 And I think my last point is that as we think
15 about the patient community, think about our caregiver
16 community as well. Often, we talk about patients
17 because we're thinking about developing medical
18 products individually for diseases and for patients,
19 but as we have compassion for each other, we also have
20 to have compassion for caregivers, because it is also
21 a huge part of the story. So, with that, I just
22 wanted to say thank you. I'm here to answer

1 questions, and thank you for all that you do. So, I'm
2 going to do this or should do questions?

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

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

22 I was in a two-and-a-half-year study, natural

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

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

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

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

22 KRISTEN: Hi. I'm Kristin, and I represent a

1 community of PTEN hamartoma tumor syndrome patients, a
2 rare genetic heredity cancer syndrome with a whole
3 neurocognitive component. This is more just a comment
4 to what he said and what you said. The importance for
5 sharing data and being able to collect that data for
6 patients is critical. And what we're seeing more and
7 more in the rare disease community is patient
8 organizations are becoming wise to that in starting
9 patient-driven registries, which we have recently
10 done. But the purpose is not to hold the data for
11 ourselves; it's to be able to open it up to all
12 researchers and also share snapshots of that data with
13 our patient community, which we're doing. So, it's
14 possible; you just have to have motivated patient
15 organizations.

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

21 I am going to stop and switch gears for a
22 moment, because we have a special announcement. So,

1 you've already heard earlier about the Beyond the
2 Diagnosis exhibit, which is really intending to
3 provide a face to all 7,000 and more rare disease.
4 This whole exhibit is traveling across the country.
5 It's going to medical schools and research institutes
6 and hospitals around the globe, even, so even beyond
7 United States, to look beyond the diagnosis of the
8 patient. And so today the founder of the Beyond the
9 Diagnosis exhibit -- oh, she's right next to me, there
10 you go -- is Patricia Welton, and she's joined us to
11 unveil the newest piece.

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

21 MS. CHITTOORAN: Yes.

22 MS. WELTON: You guys are the first to see

1 this. [Applause.]

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

11 [Break.]

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

20 So, just some reminders before we get
21 started. If you don't get to provide feedback today,
22 please do so on our docket, and the just so everybody

1 knows, we do have a large audience on the web as well.
2 There's almost -- about 500 people or so on the web as
3 well, so in addition to what we have in the room, so
4 that's very exciting.

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

17 MS. RASKIN: My name is Julie Raskin and I
18 live and work in New Jersey with my husband, and we
19 have two children, Hannah and Ben. They're both young
20 adults. And Ben, who is the younger one, was born 22
21 years ago, almost 23, with congenital hyperinsulinism.
22 And congenital hyperinsulinism is a disease that

1 causes the overproduction of insulin, and that causes
2 severe hypoglycemia, or low blood sugar. And the
3 brain and the body need blood sugar to grow and
4 develop, so if it's not controlled early on, it could
5 cause brain damage or death. And a lot of what you
6 all talked about this morning really, really resonated
7 with me. And we sort of think of hyperinsulinism, a
8 lot of us it can be like a global insult to the
9 family, not necessarily just the brain, but to the
10 family, for all the reasons that you all spoke about.
11 And I think that in and of itself is a commonality
12 among so many of the rare diseases. So, thank you for
13 giving an opportunity to meet you all.

14 MS. CHITTOORAN: Thank you, Julie. Michael?

15 MR. BUSBY: Good afternoon, everyone. My
16 name is Michael Busby. My wife Kristin and I have
17 three children, Alexandra, 8 years old; Michael, 6;
18 and Joseph, 3. Alexandra and Joseph were both born
19 with progressive familial intrahepatic cholestasis, or
20 PFIC2. We are -- anyhow, sorry. We are -- I'm happy
21 to be here to talk about rare disease. Like Julie
22 just said, a lot of what you all said this morning

1 certainly resonated with us. One of the topics was,
2 you know, sleep disorder, or patient care due to lack
3 of sleep, so that definitely hit home. I also sit on
4 the board of directors for the American Liver
5 Foundation in Greater New York. Thank you.

6 MS. CHITTOORAN: Thank you, Michael. Monica?

7 MS. WELDON: I'm Monica Weldon, and I am the
8 mother of five children. I'm married to my husband
9 Chris. My children, I should start, I guess, with my
10 oldest three: Hailey, Taylor and Sawyer. They are my
11 three adult children. Started over and I have twins,
12 11-year-old twins next week, and one of my twins,
13 Beckett, has a condition called SYNGAP1, and this is a
14 neurological disorder, developmental disorder that
15 causes intellectual disability. It is also an
16 epilepsy gene or condition, where he has absence
17 seizures and it is also an autism gene, where we
18 struggle, of course, with the behaviors, sleep issues,
19 a lot of sensory processing issues, muscle
20 coordination problems. And, of course, now, as we
21 move through to learning more about this disorder,
22 because it's newly -- pretty much newly discovered, a

1 lot of immune system problems, a lot of digestive
2 problems. And I am also the president and CEO of the
3 Bridge the Gap SYNGAP Education Research Foundation,
4 who is focused on research for this disorder, and I
5 appreciate the opportunity to come and share.

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

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

18 MS. RASKIN: Sure. So, I have those
19 experiences personally with my son, and also as the
20 executive director of Congenital Hyperinsulinism
21 International. And in terms of clinical trials, we --
22 when my son was born, there weren't any FDA clinical

1 trials, but there were some -- well, they might have
2 been FDA, but they were smaller, investigator-led
3 trials. And we very much benefited from some
4 activities like that that were at one of the leading
5 centers in the world, the Children's Hospital
6 Philadelphia, for treating congenital hyperinsulinism.
7 My son basically could not get home from the hospital
8 and start his life without clinical experimental
9 protocol that included using two off-label medications
10 in an off-label device. And so after some surgeries,
11 we were able to go home on that kind of regime. So,
12 that was an absolute godsend.

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

1 MS. CHITTOORAN: Sure.

2 MS. RASKIN: Okay, great. So, as a
3 community, our congenital hyperinsulinism community
4 started a -- just an Excel spreadsheet, where we
5 collected some information, natural history
6 information about the condition, and that was done by
7 a lovely colleague of mine, Isabel Calderon. And it
8 was really a backbone, very important to our community
9 in understanding how the condition affected others in
10 our community and that helped us to benchmark sort of
11 where we are and what was happening to our children.
12 And that was our sort of launching pad. And then we
13 wanted to go farther and develop a really -- a real
14 patient registry with an institutional review board
15 and with steering community members, professional
16 scientists and researchers, and patient advocates from
17 around the world to really guide this work. And so we
18 did that and it took us years and years and years.
19 We're the opposite of Monica. Very slow in our
20 development, but with a very focused purpose to try
21 and be as comprehensive as we could in creating it,
22 and we went live in October. And then I've had the

1 experience with Benjamin, my son, being part of that.
2 And so that was extremely interesting, and to see the
3 effect on him of sharing his data and what it meant to
4 him to be part of that was very meaningful and
5 compelling for him.

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

10 MS. RASKIN: Well, as I said, this disease
11 was such a global insult to the family. My son was
12 always just a love, just delightful, and we adored
13 him. And he brought us so much happiness even in the
14 depths of our depression and grief over the disease.
15 But we were really desperate, and there was no way to
16 go home without participating. And we, you know, in
17 terms of -- we were already in a hospital. We were
18 already cycling through potential different treatment
19 possibilities, and so it wasn't even in our mind that
20 this was somewhat experimental, because everything
21 seemed kind of experimental. There was no treatment.
22 So, our biggest consideration really was listening to

1 the professionals, and we were so lucky that CHOP had
2 been studying and caring for patients with this
3 disease for already a pretty long time, even though it
4 was so rare. And so we really trusted in them in
5 terms of deciding to do this, but over time, fast-
6 forward to know, and my son was in -- he traded his
7 rare disease for a common disease, because his
8 pancreas was removed. So, he went from having
9 hyperinsulinism to being diabetic. And so he had an
10 opportunity to participate in a trial that was a pilot
11 study also at CHOP, and for the artificial pancreas.
12 And it was an incredible experience for him to be able
13 to give back to science and to be part of something
14 that could really be life-changing for him in the
15 future.

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

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

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

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

1 out of it."

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

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

22 Twenty-four months old, it was incredible

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

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

22 So, it's a lot. That's a lot to handle. She

1 was just about two and a half years old at that point.

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

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

21 You know, about a year after that we kept
22 reading and reading, and ultimately on

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

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

15 MR. BUSBY: So, for my family, when you're
16 faced with the -- and much like everybody. You know,
17 when you're faced with the decision of the end result
18 is a transplant, you kind of look at every solution
19 before you have to get to that decision. For us, it
20 just seemed -- to me it seemed unreasonable that there
21 was not some type of medication that could help this,
22 or at least prolong it to get to me not making a

1 decision at two years old or three years old to have
2 my daughter liver transplanted. And just to kind of
3 going back to how far we would have gone, I would have
4 gone all the way to that point of transplant to try
5 something. You know, and we were told very
6 specifically that there was no guarantees and side
7 effects, and so forth. And fortunately for us, the
8 side effects are minimal and she's doing really well.

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

18 MR. BUSBY: No. And I'll back that up by
19 saying that we currently, much like Julie, travel from
20 Long Island, New York to Children's Hospital in
21 Philadelphia on a regular basis for that treatment.
22 And I would have gone to California. Oh, yeah, I

1 would have gone anywhere. It would not have stopped
2 us, and fortunately Philadelphia is a three-hour trip,
3 you know. And I look at that, to me there is nothing
4 I would stop doing or say, oh, that's just too far or
5 too much. I wouldn't.

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

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

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

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

22 MR. BUSBY: Yes. The itching for this

1 specific one was the primary endpoint.

2 DR. SILVERSTEIN: I wanted to follow up on
3 Dr. McCune's comment, and I think it's really
4 important. This is more of a statement as opposed to
5 a question. But I get from all three of you who are
6 up here and those who were here before that you're
7 very, very intelligent, well-informed persons. But
8 not everybody out there in the world is as informative
9 as I think many of you. You may be more of a selected
10 group. If you come to this meeting you're very
11 engaged in all the aspects of your children's care and
12 the care of other children who have similar diseases.
13 But I think it's important when you're considering
14 putting your child in a clinical trial, is to consider
15 exactly what Dr. McCune is saying, what are the
16 endpoints? So, basically, what are they trying to
17 show? What are they trying to assess as an outcome of
18 the study? And so if your child, as in your child's
19 situation, the itching was the most problematic part
20 of her disease at that time, you would want to find
21 something where they're addressing that particular
22 outcome. That doesn't mean that they don't -- if the

1 outcome of that endpoint is not achieved in the trial
2 that your child may not benefit from that, because the
3 outcome is a general result. But it's important to
4 know when you look on clinicaltrials.gov, and I think
5 also when you talk to your child's physician is, what
6 problems are being addressed in the trial, and is that
7 appropriate for your child's problem? Because disease
8 may have various symptoms and it depends what you're
9 trying to achieve with that trial.

10 So, being in a clinical trial is only useful
11 if it is appropriate for your child. We talked about
12 the preferences of the family and of the child
13 especially, if the child is the one with the disease,
14 and to try to match it together. Because there's a
15 desperation to try and get yourself or a child into a
16 clinical trial, which I can only understand through
17 patients I've had and friends I've had who have had
18 children who have diseases. But at the same time you
19 want to make sure it matches well so that you're
20 giving your child the best chance to have the symptom
21 relieved that needs to be relieved. And is that how
22 you guys approached it, you all approached it? I'm

1 sorry, I'm from New York; we say guys. Is that how
2 you all approached it? How did you figure out which
3 trial? What got you to that point where you can say
4 this is the right trial for my child, or --

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

22 MS. CHITTOORAN: Thank you.

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

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

16 MS. WELDON: Well, I started out, I'll give
17 you a brief synopsis of my son's story. It kind of
18 was similar to yours. And you notice when they're
19 young infants and they're not progressing the way they
20 need, and we knew that Beckett was not progressing the
21 way he should at four months -- not sitting up in
22 comparison to his twin sister Piper, and noticed

1 different things along with him. And, of course,
2 after having five children, I knew that there was
3 something wrong with him not being able to walk within
4 the normal range and meet his milestones.

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

12 But fast-forward, we finally ended up getting
13 the genetics and he was diagnosed at the age of 4.
14 And so when we had gone to the genetics doctor and he
15 handed me one paper that had been written on this --
16 you know, written about this disorder, SYNGAP1, saying
17 it just caused intellectual disability. We didn't
18 even know at the time it was an epilepsy gene, or a
19 gene that caused a multitude of different types of
20 epilepsy. And so I knew then that -- I remember
21 looking at my geneticist and said, "Is this it?" And
22 he goes, "That's all we have." And I said, "Well, are

1 there any others?" And he said, "Well, we only know
2 of about five others in literature, and he's No. 6."
3 And I said, "Oh, wow, okay," just kind of sitting
4 there in shock and feeling probably the most alone
5 I've ever felt. Drove home. I think it took me about
6 two days to process and realized I couldn't live -- I
7 could not allow my child to continue living the
8 quality of life he was living with the sensory
9 processing -- we didn't know at the time he was having
10 seizures with the behavior problems and things like
11 that. I had to do something.

12 And so I started the organization and we
13 found, of course, a group of people in between by the
14 time I started on Facebook, started out with three
15 families on Facebook. And that grew into the
16 organization, and within the first year, after getting
17 involved with the rare diseases community, I realized
18 everything is revolving around data, and I had to
19 educate myself on the drug development process. And
20 so I took a shot at writing my very first grant. I
21 taught school for 23 years and my background was
22 science, so I knew there was something there. Ended

1 up winning one of the FDA pilot program registries
2 through the National Organization of Rare Disorders,
3 which has been up and running for two and a half years
4 now, and it was a lifesaver for our organization.
5 Launched at Christmas Day. That as the best Christmas
6 present anybody could ever have, because with that
7 registry we ended up finding trends. We found that
8 SYNGAP1 is the gene, that mechanism that controls
9 sensory processing in our patient community, possibly
10 overlapping into other autism communities as well.
11 And I just realized that watching my own son and the
12 symptoms that he had at home, and reading through the
13 trends, of course, on our social media, that we needed
14 to start asking these questions under an IRB-approved,
15 organized way of collecting this data.

16 And that brought us to our new finding with
17 the scientist who used our data to find our very first
18 biomarker that was just published on Friday this last
19 week. And it has just been phenomenal, and those
20 types of things has motivated our community, those
21 results, to showing them how the data and how these --
22 and we're not in a clinical trial right now. I'm

1 shooting for that. I'm going to get there with our
2 group, I'm bound and determined. But on a side, the
3 clinical studies that we are involved in, that we have
4 set up with our researchers, and gathering all those
5 scientists together, basically pleading and begging.
6 I think I begged Dr. Jimmy Holder, which I love him to
7 death. He's at Texas Children's, and he goes, "Okay,
8 I'll study." No, he was excited to come and study
9 with us, but he was our first clinician ever to study
10 SYNGAP1. And being a part -- involving these
11 scientists and these clinician researchers in on our
12 disorder changed the game for us. And so now we're in
13 these clinical studies to help find more biomarkers
14 and more clinical endpoints, because you made a really
15 good point that I didn't think about is, what is going
16 to be primary for us? And we're only going to get
17 that from the patient community, which we have to
18 prioritize. What symptom do we want to treat? And,
19 of course, seizures is probably our primary. But then
20 we have behavior, then we have sleep, then we have all
21 these different things. And how are we going to
22 incorporate and measure those endpoints and get those

1 biomarkers? And the only way to do it is through data
2 and through our registry. And I hope I didn't talk
3 too long and I hope I answered your question.

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

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

1 European families to get to clinical study in Europe.
2 And I truly believe that all that tied together, and
3 it's not just about policy, driving policy and
4 legislation. It's not just about advocacy and spread
5 awareness, but you also -- in parallel with all of
6 that, you've got all these gears that you need to
7 focus on, and I think that as an organization, you
8 need to try to help create protocols, like with our
9 gait study that we're doing at Texas Children's right
10 now. All of those are to look for these endpoints,
11 and we want as many families to be involved with those
12 pilot programs as possible so that we know exactly how
13 to design this clinical trial. Because, like most of
14 you know, 95% of all clinical trials fail. Why? Why?
15 Because, well, participation, retaining your patients,
16 but also some of the clinical designs suck. I mean, I
17 don't mean to be blunt, but, you know, I'm from Texas,
18 I'm blunt, so I just speak my mind. And that's
19 because the patient voice wasn't included on that.
20 And I believe that real world data, along with the
21 clinical data and all of the -- all of that has to tie
22 in together, and if you're not designing a trial to

1 make sure it is waterproof, you're setting yourself up
2 for failure. And I'd rather have a 50/50 chance than
3 a 5% of it succeeding.

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

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

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

20 MS. CHITTOORAN: Well, thank you very much.
21 So, before I move into the audience and expand this
22 conversation to you all, I just want to check. Does

1 anybody on the FDA table have any questions before we
2 move on?

3 MS. WITTEN: I have a question.

4 MS. CHITTOORAN: Sure.

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

14 MS. WELDON: Well, it all started, I guess,
15 if you've ever been to Houston, just like in DC,
16 traffic is horrible. So, I'm stuck in traffic on my
17 way home and I realized I was alone in the world, but
18 I knew, I knew that he wasn't the only one. There had
19 to be more. I mean, you've got 8 billion people on
20 this planet; what are the chances of him being the
21 only one? And I've heard of more even ultra-rare
22 disorders, but I had to -- how I processed is I

1 started to blog. And I started to actually track my
2 own natural history of my son's symptoms and his and
3 own lives dealing with this. And I started putting,
4 you know, the hashtag thing was the -- I don't know
5 what people did before social media and hashtags. But
6 that's how, you know, finding -- actually, I didn't go
7 out finding anyone; they found me. They put in, I
8 guess, in search SYNGAP1, and then all of a sudden, I
9 guess six months later, after I was blogging and just
10 praying that something had to change, she reached out.
11 And I think we stayed on the phone until 2:00 or 3:00
12 -- it was 3 a.m., I know, Eastern. It was 2 a.m.
13 Central, but we stayed on the phone for about two or
14 three hours talking about our kids, and we were, like,
15 I think I've found my child's you know,
16 boyfriend/girlfriend, because, you know, she was a
17 little girl and my son was, you know, my son. And
18 we're like, "We're not alone anymore." "Oh, you don't
19 sleep, either?" "Yeah, okay." You know, it was
20 crazy. And she goes, "Well, you know I know of one
21 other person," and I was like, "Can you contact her?"
22 And then we said, okay, well, let's do the Facebook

1 group thing. Well, there's only three of us. I said,
2 "Well, let's do it anyway."

3 And then I started a page an open page, and I
4 started researching all of the papers I could find. I
5 also found a lot of mouse model data, but no human
6 data. But I posted it anyway, because then people
7 started going, oh, well, you know, and it snowballed.
8 And so not all of the -- we have two -- I know that
9 there are right now in one of the databases here in
10 the United States -- I can't remember all of the
11 acronyms, but it's -- I think we have 262 different
12 SYNGAP1 variants. I know that we currently have about
13 209 registrants in our database. I know that we have
14 close to about 350 families within our Facebook group.
15 Not all of them participate in the research, and I'm
16 trying to coerce them to do that because we're such a
17 small population. And that's when I just took a leap
18 of faith and quit my job teaching and went into this
19 full time and started just telling my story. Anybody
20 who would listen. And the people out in the audience
21 who know me, know I never shut up. You can probably
22 tell right now.

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

12 MR. LACEY: Sure. My name is Patrick Lacey.
13 I'm with Beat Nb, a nonprofit in Boston. My son was
14 diagnosed with neuroblastoma -- it's a pediatric
15 cancer -- as a child, and he enrolled in probably nine
16 or 10 different clinical trials, Phase 1s and Phase
17 2s. I founded the nonprofit and we've funded probably
18 18 clinical trials at this point. And what I've
19 discovered first as a father searching for clinical
20 trial options, hoping to save my child, I discovered a
21 lot of things about study design that I would change
22 if I had the power to do so. And one of those is the

1 patient voice, as many people have mentioned.

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

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

17 Looking at travel considerations, cost. You
18 know, everyone in this room is here for a reason --
19 they're passionate, they have the desire to help, and
20 we have the ability. And as you alluded to earlier,
21 not everyone has that same capacity to either attend
22 these meetings or to search for those clinical trial

1 options. So, having clinical trial options that are
2 available close to home, that travel and losing a job
3 and doing all these other commitments makes it
4 challenging for families to access clinical trials.
5 So, having them available in regional locations is
6 really important as well so that families, if they
7 want to make that choice and they think it's a good
8 study, they're not precluded from doing so because
9 they have to travel halfway across the country and
10 make sacrifices that would be impossible for some
11 families to do.

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

20 When you see a clinical trial consortium
21 that's enrolling patients, patients are traveling from
22 other countries and all over the globe to get on those

1 studies, that's because of great trial design. And
2 that's because of trials that are putting the patient
3 and their outcome, both of those things, and the
4 questions that are asked in the study, those all-
5 important considerations, and melding all those
6 together in such a manner that you address all of
7 those needs, is something that I find to be critically
8 important going forward in helping all these patients.

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

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

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

21 So, thank you very much. This meeting has
22 been just really informative for me. I'm new to the

1 patient advocacy world. My spouse was diagnosed with
2 ACPMP about six months ago. I'm an FDA regulatory
3 lawyer by day, by training, and so now I'm trying to
4 kind of use my skills to do some patient advocacy
5 work.

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

17 And so one of the reasons is eligibility
18 criteria, which I've heard a lot of discussion about,
19 is very, very narrow. And when we're talking about
20 randomized clinical trials, that has its own set of
21 issues. Some of the eligibility criteria, just for
22 example, a big one is to do with the dosage form. So,

1 a lot of our patients have small bowel obstruction as
2 a result of the appendix cancer, which essentially
3 produces mucinous tumors throughout the abdomen and
4 just compresses the digestive system, compresses the
5 lungs. But with a small bowel obstruction, so many of
6 these trials are for immunotherapies and are capsules,
7 and so that's an exclusion criteria. Even if the
8 patient wanted to, could not participate because they
9 just can't swallow and have bioavailability issues.

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

22 Very quickly, just a couple of the other big

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

17 MS. CHITTOORAN: Thank you.

18 MS. SHELTON: It gets me emotional. Just
19 last but not least, the real shocker of the reason for
20 why our patients are having problems with clinical
21 trial is they have no knowledge of them. Their
22 doctors are not talking to them about them unless

1 they're clinical trials at their own institution, and
2 even then it's a longshot. And, you know, I sat in
3 with a patient and they were told, "Just go to
4 clinicaltrials.gov." I'm a lawyer. I helped with the
5 legislation that created clinicaltrials.gov. It's
6 difficult for me to navigate, and so to tell some of
7 these patients, just go do that, especially when
8 you're searching for biomarkers and whatnot, it's just
9 a real challenge. Thanks for listening.

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

15 MS. SLAVIT: Yeah, so we've actually heard a
16 lot of the same things that people have been talking
17 about in the room. The difficulty of the time
18 commitment, that it can be disruptive. There are also
19 concerns about the treatment being conflicting with
20 what the treatment regimen they are currently on.
21 Also not knowing maybe what some of the side effects
22 of some of the medications will be. A few people are

1 concerned about being on the placebo and not getting
2 the drug that's being tested. As a lot of people have
3 mentioned, the location of the trial, and so just the
4 cost of getting there. People have talked about the
5 endpoints and really looking at the endpoints as a
6 decision of whether they're going to participate or
7 not.

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

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

19 MS. CHITTOORAN: Okay, thank you. So, just a
20 show of hands. Has anybody here who is a patient or
21 caregiver wanted to participate in a clinical trial
22 and wasn't able to? Okay. So, I'd like to hear from

1 a couple folks about that, if you wouldn't mind
2 sharing. Do we have a mic coming up?

3 MARIE: Hi. Marie again. So, my daughter is
4 6, she has Prader-Willi syndrome. And I didn't
5 mention before, I do also have a for-profit company
6 called TREND Community. But all the clinical trials
7 that are currently recruiting, the primary endpoint is
8 hyperphagia, and though I think she might benefit with
9 regards to some of the secondary endpoints, she's not
10 in hyperphagia, so she doesn't qualify for any of the
11 clinical trials.

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

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

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

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

11 LENNIE WOODS: Hi. My name is Lennie Woods.
12 I'm with Sarascure.org. We are a patient advocacy
13 group, but I'm also the mother of Sarah, and I feel
14 like I've got a sister in Monica, because we were told
15 my daughter was the only living one with clear cell
16 sarcoma at the time. An interesting fact, there was
17 another patient in the same hospital being seen by
18 another doctor with a different pathologist. He found
19 us, God bless social media and Facebook. And when we
20 -- we didn't confront, but when we brought it to the
21 attention of the hospital, Memorial Sloan Kettering,
22 there were some very upset people. But there were

1 papers being written on him and studies being done on
2 my daughter, and no one was communicating. And we've
3 since -- I mean, that's hurtful. We've since found 25
4 patients living and about 10 years of natural history
5 data on a Facebook page, yes. It was a secret page,
6 so it wasn't infiltrated by others, and I want to talk
7 to you.

8 But we have problems with trials in that
9 we're considered soft tissue sarcoma, and clear cell
10 is extremely different. We're almost hurt by being
11 called that. So, they want to throw us into trials
12 for soft tissue sarcomas and they're never successful.
13 And on papers, when you read papers and you try to out
14 clear cell sarcoma patients, they're thrown in with
15 other soft tissue sarcomas. And this is also a
16 problem. We support other small groups, like
17 epithelioid sarcoma, who are parents doing the same
18 thing we are. So, there's a whole bunch of us out
19 here with a lot of good information. But I will tell
20 you, the people from the FDA should know, when we try
21 to share information and talk to our doctors, we get
22 the eye-roll, we get -- I mean, we are shut down. I

1 call them the gatekeepers. They will not let us
2 patients get beyond to make the change. So, I say I
3 had to jump over them, but thank you.

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

8 MS. SLAVIT: Nothing additional at this point.

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

12 DR. SILVERSTEIN: Yeah, I'm sorry to hear
13 about your experience. As a physician, that's
14 disappointing, obviously, but it's disappointing for
15 all of us. Just the one comment, and the question, I
16 think, focused on two different, very different
17 aspects of getting patient data, clinical study and
18 registry, and I think it's appropriate to put it in
19 the same question. But I would also say that registry
20 data is what we consider real world evidence, or real
21 world data. Five years ago I don't think we put much
22 stock into the value of registry data. I think

1 nowadays at the FDA, especially for children, where
2 data is very, very hard to generate under the best of
3 circumstances, we really do take seriously registered
4 data. As a reviewer myself, on several applications
5 I've accepted registry data as the proof either as a
6 control group or whatever. So, I would encourage
7 everybody, especially those that are here and on the
8 phone, to consider entering your child or your own
9 data into registries. And if you need to, I'm sure
10 Monica would be able to show you how to basically just
11 Google "registry" and put in -- and I'll bet you'll
12 find somebody who will get you some information about
13 how to do it. Because that data, even if it's just as
14 a control group, can be very, very useful to help
15 assess whether an intervention, a device or a drug is
16 beneficial.

17 So, I'm just curious, how many of you here
18 either entered your own or your child's data into a
19 registry over the last 10 years? That's great. For
20 those who didn't raise your hand, try every way you
21 possibly can to connect with people on social media.
22 I'm not a social media person myself, but connect with

1 people. I'll bet if I had a situation like yours and
2 I needed to, I would become a social media person
3 tomorrow. But try to use that, because it's extremely
4 important. And I'm speaking from the device world --
5 we do look at registry data very differently than we
6 did a few years ago. We see the value in it,
7 especially for rare diseases, which includes a lot of
8 pediatric diseases. So, it's a small pitch, but I'm
9 glad a lot of you are doing it.

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

21 So, I just want to turn over to Andrea, who
22 is going to be moving to the next portion of the

1 meeting, which is the open public hearing. Thank you
2 so much.

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

18 For transparency purposes, again, we ask,
19 please disclose if you are affiliated with an
20 organization or if your travel has been funded, or if
21 you have significant financial interest in rare
22 disease medical product development. As you are

1 speaking, you will notice that there will be a timer
2 and lights to guide you. The light will indicate you
3 can begin speaking, when it is green. It will turn
4 yellow when you have 30 seconds left in your time, and
5 the timer will turn red when your time has come to an
6 end. If you have not concluded your remarks at the
7 end of the allotted time, I will ask you to do so,
8 gently. As a reminder, you also have the option to
9 submit comments to the docket, which will remain open
10 until May 30th. You can find additional information
11 about this in the federal registered notice. So, with
12 that, let's get started with the first speaker. And
13 I'm calling up the first speaker, who is Kristin Moro
14 (ph).

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

21 I guess four years ago, when she was
22 diagnosed at age 9, we were noticing that her symptoms

1 of fatigue were minimal at that point, but upon her
2 diagnosis realizing that she would lose mobility,
3 there was risk of speech and vision loss, scoliosis,
4 cardiomyopathy, potential diabetes. We were very
5 eager to participate in any clinical trial.

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

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

22 MR. CAMPIAN: Good afternoon. Thank you. My

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

12 The plea is for cooperation. It is spelled
13 out in our recent whitepaper that we submitted,
14 Registries for Rare Diseases, a foundation for multi-
15 arm, multi-company trials. By working together, rare
16 disease stakeholders have an opportunity to create
17 broad-based registries that share common technology
18 platform and collect data to address all their needs.
19 The toughest challenge for these partnerships is not
20 finding a multi-tenant technology platform, but
21 getting people to cooperate, to agree on common data
22 definitions and to use a common data hub rather than

1 setting up separate registries for their natural
2 history studies, quality improvement projects, post-
3 market studies, or other projects.

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

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

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

1 MS. SHER: Good afternoon. I'm Rachel Sher,
2 Vice President for Policy and Regulatory Affairs at
3 NORD, the National Organization for Rare Disorders.
4 For those of you who don't know, NORD was founded in
5 1983, and we represent more than 290 individual rare
6 disease patient groups. We have been focused this
7 whole time on the identification, treatment and cure
8 of rare disorders through programs of education,
9 advocacy, research and patient services. We really
10 today just want to thank FDA for holding this meeting
11 and for its leadership on these issues.

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

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

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

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

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

21 MS. FURIA-HELMS: Thank you so much. And I
22 apologize if I mess up people's names. So, don't take

1 it personally; I'm doing my best. Next speaker is
2 Robyn Himick.

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

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

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

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

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

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

17 MS. CISCO: Hi there. Jill Cisco with
18 Acromegaly Community. I wanted to discuss just for a
19 couple moments, you know, we have an online community,
20 and although it sounds like some of the things that
21 happen online, that they're open. We have a closed
22 group that we interview every single person before we

1 allow them in. We only allow medically approved
2 documents to be posted. They have to be from
3 accredited sites. You know, we try to educate our
4 patients. Our last conference that we did, we held in
5 concession with the Pituitary Society, because we try
6 to put the correct information out to our patients.

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

22 MS. FURIA-HELMS: Thank you very much. The

1 next speaker is Christina Hartman.

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

21 But one of the challenges that I've seen --
22 you know, I've worked for HHS for the first third of

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

19 So, one of the things that EveryLife is doing
20 is we are asking Congress for \$1.5 million to do a
21 burden study to demonstrate the true public health
22 crisis of rare disease in the United States. And so

1 this would be a comprehensive study that the National
2 Academy of Medicine would do, and it would look not
3 only at direct medical costs of rare diseases, but it
4 would also look at the cost to caregivers and
5 families, the comprehensive societal burden. And I
6 hope that that would provide the justification
7 necessary to put the resources behind this and to
8 justify the collaboration across the Department of
9 Health and Human Services, including FDA.

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

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

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

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

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

21 In the past several years I've had the
22 pleasure and opportunity to help plan and moderate 16

1 externally led patient-focused drug development
2 meetings, four rare disease patient communities. Of
3 those 16 meetings I was involved with, my colleague,
4 Larry Bauer, and I, looked at the 11 published Voice
5 of the Patient documents that summarize the findings
6 of those meetings, and we want to share some of what
7 we found for the theme of this meeting today.

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

20 All the rare diseases except one that we
21 looked at shared the commonality affecting multiple
22 body systems; however, every community was still able

1 to identify one or two symptoms that most patients had
2 that caused the most severe impact. Every disease has
3 phenotypic variability with different symptom clusters
4 and different levels of disease severity, and every
5 rare disease has unmet medical need, and 8 out of 11
6 diseases cause premature death.

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

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

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

1 So, in the near future we plan to provide a
2 more detailed analysis of our observations from these
3 16 externally led meetings, including looking to
4 themes that we heard today -- things like pain, speech
5 impairment, sleep disorder, caregiver burden and more,
6 and we will be sure to provide those to the docket.
7 Thank you.

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

12 MS. YOUNG: Thank you. My name is Ni Young.
13 My name is Ni Young. I congratulate FDA at this time,
14 allow people to speak their own voices, but I have my
15 own consideration. One is this type of disease, I
16 need some professional to tell me is it preventable
17 and how many from here are allowed to speak, but how
18 many lost their loved ones? I suppose the statistics
19 should be variable, and this is maybe the result of
20 many call malpractice, and how are we going to train
21 the physician to do a better job, or the government to
22 have a better responsibility to supervise them, in a

1 sense? Otherwise, the people's complaint should be
2 documented. So, to count on physicians should be
3 avoided.

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

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

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

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

14 MS. FURIA-HELMS: Thank you very much. This
15 concludes the open public comment period, and we
16 appreciate and thank everyone for participating today,
17 not only in the OPC, but also today in the audience,
18 especially our panel members, the FDA panelists, the
19 folks online. Thank you so much for participating
20 today. And I just want to briefly thank the Patient
21 Affairs staff for all your hard work, along with the
22 Office of Orphan Products staff that has been really

1 working really hard to get this meeting to be
2 successful today, that I think we might have done a
3 good job there. So, thank you all.

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

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

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

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

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

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

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

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

19 And as you have heard, we really encourage
20 you to submit comments to the docket, which will
21 remain open until May 30th. We appreciate all the
22 feedback that we receive into the docket, especially

1 as follow-up today, as you maybe think about
2 additional issues or considerations that we didn't
3 have time to address today.

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

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

21 A transcript of this meeting should be
22 available within 30 days. And as I mentioned at the

1 beginning, we will work on a meeting summary document,
2 but we'll need to incorporate information from the
3 docket, which will remain open until the end of May.

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

8 [Applause.]

9

10

11

12

13

14

15

16

17

18

19

20

21

22

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

CERTIFICATE OF NOTARY PUBLIC

I, SAMUEL HONIG, the officer before whom the foregoing proceedings were taken, do hereby certify that any witness(es) in the foregoing proceedings, prior to testifying, were duly sworn; that the proceedings were recorded by me and thereafter reduced to typewriting by a qualified transcriptionist; that said digital audio recording of said proceedings are a true and accurate record to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.



SAMUEL HONIG

Notary Public in and for the

District of Columbia

1 CERTIFICATE OF TRANSCRIBER

2 I, SANDRA TELLER, do hereby certify that this
3 transcript was prepared from the digital audio
4 recording of the foregoing proceeding, that said
5 transcript is a true and accurate record of the
6 proceedings to the best of my knowledge, skills, and
7 ability; that I am neither counsel for, related to,
8 nor employed by any of the parties to the action in
9 which this was taken; and, further, that I am not a
10 relative or employee of any counsel or attorney
11 employed by the parties hereto, nor financially or
12 otherwise interested in the outcome of this action.

13
14 

15 SANDRA TELLER
16
17
18
19
20
21
22

&	20 18:14 79:2	3:01 95:8	66:12 70:21,22,22
& 155:17	90:12 107:13	3:15 95:9	71:1 103:19
1	152:4	4	127:20 166:10
1 44:9 63:2 78:15	20/20 78:3	4 49:14 115:13	167:7
127:6,7 142:18	2000s 82:6	123:9	able 27:5 31:13
1.5 153:20	2016 84:20	45 19:6	35:9 37:17 38:1
10 2:4 15:10,18	2019 1:10	5	38:21 43:14 47:10
32:7 39:11 63:16	209 125:13	5 121:3	66:2,14,18 69:4
77:22 83:22	20993 1:15	50,000 78:16	70:9 79:6,8 83:10
126:16 137:4	21 73:9	50/50 121:2,9	83:12,14 86:19
139:19 144:3	21st 84:21 85:5	500 96:2	88:2,5 89:12 93:5
100 26:6 93:16	22 70:1 96:20	6	93:11 100:11
152:17	22nd 74:5	6 55:21 97:17	103:12 113:8
10903 1:13	23 2:5 96:21	116:2 123:9 135:4	115:3 130:11
10th 143:6	107:18 116:21	60 25:8 55:3	134:12,22 139:10
11 71:14,18 98:12	24 50:17 105:12	60,000 78:16	141:13 156:22
156:4 157:5	113:9	7	abnormal 148:10
12 106:2	25 137:3	7 77:22	absence 98:16
13 25:7 105:16	26 77:8	7,000 4:21 94:3	absolute 100:12
142:17	262 125:11	8	absolutely 29:3
14 105:16	28 18:14 34:22	8 77:22 97:17	49:22
142 3:9	73:8,10	108:7 123:19	academia 11:12
14826 167:14	29 1:10	157:5	academy 154:2
15 32:7 33:20	290 146:5	80 55:3	accelerate 119:11
63:16 83:22 95:8	2:00 124:11	81 2:18	119:11
1503 1:14	2s 126:17	9	accelerating 148:6
16 46:18 155:22	3	9 142:22	accepted 41:10
156:3 158:3	3 2:3 44:3,9 63:1	95 61:22 62:2	139:5
160 3:10	64:21 74:6 97:18	120:14 121:8	access 5:7 50:6
16351 166:17	124:12 127:7,7	153:9	91:19 128:4
17 32:9	135:16 154:18	96 2:19	134:12 148:7
18 25:4,7 74:15	3,200 130:8	a	150:9
126:18	30 4:22 12:19	a.m. 124:12,12	accessibility 149:6
19 115:8	59:10 74:10 79:2	abdomen 131:3	accessing 103:21
1983 6:8 146:5	107:13 142:4	abernathy 2:18	accident 106:6
1:00 1:11	164:22	15:6 79:22 80:1	accommodate
1s 126:16	30th 12:14 22:19	80:10,18 81:2,3	22:13
2	59:5 79:17 142:10	90:5 92:1 93:16	accommodated
2 15:8 92:10 95:15	163:21	abilities 18:12	15:17
108:2 124:12	31 1:14	ability 32:14	accomplish 13:12
127:6	3156041 1:17	48:11 65:21 66:3	162:12
2-1/2 43:20	35 82:8		account 127:5
	350 125:14		144:1

<p>accredited 151:3 accurate 37:6 166:9 167:5 accurately 9:6 achieve 6:21 112:9 achieved 112:1 acids 108:6 acknowledge 6:17 acknowledges 14:15 acpmp 129:15 130:2 acromegaly 73:3 73:15,16 150:18 acronyms 125:11 act 84:22 acting 2:17 15:5 17:15 58:5 73:7 73:22 80:2,7 86:11 action 70:3 166:12 166:16 167:8,12 active 29:22 40:1 activities 16:8 19:13 26:19 66:5 100:4 149:21 157:8 activity 45:15 actual 68:10 acute 24:1 59:22 60:1,2 106:21 add 43:11 55:8,19 57:17 69:10 114:1 adding 59:8 addition 6:3 38:16 96:3 153:6 additional 99:10 138:8 142:10 148:21 158:9 164:2,13 address 7:15 46:12 48:1 99:8 129:6 144:18 164:3</p>	<p>addressed 14:5 27:20 112:6 addressing 7:12 16:9 111:21 adds 148:21 162:8 adequately 28:20 adjustment 47:6 48:19 administer 79:11 administered 122:6 administration 1:1 47:16 157:20 administrative 11:18 adobe 15:1 adored 102:12 adrienne 2:14 18:19 23:7 30:15 38:19 44:18 45:22 59:13 62:15 67:22 adult 25:9,10 32:21 36:18,18 98:11 127:6 adults 19:10 24:10 29:7 40:19 64:1,1 96:20 127:8 advance 6:1 7:19 13:11 80:10,19 86:3 91:19 advanced 2:12 3:3 19:13 25:10 81:21 82:17 91:5 advancement 114:10 advances 5:9,15 adversely 159:6 advice 88:10,11 88:18 92:13 advocacy 11:11 19:8 29:7,22 120:4 130:1,4 136:12 146:9 152:5 155:8</p>	<p>161:12 advocate 18:6 19:9 68:11 80:21 85:17 154:17 advocates 8:3 16:16 101:16 144:4 aetna 55:18 affairs 2:6,7,20 6:16 10:19 11:2 13:14 16:5 17:1 20:12 21:4 86:4 146:2 147:12 160:21 163:15 affect 5:4 61:16 65:20 69:17 86:14 affiliated 14:16 141:19 affordability 149:6 afternoon 4:2 10:20 13:7 15:8 15:12 20:2,13 54:14 97:15 143:22 146:1 155:11 age 18:14 34:2 37:2 44:21 115:13 142:22 154:18 agency 6:18 agency's 80:4 agenda 13:7 80:10 agent 127:10 aggressive 73:19 agitate 92:18 agnostic 131:13 ago 39:6,12 96:21 130:2 138:21 140:6 142:21 144:9 149:18 agree 93:16 144:21 146:17 aha 106:6</p>	<p>ahead 26:4 41:14 136:10 ahmad 154:11,12 154:12 aid 41:9 air 23:16 aisle 14:21 141:15 alexandra 97:17 97:18 align 88:4 allergic 71:21 allotted 142:7 allow 4:11 17:5 116:7 151:1,1 158:14 allowed 15:21 158:17 alluded 33:7 127:20 als 18:12 32:3 alternative 54:3 146:21 alternatives 63:20 alzheimer's 18:13 amazing 51:13 108:8 ambassador 70:4 ambulation 18:2 american 98:4 amount 54:1 71:3 73:13 135:19 156:18 amy 2:18 15:6 79:22,22 amyloid 148:11 amyloidosis 148:4 148:9,13,16 149:2 149:4 150:1,8 analyses 145:13 analysis 158:2 andrea 2:4,7,20 10:18 11:1 20:12 21:4,11 22:22 140:21 155:12</p>
--	---	--	---

<p>anemia 26:16 anemic 23:21 angelman 49:15 49:20,21 50:15,20 52:8 angry 31:11 animal 63:21 ankrd11 51:5 anna 142:16 annette 51:2 announcement 93:22 announcements 11:18 anonymous 14:11 answer 29:3 53:3 82:22 83:10 89:22 162:19 answered 104:7 119:3 answers 83:4 anti 74:15 75:1 antibiotic 71:21 antibiotics 71:22 anticipate 38:22 anxiety 53:20 anybody 26:12 35:20 45:20 46:14 50:21 52:3,12 66:22 69:9 104:1 104:6 117:6 123:1 125:19 134:20 138:10 anymore 124:18 anyone's 34:8 anyway 66:15 125:2,6 apologize 147:22 apparent 39:9 appearance 73:18 appendix 129:17 131:2,11,12 applause 95:1 165:8</p>	<p>applications 139:4 appreciate 8:11 11:8 77:4 81:6,7 99:5 160:16 161:8 163:21 165:6 appreciated 163:1 appreciation 28:10 appreciative 77:7 81:4 164:12 approach 141:13 146:17 approached 112:22,22 113:2 appropriate 50:3 50:7 112:7,11 138:18 148:19 approval 64:9 approved 5:6 31:19 66:17 73:5 117:14 148:12 149:3,5 151:1 153:11 approximately 12:17,19 april 1:10 arc 148:5,5 149:12 archived 20:16 area 12:2 14:13 29:8 134:10 154:16 155:1 areas 86:4 arm 144:15 art 9:18 10:3 articulate 156:16 artificial 103:11 artists 10:3 aside 15:11 66:14 asked 40:15 42:5 45:9 77:5 88:9 129:4 asking 22:2 23:5 69:21 82:19 117:14 153:20</p>	<p>asks 84:22 85:7,12 aspect 31:20 32:6 53:11,13 73:20 151:16 aspects 9:11 28:16 28:19 65:3 87:18 111:11 138:17 150:3 assess 4:13 7:5 8:13 111:17 139:15 assistance 66:1,2 associate 17:15 155:16 associated 162:20 association 145:5 asthma 45:2 asymptomatic 30:20 ataxia 2:15 17:19 17:21 49:1 142:18 attend 94:16 127:21 attended 161:6 attendees 11:21 15:3 17:9 attending 10:11 164:19 attention 48:13 57:4,10 136:21 attorney 166:14 167:10 attr 149:4 audience 8:3 15:13 40:11 41:19 41:22 42:4 43:2 54:12 55:8 56:16 59:12 69:12 71:5 71:8,11 75:12 95:7,16 96:1 99:12 122:21 125:20 126:3 138:10 140:13 160:17 161:7</p>	<p>audio 11:20 166:8 167:3 autism 51:19,19 58:8 74:8 75:3 98:17 117:10 availability 5:7 available 12:10,17 12:18 62:16 76:8 90:17 91:21,22 92:11 107:15 128:2,5 149:12 162:16,18 164:22 avenue 1:13 aversion 77:13 avoided 159:3 aware 143:9 awareness 120:5 154:21 155:7 awful 60:2 axis 19:8</p> <p style="text-align: center;">b</p> <p>baby 105:11 back 22:2,10 46:14 56:10 59:9 59:11 76:13 95:9 96:7 102:7 103:13 106:1,4,11,15 109:3,18 134:11 145:14 164:16 backbone 101:8 backed 36:7 background 20:5 20:11 67:9 116:21 bad 41:13 60:20 107:20 badges 164:17 baffling 104:19 balance 31:6 38:9 38:15 39:14 40:8 41:8 65:21 150:12 162:17 balancing 40:2 baltimore 143:8</p>
---	--	--	---

<p>barrier 134:18</p> <p>barriers 54:19 55:5 121:22</p> <p>basal 46:22</p> <p>based 65:7,19 144:10,17</p> <p>baseline 92:3</p> <p>basic 50:2 149:21</p> <p>basically 23:14 100:7 108:2 111:16 118:5 139:10</p> <p>basics 103:21</p> <p>basis 58:15 109:21 130:15 162:10</p> <p>battled 32:9</p> <p>bauer 156:4</p> <p>beat 126:13</p> <p>beautiful 10:4 95:3</p> <p>beckett 98:13 114:20</p> <p>becoming 72:5 93:8</p> <p>bed 105:9</p> <p>begged 118:6</p> <p>begging 118:5</p> <p>beginning 61:21 63:5 64:2 68:10 69:2 143:10 165:1</p> <p>behalf 52:8 129:15 148:4 161:5</p> <p>behavior 31:9 56:8 116:10 118:20</p> <p>behavioral 51:6 51:10</p> <p>behaviors 98:18</p> <p>belief 30:6 127:15</p> <p>believe 45:9 52:19 120:2,20 121:6 160:3</p> <p>ben 96:19,20</p>	<p>benadryl 60:18</p> <p>benchmark 101:10</p> <p>beneficial 139:16</p> <p>benefit 53:1 66:6 67:15,17 112:2 135:8 160:6</p> <p>benefited 100:3</p> <p>benefits 37:9 59:15,18 61:4 62:16 65:17 71:9 78:13 157:15</p> <p>benjamin 102:1</p> <p>best 22:13 36:16 50:8 112:20 117:5 127:15 139:2 148:1 166:9 167:6</p> <p>bet 139:11 140:1</p> <p>beth 77:1</p> <p>better 40:5 56:10 65:20,21 74:1 85:8 87:5 114:9 158:21,22 159:7 159:16 160:12 163:8</p> <p>beyond 9:17,21 10:1,7 39:20 94:1 94:6,7,8 138:2</p> <p>big 31:9 32:4 34:8 44:4,15 58:13 64:6 130:22 131:22 159:5</p> <p>biggest 53:9 63:2 66:11 90:14 102:22 119:10,14 151:7</p> <p>bile 107:7,7 108:3 108:6</p> <p>bilirubin 107:18</p> <p>billion 123:19</p> <p>bioavailability 131:9</p> <p>bioinformatics 80:18</p>	<p>biologics 5:16 6:7</p> <p>biomarker 117:18</p> <p>biomarkers 32:5 32:11 118:13 119:1 133:8 143:14</p> <p>biomedical 86:21 88:6</p> <p>biorhythms 70:15</p> <p>biotech 100:16</p> <p>biotin 46:21 47:11</p> <p>bipolar 33:16</p> <p>birthday 143:6</p> <p>bit 11:4 14:2 24:16 25:12 26:18 33:7 41:15 42:16 46:3,12 49:7,7 54:7,10 81:14 87:2 96:11,15 99:16 104:9,10 114:14 122:12</p> <p>bite 122:19</p> <p>bitty 122:17</p> <p>bless 136:19</p> <p>blind 77:19</p> <p>blindness 77:21</p> <p>block 25:3</p> <p>blog 124:1</p> <p>blogging 124:9</p> <p>blood 19:1 23:14 25:2 70:10 97:2,3</p> <p>bloodstream 107:8</p> <p>bloodwork 74:19 74:20</p> <p>bloody 84:16</p> <p>blow 44:16</p> <p>blunt 120:17,18</p> <p>board 18:15 55:14 98:4 101:14</p> <p>bodies 30:9</p> <p>body 19:5 23:15 25:7 44:17 73:17 97:3 107:8 156:22</p>	<p>157:17</p> <p>bone 19:4 23:18 30:1 61:6</p> <p>bones 60:18</p> <p>bonita 54:14</p> <p>bonita's 55:9</p> <p>bootstrapped 132:16</p> <p>born 18:21 96:20 97:18 99:22</p> <p>boston 126:13</p> <p>bound 118:2</p> <p>boundaries 84:9</p> <p>bounding 82:11</p> <p>bowel 131:1,5</p> <p>box 15:3</p> <p>boy 132:4,9</p> <p>boyfriend 124:16</p> <p>boys 43:11 72:11 152:9,9</p> <p>brain 24:8 58:2 60:16 94:15 97:3 97:5,9</p> <p>brainstorming 130:13</p> <p>branch 20:1</p> <p>brave 61:5 155:15</p> <p>break 15:7 88:16 95:8,11</p> <p>breath 48:4</p> <p>breathing 45:4</p> <p>breathless 48:5</p> <p>bridge 10:17 99:3</p> <p>bridging 1:7 4:5 10:22</p> <p>brief 114:17</p> <p>briefly 47:17 160:20</p> <p>bright 106:13</p> <p>bring 14:10 49:18 81:15 141:16</p> <p>bringing 145:7</p> <p>british 90:13</p>
--	---	---	---

broad 144:17 broken 140:18 brought 34:6 47:2 102:13 117:16 136:20 build 33:1 86:18 144:4 building 1:14 13:2 84:6 107:7 builds 8:7 bunch 137:18 burden 24:3 34:13 148:22 149:15 150:2 153:21 154:5 158:5 159:4 burdens 149:11 burdensome 23:11 38:6 49:10 49:17 56:3 149:18 busby 3:6 97:15 97:16 104:12 108:15 109:18 110:12,22 114:1 businesses 159:12	cancer 80:14 82:17 93:2 126:15 129:17,19 131:2 131:11,12 capabilities 86:16 87:21 capacity 127:21 capillary 25:3 caps 54:20 capsules 131:6 capture 9:6 22:9 42:7 140:20 capturing 20:18 car 143:12 159:13 159:15 cardiac 18:2 cardiomyopathy 143:4 care 20:6 26:15 28:12,22 29:1,6 29:11 32:20,20,21 45:11 50:7,11 57:1 70:10,22 80:20 81:19 82:18 83:19 98:2 111:11 111:12 143:11 144:7 145:18 150:11 career 33:2 79:7 81:19 153:1 caregiver 18:9 22:9 23:8,10 68:14 76:16 85:16 89:15 96:11 104:9 134:21 158:5 caregivers 4:10,20 7:11,14,17 8:3,8 8:13 11:15 12:9 13:21,22 16:15 21:6 42:13 50:14 50:18 51:14 64:1 89:20 126:3 129:17 130:14 149:14 150:6,10	154:4 155:14 156:13 caretaker 44:11 caring 30:18 79:8 103:2 caroline 2:15 17:18 38:3 40:12 41:1 48:3,10 65:14 142:18 carrier 77:18 cart 65:22 case 12:22 70:18 catches 45:1 category 27:14 cause 18:2 19:3 60:14 97:5 157:6 157:10 162:21 caused 51:4 115:17,19 157:2 causes 27:19 75:2 97:1,1 98:15 150:1 causing 71:20 cber 2:13 6:14 19:12 69:12 75:15 cder 2:8 6:14 17:17 cdrh 2:11 3:2 6:14 cell 2:14 18:21,21 19:9 23:9 26:16 29:15 40:16 62:1 62:1 68:9 91:7 136:15 137:9,14 cellphones 11:19 cells 19:1 25:3 68:20 center 17:17 19:22 28:21 67:2,3 68:9 146:15 centered 80:20 centers 6:14 67:3 100:5 central 32:2 78:2 78:3 91:4 113:21	124:13 136:3 century 84:21 85:5 ceo 51:3 99:2 certain 67:17 135:18 certainly 98:1 certificate 166:1 167:1 certify 166:3 167:2 chair 122:4 challenge 31:20 34:10 42:20 64:18 77:16 133:9 144:19 153:4 challenges 7:1,12 34:20 38:22 43:13 55:12 119:20 121:6 152:21 157:18,20 challenging 27:7 31:16 36:5,9 42:17 65:13 77:11 128:4 148:19 chance 49:2 79:15 112:20 121:2 151:13,17 chances 123:20 change 24:15 29:11,14 41:8 68:18 77:13 121:8 124:10 126:21 138:2 changed 39:4 118:12 149:2 changes 39:8 51:15 changing 68:12 103:14 channel 37:21 channeling 130:6 130:14
c			
c 1:14 4:1 calderon 101:7 calendars 27:3 california 109:22 143:8 call 29:7 70:5 89:11 121:9 138:1 141:11 158:20 called 19:8 43:10 44:10 49:15 57:16 84:21 98:13 135:6 137:11 141:16 147:2 calling 142:13 campaign 70:5 campian 143:21 143:22 144:1 campus 1:12 11:5 39:14			

<p>channels 86:8</p> <p>charlotte 43:9,14 43:19</p> <p>chat 15:1,3</p> <p>chattanooga 155:1</p> <p>check 122:22 147:7</p> <p>checking 15:2 70:10</p> <p>chi 70:5 100:14</p> <p>chief 2:18 15:5 80:2,7 81:12 86:11</p> <p>child 18:21 25:9 26:20 28:2 32:20 32:20 36:19 50:1 67:11 76:1,10,12 79:7,9 111:14,18 112:2,11,12,13,15 112:20 113:4 116:7 122:4 123:7 126:15,20 139:8</p> <p>child's 111:18 112:5,7 124:15 139:18</p> <p>childhood 33:22 152:10</p> <p>children 5:4 19:7 24:9 40:16 45:8 46:4 49:20 50:4 56:19 57:1 61:22 62:2 71:1 78:11 78:18 79:11 96:19 97:17 98:8,9,11 101:11 111:12 112:18 115:2 121:18 139:1 153:9</p> <p>children's 100:5 109:20 111:11 115:11 118:7 120:9</p>	<p>chittooran 2:6 13:14 20:10,10 21:1,2,3 24:14 25:11 26:12 28:8 30:15 33:6 35:1 35:19 38:3 39:3 39:16 40:10,21 41:16 42:3 44:6 45:19 46:11 47:18 49:4,6 50:21 52:2 52:10,16 54:6 55:6 56:15 57:14 58:16 59:2 62:9 64:10 65:14 66:7 66:21 67:22 69:9 69:20 71:4 73:2 74:2 75:10 76:20 79:1,12 90:3 94:21 95:2,12 97:14 98:6 99:6 101:1 102:6 104:1 108:9 109:9 110:6 113:22 114:11 119:4 122:20 123:4 126:1 129:12 132:17 133:10 134:19 135:12 136:9 138:4,9 140:10</p> <p>chock 47:14</p> <p>chocked 90:6</p> <p>choice 127:16 128:7</p> <p>choices 33:2 128:14</p> <p>choked 90:7,9</p> <p>cholestasis 97:19</p> <p>choose 16:12 65:3 132:7</p> <p>chop 103:1,11</p> <p>chorea 31:5</p> <p>choroideremia 77:2,18 78:14 135:15</p>	<p>chose 136:7</p> <p>chris 98:9</p> <p>christina 43:8 152:1,2</p> <p>christmas 117:5,5</p> <p>chromosome 74:6</p> <p>chronic 28:2,3 56:2 59:22 71:21 72:4</p> <p>cincinnati 17:20 39:11</p> <p>circulate 19:3</p> <p>circumstances 139:3</p> <p>cisco 73:3,3 150:16,17,17</p> <p>clarify 26:13 40:14,20</p> <p>clark 38:10 39:17 48:15 54:10</p> <p>clear 136:15 137:9 137:14 164:6</p> <p>clearly 52:22</p> <p>clinic 82:2,7,14,16 83:7</p> <p>clinical 4:14 5:20 9:13 13:19 19:14 19:14 29:18,19 30:5 35:8 36:20 46:21 63:4 67:7 68:7 75:19 76:1,7 76:10,12,14 77:3 80:16,16 85:9 88:1 95:18 99:15 99:21,22 100:8,20 100:21 102:7 103:18 104:11 108:14 109:10,14 110:10,11 111:14 112:10,16 117:22 118:3,13,14 119:6 120:1,13,14,16,21 126:8,8,16,18,19 127:22 128:1,4,13</p>	<p>128:14,20 130:20 131:13,19 132:15 132:20 133:1,12 134:21 135:6,11 138:17 142:20 143:5,16 151:9,21 153:7 160:4,13 163:1</p> <p>clinicaltrials.gov 107:14 108:1,12 112:4</p> <p>clinicaltrials.gov. 133:4,5</p> <p>clinician 72:9 118:9,11</p> <p>clos 155:6</p> <p>close 104:4 125:14 128:2 140:15 165:7</p> <p>closed 150:21</p> <p>closely 147:16</p> <p>closest 37:15</p> <p>closing 3:10 16:1 20:20</p> <p>clusters 157:3</p> <p>cocktails 74:17</p> <p>coerce 125:16</p> <p>coffee 12:1</p> <p>cognition 52:18</p> <p>cognitive 18:12 24:10 28:18 31:3 31:13 32:5,12 53:14 57:11 65:5</p> <p>cohort 57:19 127:9</p> <p>cold 45:1,5,6</p> <p>colicky 104:22 105:21</p> <p>collaborates 6:9</p> <p>collaboration 6:18 148:8 153:2 154:8</p> <p>colleague 22:6 77:17 101:7 156:3</p>
--	--	--	---

colleagues 17:12 22:3 75:11 99:9 144:8 collect 14:22 93:5 144:18 collected 101:5 collecting 117:15 collects 144:5 color 13:15 columbia 166:20 combination 60:5 come 15:17 24:7 64:7 84:17 87:14 88:16 99:5 104:20 111:10 118:8 131:19 142:5 comes 36:20 50:2 67:11 72:2 122:3 130:9 comfortable 29:14 43:4 48:22 coming 9:14 77:4 80:12 82:2,6 131:14 135:2 146:12 comment 3:9 14:14,20 15:9,10 15:12,14,19,22 26:17 40:17 55:9 75:14 76:21 93:3 111:3 138:15 141:8 158:11 160:15 commenters 15:18 comments 8:19 12:15 15:1 28:10 59:1,6 76:16 79:16 140:19 141:14,17 142:9 144:9,10 145:10 163:20 commissioner 2:17 15:5 19:18 20:4 80:2,3 81:12	85:21 86:11 commitment 64:6 81:1 109:14 133:18 commitments 85:22 128:3 committed 6:20 7:14 common 7:18 13:10 37:3 45:7 47:1 55:13 66:10 66:10 78:13 103:7 113:7 144:17,21 144:22 156:8 commonalities 1:7 4:5,13 7:5,10 8:1 8:13 10:22 44:13 87:8,10,14 95:18 161:16,17 162:1,2 162:5,13 commonality 90:10,15 97:11 156:21 commonly 69:14 communicate 43:14,22 50:1 88:6 communicating 137:2 communication 50:4 51:11 86:8 162:3 communities 35:14 37:10 61:4 71:12 76:2 88:10 117:10 145:7 156:2,11 157:19 community 10:7 18:7,7 27:17 36:1 45:10,12 50:13,15 50:20 58:7 61:11 69:16 70:16 73:4 74:18 75:17,21 80:22 86:21 89:15	89:16 91:11,11,14 91:18,18 92:9,17 92:18 93:1,7,13 101:3,3,8,10,15 116:17 117:9,20 118:17 119:13,17 123:11 135:6 150:18,19 153:5 153:10 154:22 156:22 157:11 community's 30:6 comorbid 18:3 44:18 comorbidities 74:14 75:5 compadres 89:10 companies 54:19 67:7 100:16 company 80:15 84:11 135:5 144:2 144:15 compare 92:6 compared 39:15 92:4 comparing 62:18 comparison 114:22 compassion 88:21 89:1,4,19,20 compelling 102:5 complaint 51:6 151:10 159:1 complaints 151:7 complete 106:6 164:11 completed 164:20 completely 40:18 49:21 complex 50:4 150:8 163:2 complexity 162:9 complicated 121:5 complications 61:1 149:10	component 58:8 93:3 compound 47:8 47:11 comprehensive 101:21 154:1,5 compresses 131:4 131:4 computer 80:9 83:16 84:6 concern 44:4,15 143:17 concerned 30:22 134:1 concerns 46:6 133:19 136:2 concession 151:5 conclude 15:8 concluded 142:6 concludes 15:4 160:15 condition 37:18 37:18 43:7 71:9 73:5 75:22 96:12 98:13,16 101:6,9 conditions 5:18 8:10 9:20 21:18 32:3 43:13 45:3 87:6 153:12 conducting 67:19 conference 151:4 confident 83:5 conflicting 133:19 confront 136:20 congenital 3:5 70:1,2 96:21,22 99:20 100:6,14 101:3 113:5 congratulate 158:13 congress 84:20 153:20 connect 15:1 37:17 38:1 139:21
--	---	--	--

<p>139:22 163:14,15 163:16 connected 16:2,7 16:8 37:20 113:15 connection 37:16 consequences 157:10 consider 8:18 9:11 59:19 65:17 66:8 67:4 102:8 109:13 109:17 111:14 138:20 139:8 consideration 7:21 102:22 158:15 considerations 4:14,15 13:18 21:14 95:19 127:17 129:5 164:2 considered 29:18 67:12,15,18 108:13 137:9 considering 79:19 111:13 113:11 114:4 119:7 133:13 149:12 considers 126:10 consistent 156:11 consistently 104:14 consortium 128:16,20 148:5 constipation 57:20 60:15 constituents 130:7 constraints 132:12 contact 12:7 16:10 16:11 124:21 context 88:3,7 continue 80:9,19 81:9 84:5,14 88:14 92:14,18</p>	<p>116:7 147:15,18 163:10 164:10 continued 3:1 146:18 continuing 89:8 continuity 27:15 continuous 73:13 86:15 contribute 11:9 16:19 contributed 10:4 161:8 contributing 81:6 control 51:7,15 127:13 139:6,14 151:9 controlled 97:4 controls 117:8 conveniently 148:20 conversation 31:10 48:20 56:5 68:4 81:15 87:15 122:22 conversations 82:14 cool 69:4 cooperate 144:21 cooperation 144:12 coordination 13:15 98:20 copays 54:20 copies 12:18 copy 91:14 core 85:20 correct 30:20 151:6 corrected 30:10 correctly 58:4 cost 127:17 134:4 154:4 costs 91:20 154:3</p>	<p>couch 82:12,14 counsel 166:10,13 167:7,10 counseling 57:7 count 159:2 counter 47:13 countless 74:7 countries 128:22 country 94:4 128:9 132:7 couple 22:18 43:1 54:12 59:10 69:12 87:4 95:4 96:14 131:22 132:14 135:1 136:10 144:9,11 150:19 151:9 coupled 150:9 course 24:3 26:1 30:7 58:2,6 60:2 98:18,20 115:1,7 116:13 117:13 118:19 119:13 152:11 153:18 courtesy 17:5 cover 55:14 104:16 131:17 coverage 50:3 55:17 72:18 153:15 covered 56:14 57:3 crazy 121:10 124:20 create 69:3 89:12 120:8 144:16 147:5 created 133:5 creating 101:21 crew 20:17 crisis 153:22 criteria 35:8 64:19 130:18,21 131:7 131:10</p>	<p>critical 7:12 86:3 92:2 93:6 110:9 121:13 critically 5:8 7:4 129:7 cross 6:18 crossed 152:20 crossover 75:3 culmination 41:11 curation 37:5 curative 30:2 cure 30:7 32:7 79:7 146:7 148:12 cured 30:9 cures 36:21 37:8 84:22 85:6 curious 49:9 67:9 126:6 139:17 curly 82:7 currently 47:5 64:20 66:16 109:19 125:12 133:20 135:7 148:12 152:16,18 153:10 159:8,13 cut 80:5 cycling 102:18 cystic 145:4</p>
			d
			<p>d 2:1 4:1 da 44:1,1 dad 34:11 daily 7:18 49:22 62:7,7 66:5 149:21 157:8 damage 19:5 26:10 30:8 97:5 dan 144:1 daniel 143:21 danlos 46:2 54:15 54:18 94:14 data 5:21 63:21 80:8,15,16 85:8 86:17 90:10 91:8</p>

<p>91:19 92:2 93:5,5 93:10,12 102:3 116:18 117:15,17 117:21 119:1 120:20,21 125:5,6 127:5,6,6 134:15 137:5 138:17,20 138:21,22 139:2,4 139:5,9,13,18 140:5 144:2,18,21 144:22 145:12 146:21,21 147:5 163:4,4</p> <p>database 125:13 databases 125:9 date 1:10 daughter 23:8,11 28:12,16 29:1 43:9,14 49:14 55:10,22 56:3,18 56:22 57:5,6 61:15 74:13 88:22 104:13 105:7 106:12,20 109:2 132:13 135:3 136:15 137:2 142:16 152:7 153:7 154:17</p> <p>daughter's 26:18 28:3,22 104:10 153:5</p> <p>daughters 152:13 david 159:19 day 1:2 9:22,22 32:8 36:2,2 38:18 40:7 42:20,20 50:17 69:18 70:16 73:9,14 77:12,13 80:4,4 81:22 87:8 105:12 107:13 113:9 114:2 117:5 122:3 128:18 130:3 162:10,10</p>	<p>days 12:19 34:18 73:8,10,10,21 116:6 164:22</p> <p>dc 123:15 152:6 deal 24:13 25:10 38:20 53:13 78:18 87:20 113:6</p> <p>dealing 65:11 70:13 124:3</p> <p>death 97:5 118:7 122:3 157:6</p> <p>deborah 129:15 december 84:20 decided 33:10 deciding 102:8 103:5 126:11 133:13</p> <p>decision 33:13 34:6,7,8 36:3 59:19 60:6,7 65:17 108:17,19 109:1 128:13 134:6</p> <p>decisions 31:14 163:2</p> <p>decline 31:13 57:11</p> <p>decreased 143:15 dedicated 5:12 dedication 6:12 deductibles 54:20 deficiencies 71:18 deficiency 71:15 72:13</p> <p>definitely 33:21 34:7 36:5 37:13 38:8 41:8 53:12 64:17 98:3 113:11 123:6 164:4</p> <p>definitions 144:22 degenerative 17:22</p> <p>degree 91:4 136:3</p>	<p>delay 35:2 delayed 51:12,12 64:11 148:16</p> <p>delays 148:17 delighted 15:4 delightful 102:12 delivery 136:6 demonstrate 5:17 153:21</p> <p>denial 33:21 department 154:8 depending 36:17 114:5</p> <p>depends 59:21 112:8</p> <p>deposit 148:10 depressed 31:12 65:8</p> <p>depression 31:22 33:16,17 53:20 102:14</p> <p>depths 102:14 deputy 2:17 15:5 80:2,3 81:12 85:21 86:10</p> <p>derived 83:6 derm 106:7 dermatologist 106:4,7</p> <p>description 26:15 design 7:22 9:12 68:10 76:17 120:13 126:21 127:7 129:1 160:5 160:13</p> <p>designate 5:22 designed 21:21 127:2 128:18 131:19 149:13</p> <p>designing 120:22 145:19</p> <p>designs 120:16 desire 127:19 157:12</p>	<p>desk 12:20 desperate 102:15 122:10</p> <p>desperation 112:15 122:10</p> <p>detail 110:14 detailed 158:2 deteriorates 18:11 determination 143:19</p> <p>determined 118:2 develop 6:5 9:3 88:4 97:4 101:13 113:18 148:13,14</p> <p>developed 149:13 developing 6:21 7:13 9:9 85:11 89:17 100:20</p> <p>development 5:10 5:13,14,15,20 6:1 6:4,6,9,12,16 7:6 7:20,21 9:5,11 10:14 13:12 14:18 16:6 19:18 63:4 64:12 68:7 69:2 85:1,2,11 101:20 116:19 119:14 141:22 146:15 148:7 155:20 156:1 160:2 161:12 163:5,11 163:17 164:7</p> <p>developmental 50:12 98:14 device 90:19 100:10 139:15 140:4</p> <p>devices 2:11 5:16 6:7 11:19 19:22 20:1 67:4 80:7</p> <p>diabetes 18:3 92:10 143:4 diabetic 103:9</p>
---	--	--	---

<p>diagnosed 33:19 56:6 71:13,19 77:20 107:10 115:13 123:8 126:14 130:1 132:3 142:17,22 149:17 152:8 154:17 155:2</p> <p>diagnosis 5:17 9:18,21 10:1,7 26:22 39:13 41:11 41:12 46:20 55:15 55:16 56:13 61:19 94:2,7,9 123:10 143:2 148:16,18 153:17,17 157:19</p> <p>dialogue 13:9 16:19</p> <p>dicey 113:19</p> <p>die 62:2 121:15 152:10</p> <p>difference 26:7 34:16</p> <p>differences 7:3 44:20 87:9,11 161:15</p> <p>different 21:16,17 21:19 24:21 35:14 35:15 37:18 39:15 39:15 45:13 52:4 52:18 54:16 55:1 61:19 65:3 74:10 76:2 82:2 86:20 92:3,8 102:18 106:2 113:12 115:1,8,19 118:21 125:11 126:16 136:18 137:10 138:16,16 157:3,4</p> <p>differentiate 28:1</p> <p>differently 53:4 140:5</p> <p>difficult 28:10 43:15 47:7 48:7</p>	<p>57:13 74:17 79:11 123:10 133:6 136:5 160:8 162:7</p> <p>difficulties 18:4 43:12 45:4 162:14 162:21</p> <p>difficulty 42:11 52:9 133:17 162:4</p> <p>digestive 99:1 131:4</p> <p>digital 166:8 167:3</p> <p>direct 154:3</p> <p>direction 84:13 159:8</p> <p>directly 4:10 8:8 8:12 144:7</p> <p>director 4:6 11:1 17:15 19:17 20:3 70:2 99:20 144:2</p> <p>directors 98:4</p> <p>directs 80:5</p> <p>disabilities 103:16</p> <p>disability 74:8 98:15 103:19 115:17</p> <p>disabling 5:1</p> <p>disappointing 138:14,14</p> <p>disclaimer 13:15</p> <p>disclose 14:15 141:19 154:13</p> <p>discovered 84:8 98:22 126:19,20</p> <p>discovery 63:22</p> <p>discuss 150:18</p> <p>discussing 53:5</p> <p>discussion 14:6,8 16:15 22:12 53:1 59:12 61:14 72:6 95:16 130:18 145:9</p> <p>discussions 13:13</p>	<p>disease 1:2 2:16 5:13 6:8,12,22 8:11 9:17 14:13 14:18 17:22 18:1 18:7,7,9,10,15,17 18:21,22,22 19:10 20:8 21:16 23:9 23:13,14 24:20 25:5,5,6,6,10 26:5 27:1,18 28:2,3,16 28:19 29:15 30:18 30:19 31:2,19 32:2,13 33:18 34:21 36:22 37:4 41:1 42:14 43:7 44:8,20 54:1 57:19 58:7 59:18 62:16,21 65:16 71:9 73:1,4 76:9 76:10 78:16 81:22 87:19 91:10,11 92:9 93:7 94:3 96:12,22 97:21 102:10,14 103:3,7 103:7 107:4 111:20 112:7,13 113:19 114:9 123:8 127:13 135:17 141:22 144:16 146:6,20 147:9 148:12 149:8,10,15 150:4 151:15 152:15 153:5,10,22 154:16,18 156:2 157:2,4,5,13 158:15 161:21 162:8,16 163:5,11</p> <p>diseases 1:6 4:5,11 4:12,19,20,21 5:1 5:4,5,6,8,11,18,22 6:5,7 7:4,6,13,18 7:19 8:1,10,14 9:9 9:16,20 10:2,15</p>	<p>10:18,22 13:11 17:15 19:15,20,21 21:16,18 32:14 37:15 45:8 65:11 69:13 70:17,17 79:4 81:17 86:1,5 86:14 87:3 89:18 90:16 94:17 97:12 111:12 112:18 113:7 116:17 140:7,8 144:14 147:2 148:10 150:1 152:4 154:3 154:22 156:9,10 156:13,15,20 157:6 163:8 164:7</p> <p>disk 19:1</p> <p>dismissed 46:5,7</p> <p>disorder 31:3 32:4 43:10 44:9 46:22 50:15 51:4 57:16 70:19 76:3,3 98:2 98:14,14,21 99:4 115:16 118:12 142:18 152:8,11 158:5</p> <p>disordered 56:3</p> <p>disorders 50:5,12 65:4 117:2 123:22 146:3,8 162:4</p> <p>display 9:16 10:10</p> <p>displayed 12:13</p> <p>disruptive 133:18</p> <p>distance 109:15 132:1</p> <p>district 166:20</p> <p>disturbances 50:10</p> <p>dizziness 149:19</p> <p>docket 8:19,20 9:3 9:7 12:14 22:17 59:4,8 79:16 81:7 89:9,10 95:22 140:19 142:9</p>
---	--	--	---

158:6 163:20,22 165:3 doctor 29:12 41:7 106:19 115:14 136:18 doctorate 39:10 doctors 45:9 47:3 105:15 107:3 132:22 137:21 144:8 document 8:16,17 8:17 9:3,4,14 165:1 documented 24:11 159:2 documents 151:2 156:5 dog 38:10,10 48:10 doing 22:11 25:13 35:2 39:21 40:6 61:5 67:8 68:20 75:16 93:13 109:8 109:11 110:4 119:8 120:9 128:3 128:8 137:17 140:9,13 147:12 148:1 153:19 155:4 domains 52:18 door 48:21 131:20 147:15 dosage 130:22 153:13 dosages 26:3 dose 127:7,8,10 double 56:18 57:2 doubly 57:12 doug 19:19 douglas 2:11 3:2 dr 2:18 4:2 15:6 19:16,19 20:2 26:14 27:21 28:9 41:17 43:5 52:14	52:17 54:5 67:1 79:22,22 80:10,18 81:2 90:5 110:8 110:17 111:2,3,15 118:6 138:12 161:4 dramatic 151:18 dramatically 149:2 151:15 drinking 31:8 driven 93:9 driving 120:3 drop 64:7 164:17 drove 116:5 drowning 23:17 drug 1:1 17:17 31:19 35:15 54:3 63:15 85:1 106:9 106:10 116:19 119:13 127:10 134:2 139:15 146:15 153:15 155:19 156:1 160:1 161:11 drugs 2:8 5:16 6:7 17:16 29:19 74:16 80:6 107:16 drunk 31:8 dual 80:1 duchenne 71:13 71:15 72:12 due 25:2 43:17 47:4 79:8 98:2 duke 80:13 84:6 duly 166:5 duplication 44:10 duplicity 91:15 dying 132:13 153:7 dystonia 46:18,20 dystrophy 71:14 72:12 145:5	e e 2:1 4:1,1 eager 143:5 ear 77:9 earlier 21:3 58:21 88:9 94:1 127:20 129:10 early 43:18 47:8 55:10 80:17 97:4 100:17 141:10 152:10 154:21 157:19 ears 104:19 earth 132:10 easier 56:13 eastern 124:12 easy 23:2 140:14 147:4 eat 70:11,12 122:17,18 echo 28:9 49:17 49:22 edged 56:18 57:2 educate 49:2,2 116:19 122:16 151:3 educating 30:11 119:13 121:12 122:1,13 education 99:3 146:8 154:21 155:7 effect 102:3 effective 4:17 5:7 55:1 127:8 effects 25:2 28:17 31:21 53:3 59:17 62:19 64:14 66:9 66:10,12 68:15 72:20 74:16,19 109:7,8 122:1 129:19 133:21 162:20	efficacy 153:14 efficiently 85:3 86:20 effort 11:5 efforts 8:7 80:9 ehlers 46:2 54:15 54:17 94:14 either 67:10 79:15 83:4 124:19 127:21 139:5,18 144:7 162:19 163:15 elasticity 135:19 electronic 91:14 elephant 122:18 122:18 elevated 107:20 eligibility 130:17 130:21 131:10 eliminate 119:19 elizabeth 49:13 email 17:1 38:17 emailed 164:19 emergency 12:22 46:4 emotion 122:11 emotional 132:18 150:7 emphasize 63:19 employed 166:11 166:14 167:8,11 employee 76:9 166:13 167:10 employees 12:10 enabled 6:6 encompass 68:12 encourage 10:11 12:15 14:12 16:19 22:19 89:10 139:6 140:18 145:15 147:7,15 163:19 encouraged 10:15 16:16 85:5
---	---	---	---

<p>encouraging 10:6 ended 56:22 84:10 115:12 116:22 117:7 endpoint 75:20 110:18,21 111:1 112:1 113:11,20 135:7 endpoints 7:22 75:18 76:18 78:7 88:4 110:11,15,19 111:16 118:14,22 120:10 134:5,5 135:9 143:17 ends 16:3 38:12 132:10 energized 10:16 energy 24:8 82:11 89:2 engage 4:10 149:20 engaged 66:5 111:11 engagement 16:14 engagements 10:17 154:15 england 135:21 enhance 28:20 enormous 70:7 71:2 163:8 enroll 76:1,11 127:4 enrolled 126:15 128:15 enrolling 128:21 enrollment 64:8 128:19 ensure 7:15 29:5 ensuring 81:1 entered 139:18 entering 139:8 entire 150:13 environment 72:9 113:14 159:6</p>	<p>environmental 159:5 epilepsy 50:6 74:8 74:14 98:16 115:18,20 episodes 19:4 epithelioid 137:17 equation 67:20,21 er 29:9 82:9,10 eric 77:17 90:6 135:14 es 166:4 escalate 69:7 escalation 127:7 especially 20:9 34:2 36:17,20 37:14 46:5 51:8 65:11 74:17 75:2 104:5 112:13 133:7 136:5 139:1 139:7 140:7 154:22 159:21 160:18 163:22 essentially 92:3 131:2 estimated 4:22 5:3 etiologies 7:2 europe 120:1 european 120:1 evaluate 75:15 evaluates 5:20 evaluation 5:15 13:4 76:14 evenings 79:9 event 114:3 eventually 34:14 64:9 everybody 21:15 22:14 51:17 59:3 95:22 104:5 105:20 108:16 111:8 115:10 139:7 160:3</p>	<p>everylife 152:3 153:19 everyone's 165:5 evidence 85:11 138:20 exactly 28:6 37:4 67:13 88:19 93:17 111:15 120:12 example 6:11 39:10 86:1 87:14 90:21 94:19 130:22 examples 145:6 excel 101:4 excellent 29:2 excited 10:9 15:18 18:18 21:5 118:8 exciting 96:4 exclusion 103:20 131:7 excretion 107:6 executive 70:2 99:20 exercise 35:6,11 35:12 40:1 exhibit 9:18 10:2 10:5,12 94:2,4,9 exit 12:22 13:1 expand 122:21 expect 26:20 expectancy 19:6 expectations 122:9 expense 91:15 expensive 131:18 experience 7:7 9:19 23:10 24:20 41:6 68:6,16 99:14 102:1 103:12 104:11 108:8 126:10 138:13 143:15 144:7 145:18 147:14</p>	<p>experienced 23:12 42:14 157:18 experiences 7:8 8:6 13:10 14:7 16:20,22 17:6 21:10,17 23:2,18 33:9 47:1 88:3,5,7 99:17,19 100:19 140:12 141:5 155:15 156:14 experiencing 25:15 42:13 43:3 49:8,10 54:8 64:12 79:18 experimental 100:8 102:20,21 expert 80:16 expertise 148:20 experts 4:11 87:6 87:6 156:16 explain 69:21 explore 13:19 exploring 56:11 expressed 14:4 17:3 extent 74:18 externally 6:10 156:1 158:3 160:1 extremely 9:4 47:6 102:2 107:19 137:10 140:3 eye 77:9 90:7,11 91:4 135:17 137:22 eyes 104:19</p>
f			
<p>fa 17:21 66:15,17 fabulous 155:13 face 10:2 47:12 94:3 facebook 116:14 116:15 124:22 125:14 130:7 136:19 137:5</p>			

<p>152:12 faced 108:16,17 faces 37:19 facilitate 13:9 facilitated 13:13 95:15 facilitating 20:13 facilitator 2:6,20 3:8 facilities 29:2 fact 43:16 68:19 82:22 83:12,21 87:11,15 136:16 151:8 factor 71:10 factors 102:8 119:5,7 126:10 130:11 133:13 fail 120:14 failure 106:21 114:3 121:2,9 fair 81:19 fairly 28:7 82:16 127:13 faith 125:18 fall 45:14 familial 97:19 familiar 17:21 37:19 96:14 families 5:2 50:18 74:15 75:9 116:15 119:19 120:1,11 122:10,16 125:14 128:4,6,11 148:14 148:22 149:7 150:2 153:8 154:5 162:22 163:3 family 11:3 18:20 33:2 34:14 57:7 68:14 81:21 97:9 97:10 102:11 104:21 108:15 112:12 142:20 149:9 150:13</p>	<p>161:20,22 162:12 fantastic 131:14 far 25:13 26:9 33:8 38:15 42:9 56:16 59:3 66:12 82:10 109:3 110:4 farther 101:13 fashion 119:12 fast 15:10 89:3,6 103:5 105:15 115:5,12 fatal 5:1 148:12 father 77:18 126:19 fatigue 23:22,22 24:3 38:11,12,21 42:11,16 44:14 48:9 60:16 72:4 90:17 143:1 149:19 157:10 162:3 fatigued 38:13 fda 1:1,12 5:12 6:9 7:13 9:8 11:2,5,13 12:6,8,9,10,21 16:5,8,17 17:1,6 17:11 22:2 26:12 31:18 35:20 40:12 47:2 62:12 64:9 66:16 67:1 75:11 78:9 80:1,12 81:10 83:22 84:17 84:18,19 85:20,21 86:17 87:21 91:17 99:9,22 100:2 104:2,6 117:1 123:1 130:2 137:20 138:9 139:1 144:9 146:10,13,18 147:12,19 153:3 153:11 154:9 155:12,18 158:13 159:15,20 160:10</p>	<p>160:18 161:5,11 163:14 164:16 fda's 4:3,16 6:11 8:7 80:6 146:16 fda.gov. 17:2 fear 61:15 fears 164:13 feature 15:1 february 80:19 fed 94:16 federal 142:11 feed 70:13 feedback 95:21 163:22 164:16 feeding 145:15 feel 28:13,19 29:3 29:4 34:13 43:4 49:10 53:12 66:13 136:13 feeling 48:5 52:22 116:4 feels 24:4 87:7 feldman 159:19 159:19 felt 33:21 34:1 116:5 fertility 82:22 84:4 fi 12:12 fibrosis 145:4 fifth 18:20 fighting 55:16 90:16 figure 32:11 36:16 38:22 82:18 83:15 83:18 84:1 85:3 89:5 113:2 fill 164:15 filled 15:20 fillers 47:14,15 film 20:17 filtering 22:7 finally 22:21 115:12</p>	<p>financial 14:17 132:12 141:21 149:11 150:5 159:4,9 financially 166:15 167:11 find 7:9 38:5 73:12 111:20 117:17 118:13 123:11 125:4 129:7 139:12 142:10 148:19 finding 117:7,16 124:6,7 144:20 findings 156:5 fine 46:5,9 90:7 fingers 152:20 finish 17:5 140:17 finishes 141:10 firm 155:17 first 2:5 13:17 14:12 15:17,17 21:12 22:1 24:7 26:5,6 43:5 44:7 46:13 48:19 65:6 81:4 82:15 88:11 94:22 105:2 116:16,20 117:17 118:9 126:19 127:9 130:8 142:12,13 149:3 152:22 five 19:7 33:20 63:16 66:2 68:3 76:13 98:8 115:2 116:2 138:21 149:18 flexibility 146:19 flow 23:14 fly 91:1 121:13 focus 4:19 9:17 13:17 32:4 35:17 40:6 71:3 120:7</p>
--	---	---	---

focused 40:2 80:14 95:17 99:4 101:20 131:12 138:16 145:11 146:6 155:19 156:1 160:1,11	129:8 163:9,11 164:6 foss 77:1,1 found 106:18 107:9 108:1 116:13 117:7 124:7,15 125:5 136:18 137:3 156:7	fun 143:9 function 107:20 functioning 80:4 108:7 funded 14:17 126:17 141:20 funding 152:16 funny 60:5 furia 2:4,7,20 10:20 11:1 20:14 141:3 143:20 145:21 147:21 150:15 151:22 154:10 155:9 158:8 159:17 160:14	98:17 115:18,19 117:8 122:2,7 134:17 general 28:21 36:3 109:10 112:3 126:6 generate 139:2 generation 18:20 genes 74:6 genetic 18:10 30:17 34:7 43:9 44:9 46:19 51:4 74:12 75:2 93:2 107:5 114:9 148:13 152:8 genetically 83:6 geneticist 115:9 115:21 genetics 115:13,14 geneva 46:17 genomic 55:17 131:15,17 gentleman 135:12
follow 13:1 17:7 22:3 23:6 35:20 62:13 99:10 111:2 163:18 164:1	foundation 51:3 74:4 77:2 78:15 90:7,11 98:5 99:3 129:16,16 135:15 144:14 145:4 152:3,6,7 159:20	further 6:1 7:9 16:9 166:12 167:9 future 26:8 31:1 32:21 33:5 34:4 35:18 44:5 83:20 84:5 103:15 157:11,22 158:1	genetically 83:6 geneticist 115:9 115:21 genetics 115:13,14 geneva 46:17 genomic 55:17 131:15,17 gentleman 135:12
followed 71:21 following 152:6 food 1:1 80:7 foods 5:16 footage 20:19 forbid 83:9 forced 159:8 forecast 41:14 foregoing 166:3,4 167:4 forget 34:19 form 46:20 63:7,8 129:19 130:22 forms 13:4 25:3 47:7 forth 22:2 71:2 109:7 fortunate 62:5,20 90:11 fortunately 108:4 109:7 110:2 114:5 114:6 forward 16:21 20:22 84:15 85:14 85:19 91:15 100:19 103:6 105:15 115:5,12	founded 126:17 146:4 founder 94:8 four 35:12 76:13 105:22 108:6 114:21 115:8 142:21 156:2 freckles 82:8 frequency 132:1 friday 117:18 friedreich's 2:15 17:19,21 49:1 142:17 friend 77:17 friendly 76:18 friends 26:19 48:19 66:4 112:17 front 16:16 21:7 28:11 68:9 141:14 146:14 frustrated 83:12 83:13 frustration 50:2 fulfilling 5:19 full 21:5 28:15 87:22 125:19 147:17 fully 146:17	g g 4:1 47:5 gain 62:4 91:18 gait 40:2 120:9 game 118:12 ganglia 46:22 gap 99:3 gaps 10:17 gasping 23:16 gassy 104:22 gastaut 44:8,12 gastric 47:4 gastroenterologist 56:21 gatekeepers 138:1 gathering 118:4 gears 93:21 120:6 gene 19:14 29:19 29:22 30:3,5,6 51:5 63:8 75:15 77:9 90:12 98:16	gently 142:8 gerd 47:4 getting 28:22 30:2 30:12 36:19 39:14 42:17 63:4 72:3,7 74:20 76:22 90:9 95:14 108:3 110:21 115:12 116:16 131:17 134:1,4 138:17 144:21 gi 74:9 75:3 gilazzo 49:13,13 girl 124:17 girlfriend 124:16 girls 43:15,16 61:9 94:13,14 152:11 152:17 give 12:8 15:13 57:9 73:13 89:7 103:13 106:8

114:16 129:9 147:11 164:15,16 given 30:21 74:16 gives 49:2 113:16 giving 97:13 106:10 112:20 glad 11:14 77:6 140:9 global 97:8 102:11 161:20 globe 10:6 94:6 128:22 go 22:10 24:22 25:19 26:17 29:9 29:9,10 39:19 42:6 45:20 46:3 46:14,15 48:20 51:8 52:3 57:6,21 58:10,15 60:3,6,9 60:11 62:11 65:2 66:13,19 69:18 71:1 76:12,21 77:11,12 83:4,9 87:16 90:8,13 94:10 96:5 100:11 101:13 102:16 108:4 122:5 124:6 132:5 133:3,7,11 136:10 goal 7:16 10:1 13:8,12 87:9 113:12,20 goals 122:14 god 107:11 136:19 godsend 100:12 goes 67:2 70:14 85:6 113:10 115:22 118:7 124:20 going 21:1,11 26:4 27:5,6 30:12 33:12 34:1,3,16 34:17 35:18 42:6 42:20 44:21 51:1	61:1,6 63:13,14 64:3,17 65:15 68:16 69:6 71:6 72:14 74:10 82:13 82:21 83:3 84:15 85:13,19 86:13,13 86:15 89:5 90:2 92:5 93:21 94:5 95:13 99:7 102:7 104:22 109:3 110:14 118:1,15 118:16,21 119:21 121:5,16 125:7 127:9 129:8 134:6 140:22 141:7 142:19 145:11 151:10,20 158:20 gold 54:17 good 4:2 10:20 20:2 40:17 54:1 54:14 77:12 97:15 118:15 128:7 137:19 143:18,22 146:1 152:19 155:11 161:3 google 36:8 139:11 gosh 83:9 gotten 164:13 government 11:13 76:8 92:16 158:21 159:7,11,13 gradual 39:7 graft 61:8 grandchildren 44:9,12 45:1 grant 116:20 gratitude 155:13 great 11:3 12:12 12:22 23:18,18 37:19 48:20 71:5 72:10 101:2 129:1 139:19 143:13	greater 98:5 greatest 150:4 greatly 81:5 150:8 161:8 164:12 green 142:3 grew 116:15 grief 102:14 group 28:11 58:7 111:10 116:13 118:2 125:1,14 130:8 136:13 138:7 139:6,14 148:9 150:22 152:13,14 153:5 groups 36:9 137:16 145:6 146:6 152:15 155:8 161:12 grow 24:10 97:3 104:22 growing 57:8 growth 73:18 guarantees 109:6 guess 25:8 31:22 35:5 36:7,20 61:3 62:3,22 68:3 98:9 110:18 123:14 124:8,9 142:21 guide 101:17 142:2 guideposts 85:15 guilt 78:19 guilty 34:13 74:6 gut 57:19 58:2,3 guys 94:22 112:22 113:1 136:4	halfway 128:9 hallmark 56:1 hallway 12:2 hamartoma 93:1 hampshire 1:13 hand 14:9,10 22:7 84:10 126:5 129:13 131:20 139:20 141:15,16 handed 115:15 handle 16:12 106:22 hands 42:12,16 75:4 104:16 126:7 134:20 136:10 handshake 86:19 86:19 handwriting 143:15 hannah 96:19 happen 35:18 36:8 67:16 82:21 92:5 105:19 150:21 happened 41:12 82:10 happening 67:10 77:3 101:11 happiness 102:13 happy 21:19 97:20 142:15 147:9 hard 26:16 78:8 78:20 89:2 104:16 139:2 151:11 160:21 161:1 hardware 80:9 hartman 43:8,9 77:17 90:5,6 135:14,14 152:1,2 152:3 hashtag 124:4 hashtags 124:5 hat 50:11 51:2 haunted 121:16
		h	
		hailey 98:10 hair 82:7 half 5:3 39:6 42:17,22 72:20 77:13 87:13 90:22 91:3,8 107:1 117:3	

<p>hd 18:10</p> <p>head 44:2,2,18</p> <p>headaches 72:4</p> <p>health 4:17 5:13 19:22 24:7 28:18 32:14 57:5 80:10 80:14,20 90:20 152:12 153:21 154:9 157:9</p> <p>healthcare 11:12 28:13</p> <p>healthy 27:10</p> <p>hear 8:8,9,12 9:1 11:14 12:8 16:21 17:10 21:8 43:1 51:13 54:11 58:17 71:5 75:21 79:17 104:6 110:19 126:2,4 134:22 138:12 141:4,6 151:11</p> <p>heard 9:6 42:10 42:11,11,19 47:22 49:1,7,11 52:12 54:9,10 75:12 81:2,10,18 94:1 123:21 130:18 133:15 156:12 158:4 161:14,16 162:2,6,6,13,14 162:17 163:7,10 163:19 164:4</p> <p>hearing 13:20 20:7 22:8 46:13 79:3 141:1 163:2</p> <p>heart 25:5 140:15</p> <p>heartbreaking 132:16</p> <p>heartly 81:4</p> <p>heat 25:18 54:22</p> <p>heavily 77:14</p> <p>heavy 24:5</p> <p>heels 146:13</p>	<p>held 14:10 141:17 146:14 151:4</p> <p>hell 121:14</p> <p>hello 159:19</p> <p>helms 2:4,7,20 10:20 11:1 20:14 141:3 143:20 145:21 147:21 150:15 151:22 154:10 155:9 158:8 159:17 160:14</p> <p>help 7:19 9:18,20 13:11 22:8 25:14 30:13 35:6,16 36:11,11 38:10 39:21 41:2,3 49:2 57:21 61:11 63:15 69:6,16 76:19 80:9 106:8 108:21 118:13 119:19 120:8 121:21 127:19 139:14 155:22 157:22</p> <p>helped 31:19 37:1 101:10 133:4 155:19</p> <p>helpful 141:6</p> <p>helping 4:17 16:7 56:9 69:7 129:8 156:17</p> <p>helps 38:1 40:8 49:3 80:3 92:4,5</p> <p>hematologist 29:11 80:11</p> <p>hereditary 149:8</p> <p>heredity 93:2</p> <p>hereto 166:14 167:11</p> <p>heterogeneous 7:2</p> <p>hey 64:5 72:10</p> <p>hhs 152:22</p> <p>hi 17:14,18 18:5 19:11,16 20:10</p>	<p>21:2 35:22 43:8 44:7 45:22 46:17 49:13 54:14 55:7 55:21 57:15 69:11 70:5,6 73:3 74:3 92:22 95:12 135:3 135:14 136:10,11 142:15 148:3 150:17 152:2 154:12 155:11</p> <p>hidden 57:18</p> <p>hideous 74:14</p> <p>high 60:12 80:5 121:14 150:2</p> <p>higher 26:2 65:10</p> <p>highly 5:1 12:15</p> <p>himick 148:2,3,3</p> <p>hint 87:4</p> <p>hired 152:5</p> <p>historical 127:13</p> <p>history 29:19 81:21 90:18,20 91:1,12,19 92:2 101:5 124:2 135:16 137:4 145:2 147:3</p> <p>hit 84:9 98:3 140:15</p> <p>hog 45:16</p> <p>hold 93:10</p> <p>holder 118:6</p> <p>holding 146:10 147:19</p> <p>home 72:19 98:3 100:7,11 102:16 109:15 113:14 116:5 117:12 123:17 128:2 134:11 159:13,14</p> <p>homeless 159:9</p> <p>honestly 76:5</p> <p>honig 1:16 166:2 166:18</p>	<p>hooked 113:9</p> <p>hope 9:3,5,10 11:14 26:7 119:2 119:3 151:14 154:6</p> <p>hopefully 113:14</p> <p>hoping 126:20</p> <p>hopper 72:22</p> <p>horizon 63:13</p> <p>hormonal 73:17</p> <p>hormone 73:18</p> <p>horrible 72:16,20 123:16</p> <p>hospital 24:22 27:12 60:4,6 61:1 100:5,7 102:17 109:20 115:11 136:17,21 155:3</p> <p>hospitalization 27:13 71:20</p> <p>hospitalized 58:10</p> <p>hospitals 10:6 94:6</p> <p>host 61:8</p> <p>hotel 143:12</p> <p>hour 50:17 87:13 110:2</p> <p>hours 50:16 69:15 76:13 105:12 107:13 113:9 124:14</p> <p>housekeeping 41:18 164:8</p> <p>houston 123:15</p> <p>hub 144:22</p> <p>huge 34:20 50:13 50:19 89:21 91:16 131:10 151:18 159:5 163:9</p> <p>human 125:5 144:2 154:9</p> <p>hundred 92:12</p> <p>hunger 56:2</p>
--	---	---	--

<p>huntington's 2:16 18:7,9,15,17 30:18 31:2,19 32:1,13 33:18 34:21 41:13 54:1 62:16,21</p> <p>hurdles 47:13</p> <p>hurt 137:10</p> <p>hurtful 137:3</p> <p>hurting 78:21</p> <p>hurts 36:13</p> <p>husband 96:18 98:8 155:3</p> <p>hyman 155:16</p> <p>hyperinsulinism 3:5 70:1,3,6 96:21 96:22 97:7 99:20 100:6,14 101:3 103:9,17 113:6</p> <p>hypermobility 54:15</p> <p>hyperphagia 56:1 135:8,10</p> <p>hypoglycemia 97:2</p>	<p>immediate 24:22</p> <p>immune 71:14,17 72:13 99:1</p> <p>immunities 71:22</p> <p>immunity 44:17</p> <p>immunotherapies 131:6,14</p> <p>impact 1:6 4:4,12 4:19 10:22 20:8 32:13 33:13 49:22 50:18 64:8 66:18 82:20 83:3 134:16 149:15 150:4 156:15,17 157:2,7 157:8 161:21 163:7</p> <p>impacted 18:16 31:21 79:8 150:8 159:6</p> <p>impactful 38:11 51:12</p> <p>impacting 150:2 157:15</p> <p>impacts 5:2 7:17 50:14</p> <p>impaired 149:22</p> <p>impairment 158:5 162:3</p> <p>implement 155:19</p> <p>importance 93:4 161:18 163:3</p> <p>important 5:9 7:4 7:5 11:4 53:16,16 58:9 59:19 66:14 87:17 92:7 101:8 103:18 111:4,13 112:3 119:19 122:16 128:6 129:5,8 140:4 141:4 161:10 162:11,17</p> <p>impossible 55:16 128:10</p>	<p>improve 32:15 38:1 157:12 160:4 164:7,10</p> <p>improvement 66:3 145:2</p> <p>improving 66:3</p> <p>impulse 51:6,14</p> <p>inability 27:14 48:6</p> <p>inaudible 90:8</p> <p>incentives 6:4</p> <p>include 31:4 85:9 85:10</p> <p>included 100:9 120:19</p> <p>includes 6:13 86:4 86:17 140:7</p> <p>including 5:16 11:13 20:21 86:1 88:8 109:10 146:20 154:9 157:8 158:3</p> <p>inclusion 103:20</p> <p>incorporate 86:6 118:22 165:2</p> <p>incorporating 87:2 163:10</p> <p>increased 31:21 65:21</p> <p>incredible 103:12 104:17 105:7,11 105:22 106:14 147:13</p> <p>incredibly 90:11 136:5</p> <p>independence 149:22</p> <p>independently 39:6</p> <p>indicate 142:2</p> <p>indication 75:17</p> <p>indications 76:7</p> <p>indicators 78:1</p>	<p>individual 50:9 62:13 146:5</p> <p>individually 89:18</p> <p>individuals 7:1 14:7 49:21</p> <p>industry 11:12 80:14 84:12 161:13</p> <p>infancy 152:10</p> <p>infants 114:19</p> <p>infarcts 24:9</p> <p>infections 71:20</p> <p>infertile 61:9</p> <p>infiltrated 137:6</p> <p>influenced 128:14</p> <p>information 2:18 8:21 9:2 15:6,9 16:11 36:6 37:6 80:2,8 81:12 83:18 86:12 89:9 90:20 92:2 101:5 101:6 134:12 137:19,21 139:12 142:10 144:6 145:13 147:6 151:6 153:14 160:8,12 165:2</p> <p>informative 111:8 129:22 163:6</p> <p>informed 84:2 107:4 111:7</p> <p>infuse 72:17</p> <p>infusion 72:19,21</p> <p>initially 24:1 108:11</p> <p>initiatives 80:5</p> <p>injectable 73:7</p> <p>injectables 73:7</p> <p>injection 63:9 91:6 122:5 135:18 135:20</p> <p>innovation 148:8</p> <p>input 7:12 11:14 156:14</p>
i			
<p>iamrare 147:2</p> <p>idea 90:10 127:12</p> <p>ideal 54:3</p> <p>identification 28:12 146:7</p> <p>identified 14:7 57:9 156:8 157:12 157:19</p> <p>identify 5:21 7:18 13:10 41:19 43:6 87:10 109:16 157:1</p> <p>identifying 41:4</p> <p>illness 46:2 83:3,6 92:10</p> <p>imagine 60:17 105:5</p>			

inquiries 12:3 inr 107:19 ins 63:3 64:22 insatiable 56:2 inside 60:17 86:17 insisted 82:13 institutes 10:6 94:5 institution 133:1 135:22 institutional 101:14 insulin 97:1 insult 97:8 102:11 161:20 insurance 54:19 55:17,18 56:12 57:3 72:18 131:17 153:15 insurances 69:16 insurers 55:14 intellectual 74:8 98:15 115:17 intelligent 111:7 intend 141:11 intended 12:8 85:19 intending 94:2 intense 24:1 43:18 55:11 intensive 20:6 40:2 interact 48:11 interactive 21:22 interest 14:4,18 141:21 interested 12:6 15:19 20:7 21:8,9 30:11 64:18 67:8 71:17 166:15 167:12 interesting 61:13 102:2 136:16	interestingly 84:20 interests 63:10 interfere 11:20 internal 89:13 internally 6:9 international 70:3 99:21 100:15 internationally 80:15 interrupting 17:6 intervention 43:18,21 55:11 139:15 interview 150:22 intracranial 122:6 intrahepatic 97:19 intravitreal 136:6 introduce 17:12 79:21 96:10 introduced 67:11 introductions 23:4 96:6 introductory 4:7 invaluable 156:14 invasive 134:17 invest 145:11 investigator 100:2 135:21 investigators 67:7 100:16 invisible 46:2 invite 75:17 involuntary 31:4 involved 30:4,11 64:2,19,20 68:2 91:20 114:15 116:17 118:3 120:11 134:9 156:3 involvement 7:11 128:16	involves 135:17 involving 118:10 iowa 143:7 iqvia 144:2 irb 117:14 isabel 101:7 island 109:20 isolated 37:10 isolation 34:1 issue 51:10 58:13 113:21 114:4 131:10 153:16,16 159:5,10 160:6,9 issues 7:19 12:20 13:10 37:4 38:7 38:21,21 41:4 57:4,5 58:2 74:9,9 75:3 82:19 98:18 98:19 113:6 130:21 131:9,16 146:11 152:12 156:8 164:2 itchiness 108:3 itching 60:16,17 110:10,17,19,22 111:19 itchy 107:17 items 164:8 iv 79:10	jimmy 118:6 job 1:17,21 57:1 66:13,19 125:18 128:2 147:13 158:21 159:7,16 161:3 jobs 88:20 join 108:13 joined 80:19 94:10 joining 8:4 11:6 13:22 155:17 joints 73:20 joseph 97:18,18 journey 123:7 julie 3:5 69:22 96:8,16,17 97:14 97:21 99:13 104:3 109:19 114:1 161:20 jump 138:3 jumped 84:10 justification 154:6 justify 154:8
			k
			kawasaki 154:18 keep 16:10 66:3,4 113:17,17 145:10 145:15 keeping 40:4,4 kemp 2:8 17:14,14 35:22 37:1 40:22 kept 34:3 107:21 kettering 136:21 kgb 51:3 kid 34:22 72:10 127:9 kidney 25:6 159:20 kids 45:2,5 46:1,1 50:11,15 58:1,9 61:21 69:17 70:8 78:6,21 94:14 124:14
		j	
		j 47:5 james 155:10,16 159:22 janet 2:3,10,22 3:10 4:6 12:14 13:8 15:22 19:16 41:17 82:5,5 83:19 93:17 161:4 janet's 83:19 84:1 jaundiced 105:12 107:19 jersey 70:4 96:18 jill 73:3 150:16,17	

<p>kind 22:7,8 26:19 31:17 33:9 34:5 41:13 46:9 49:16 51:18 53:1 57:17 58:11 60:10,13 61:10,18 62:3 63:18,20 64:13 66:1,5,11 75:20 76:11 87:4 100:11 102:21 105:16 106:5 107:10,16 108:18 109:2 113:19 114:17 116:3 128:14 130:4,6,12,13 134:15 156:17</p> <p>kinds 45:14 54:22 145:13</p> <p>knew 33:11 104:13 106:15 114:20 115:2,20 116:22 123:18,18 132:4</p> <p>know 11:4 13:3 16:2 24:16 25:8 26:8 27:4,10 31:11 32:4,17 34:8,17,19 37:22 38:13 41:14,21 43:4,22 44:5 45:3 46:8 51:8 53:5,12 56:9 57:9,18 58:12,13 59:3 60:18 61:7 62:4 64:4 65:5,8,19,22 66:16,19 67:10 68:9 69:13 70:17 72:11 73:15,15 74:14,18 75:6,19 75:22 76:2 79:13 81:8 82:5 87:5 95:4 98:2 102:16 103:6 104:14 105:3 106:15,17</p>	<p>107:15,16,21 108:16 109:5 110:3,10,12,14 112:4 113:17,19 114:3,9 115:5,16 115:18 116:1,9 119:20 120:12,14 120:17 122:2,7,9 124:4,4,6,12,15 124:16,17,19,20 124:20 125:7,8,12 125:13,21,21 127:18 132:2,4 133:2 137:20 138:4 140:17 143:14,15 146:4 146:12 147:1 148:9 150:19 151:3 152:18,22 163:12</p> <p>knowing 37:22 63:13 65:9 133:21 136:5</p> <p>knowledge 28:15 132:21 166:9 167:6</p> <p>known 10:2 18:10 27:6 31:5 43:10 80:22 148:5 152:9</p> <p>knows 76:9 96:1 115:11</p> <p>kristen 92:22 kristin 92:22 97:16 142:13,16</p> <p style="text-align:center">I</p> <p>label 35:15 100:9 100:10 153:13</p> <p>lacey 126:12,12</p> <p>lack 23:21 48:4 50:3 51:10 57:12 58:5 69:14,17 98:2 153:17</p> <p>landed 83:22</p>	<p>landscape 149:1</p> <p>large 19:2 37:9 43:17 96:1</p> <p>larger 26:3</p> <p>larry 156:4</p> <p>late 106:11</p> <p>launched 117:5</p> <p>launching 101:12</p> <p>lawyer 130:3 133:4</p> <p>lead 30:6 113:18</p> <p>leader 122:15</p> <p>leaders 57:19</p> <p>leadership 146:11 147:20</p> <p>leading 100:4</p> <p>leads 18:1 38:8 80:8</p> <p>leap 125:17</p> <p>learn 4:12 7:9 8:15 21:19 85:8 161:14</p> <p>learned 30:17 64:3 69:1 149:17</p> <p>learning 21:9 41:6 43:16 63:3 86:15 98:21</p> <p>leave 8:19 13:2</p> <p>leaving 150:12</p> <p>led 13:13 100:2 148:5 156:1 158:3 160:1</p> <p>left 91:4 142:4 149:20</p> <p>legacy 83:20</p> <p>legislation 84:21 84:22 85:6 120:4 133:5</p> <p>legitimately 105:12 107:10</p> <p>lennie 136:11,11</p> <p>lennox 44:8,11</p> <p>lethal 129:19</p>	<p>level 47:15 60:12</p> <p>levels 157:4</p> <p>liaison 155:18</p> <p>life 7:18 19:6 27:16 32:15,17,19 33:5 34:9 36:2 38:2 42:21 50:1 57:9 66:5,14,20 69:17 73:20 82:4 87:17 100:8 103:14 108:7 113:14,18 116:8 149:16 150:3,5 151:16,16 157:12 157:15 159:11,14 162:6,9</p> <p>life's 150:12</p> <p>lifesaver 117:4</p> <p>lifestyle 27:1,2 33:4</p> <p>lifetime 63:12 148:15</p> <p>light 142:2</p> <p>lights 142:2</p> <p>limit 107:16</p> <p>limited 150:9</p> <p>line 46:10 52:7 84:10</p> <p>linked 152:11</p> <p>liquid 47:7 63:7</p> <p>list 43:12 92:14,14 130:13</p> <p>listen 16:17 125:20</p> <p>listening 21:9 87:12 89:4 102:22 133:9</p> <p>literature 116:2</p> <p>little 14:2 24:16 25:12 26:17 33:7 41:15 42:16 46:3 46:12 49:7,7 54:7 54:10 73:20 77:13 81:14 82:11 88:9</p>
---	--	--	---

<p>96:11,15 99:16 104:9,10 114:14 122:12,17 124:17 136:4 live 9:22 19:7 20:15 29:2 32:19 33:4 58:13 61:22 84:4 96:18 101:22 113:8,13 116:6 152:11 liver 98:4 106:21 107:3,6,7,20 109:2 lives 20:8 50:14 70:20,21 87:7 124:3 149:21 156:15 living 9:19 19:9 29:15 32:17 54:15 70:17 87:7 116:7 116:8 136:15 137:4 157:8 lobby 12:1 located 12:1 148:21 location 1:12 134:3 locations 128:5 locked 90:21 91:8 long 24:2 61:2 68:5,5 73:7,22 84:13 103:3 105:9 109:20 119:3 longshot 133:2 longstanding 80:21 look 10:7,12 20:22 25:7 27:2 46:5 74:7,11 76:10 94:7 108:18 110:3 112:4 114:6 120:10 140:5 154:2,4 163:9 164:6</p>	<p>looked 27:9 40:19 156:4,21 looking 27:9 32:5 58:8 67:6 68:13 78:12 113:20 115:21 127:5,17 134:5 143:16 146:20 152:16 158:3 lorie 44:7,7 lose 77:21 143:2 losing 78:4 128:2 loss 18:1 31:14 38:8 62:4,5 143:3 lost 33:21 122:13 158:18 lot 26:7 32:13,22 33:3 35:6,13 36:5 36:6 37:4,19 38:12,20 42:19 43:13 44:16 45:4 45:7 47:14 60:14 62:21 64:4 72:2 72:14 74:7,13 78:17,18 84:18 97:5,8,22 98:19 99:1,1 106:22,22 107:3,12 110:15 110:18,19 113:6 125:5 126:21 130:18 131:1 133:16 134:2 137:19 140:7,9 162:8 lots 50:11 152:12 love 56:4 73:12 79:17 102:12 118:6 121:18 130:10 132:1 loved 121:20 132:10 145:12 150:11 158:18 lovely 101:7</p>	<p>low 57:22 97:2 127:10 lower 127:8 lucas 2:8 17:13,14 lucky 103:1 155:2 lung 25:5 45:3 lungs 131:5 luxury 130:10 132:9</p> <p style="text-align: center;">m</p> <p>machine 83:9 mad 44:2 main 31:4 113:7,9 113:10 151:10 major 19:5 24:3,3 24:12 27:16,16 33:16 71:19 114:8 153:16,16 majority 51:7 making 11:6 36:3 59:20 65:18 70:11 89:7,13 108:22 128:13 malpractice 158:20 manage 25:14 31:18 39:21 60:11 65:6 150:13 management 4:13 13:18 48:9 144:1 162:14 managing 21:13 39:17 54:8,12 56:7,17 58:18 59:17 65:16 71:8 manhattan 106:20 manifestations 7:3 manner 4:18 41:5 129:6 maria 55:21,21 marie 135:3,3 marker 30:17 market 4:18 145:3</p>	<p>marketing 6:6 married 98:8 marrow 19:4 23:19 30:1 61:6 maryland 55:13 masks 25:22 mass 77:9 massage 25:18 match 30:3 112:14 matches 112:19 math 73:10 matter 104:16 maughan 51:1,3 maximize 95:13 maximizing 62:11 maynard 2:3,10 2:22 3:10 4:2,6 16:1 19:16,16 41:17,17 43:6 161:4,5 mccune 2:9,21 20:2,3 26:14 27:21 52:14,17 54:5 110:8,17 111:15 mccune's 111:3 mcdermid 74:4,5 mcnamara 155:17 md 1:15 mean 16:3 21:22 30:10 34:10 37:13 38:18 51:16 53:7 57:2 58:4 60:8,21 64:16 65:2 68:21 69:1 73:1 75:1,4,7 84:3 111:22 120:16,17 123:19 136:3 137:3,22 meaning 28:7 meaningful 102:4 meaningless 75:20 means 29:8 50:17 150:10</p>
--	---	--	--

<p>meant 28:6 102:3 measure 78:2 118:22 measures 9:12 mechanism 89:11 117:8 mecp2 44:10 45:2 med 75:1 media 12:2,4,11 37:21 117:13 124:5 136:19 139:21,22 140:2 medicaid 47:9 132:12,15 medical 5:7,16 6:2 6:7,13 7:20,21 10:5,7 13:11 14:18 16:20 28:17 37:5 41:3 45:9,11 68:20 80:7 85:1 88:2 89:17 90:18 94:5 141:22 144:4 146:19 154:3,22 157:5 164:7 medically 36:7 151:1 medication 47:5 53:20,22 54:10 63:7 64:11 72:8 79:10 108:21 medications 47:7 47:9 54:21 56:11 56:14 100:9 133:22 153:12 medicine 26:5,6 68:15,19 73:13 74:1 80:11,13 106:8 154:2 medicines 73:5 meditation 25:18 medium 10:3 meds 60:12,12 meet 48:19 97:13 115:4</p>	<p>meeting 1:2 2:4 4:4,8,11,19 6:11 6:19 7:16 8:5,7,15 8:19,20 9:1,2,14 9:15 10:10,14,21 11:4,17,22 12:7,7 12:16,17,19 13:3 13:8 14:6 16:3,13 20:13,18,19,22 81:7 85:18 111:10 129:21 141:1,6,8 144:10 146:10,12 147:20 155:13 156:7 159:22 160:10 161:1,9,10 163:6,13,18 164:21 165:1,7 meetings 127:22 146:13 156:2,3,6 156:8 157:16 158:3 160:2 164:10 megan 74:3 melanoma 81:20 81:21 82:16 83:2 83:2 melding 129:5 member 55:8 56:16 71:11 members 11:3 12:4 14:3 17:6 57:8 78:18 101:15 104:21 149:9 160:18 memorial 136:21 memory 31:14 mental 24:7 27:19 28:18 32:14 53:13 57:5 60:7 157:9 mention 54:9 58:20 135:5 mentioned 12:14 13:8 21:3,11 22:18,22 23:8</p>	<p>24:16 25:12 35:22 38:19 39:16,17,21 42:10 44:19 48:2 49:19 52:5,17 56:17 58:21 63:6 64:18 79:7,10 108:11 119:5 127:1 134:3,9 164:22 mentioning 39:18 58:18 mess 121:5 147:22 met 110:16 metabolic 70:14 method 47:16 mic 69:20 92:1 104:4 135:2 michael 3:6 97:14 97:16,17 98:6 104:8 microphone 14:11 17:9 90:4 129:9 141:13,17 mid 82:6 middle 141:13,15 mile 40:5 milestone 51:12 milestones 115:4 million 4:22 129:20 153:20 mind 33:3 41:22 53:12 94:12 102:19 120:18 126:9 130:9 135:1 164:15 mindful 22:15 minds 33:4 mine 41:15 101:7 minimal 109:8 143:1 minute 95:8 104:15 158:10 minutes 15:21 59:10 81:14 95:4</p>	<p>141:10 147:17 misdiagnosed 33:15,18 mishap 13:16 misinformation 36:6 37:5 misplaced 164:13 missed 59:7 mission 4:16 80:20 mobile 11:19 mobility 38:7,21 39:8 41:9 48:10 65:21 143:2 model 125:5 models 63:21 moderate 155:22 moderator 38:12 modernize 85:1,9 modification 56:8 mom 18:9 30:18 31:5,18 32:8 33:15 34:12 36:14 44:1 65:7 moment 13:6 27:5 27:5 93:22 106:6 107:11 moments 150:19 moms 58:12 monday 1:10 money 70:22 119:21 152:19 monica 3:4 57:15 98:6,7 101:19 114:12 136:14 139:10 monitoring 132:2 month 63:11 73:22 76:13 months 9:14 39:7 73:11 77:12 81:11 104:12 105:2,16 105:22 114:21 124:9 130:2</p>
---	---	---	--

132:14 149:1 mood 31:9 33:16 52:19,21 65:9 moods 73:19 morning 97:6,22 106:12 moro 142:13,15 142:16 mother 52:19 77:15,18 88:22 98:8 136:13 mother's 83:2 mothers 18:20 78:11 motivate 84:12,15 motivated 83:6 93:14 117:20 motivation 85:13 121:21 mount 106:19 107:2 mouse 125:5 mouth 104:5 move 16:20 30:16 52:13 85:14 89:3 89:6 91:15 98:21 99:7,12 104:8 114:11 121:14 122:21 123:2 141:11 152:6 163:11 movement 31:3,20 32:4 42:12,17 52:18,20 65:4 162:4 movements 31:5,6 31:8 53:10 moving 38:4 85:15 100:19 140:22 mucinous 131:3 multi 144:14,15 144:20 145:8 multiple 41:11 91:21 92:16 149:9	156:21 multitask 34:19 multitude 115:19 muscle 57:22 98:19 muscles 58:3 muscular 71:13 72:12 145:5 mutation 51:4 107:6 123:12 148:13 mutations 152:13 n n 2:1 4:1 naa10 43:10,15 152:9 name 4:5 11:1 14:12 19:11 21:3 42:1 43:5,6 44:7 46:1 51:2 55:21 56:21 77:1 82:4 90:6 96:10,17 97:16 99:8 115:10 126:12 129:14 136:11 141:12,16 142:16 144:1 148:3 152:2 155:15 158:12,13 names 147:22 nametag 12:21 nap 38:16 naproxen 54:21 naps 39:18 narcolepsy 56:6 56:12 narrow 130:19 national 117:2 146:3 154:1 159:20 natural 29:19 56:7 90:18,20,22 91:12 91:19 92:2 101:5 124:2 135:16 137:4 145:1 147:3	nature 23:13 149:8 150:8 nausea 72:5 navigate 133:6 nb 126:13 near 16:16 26:8 155:3 158:1 necessarily 28:21 97:9 110:20 122:11 127:3,4 162:19 necessary 154:7 need 38:16 39:1 41:1 50:17 56:19 56:20,22 60:18 64:5,5 74:1 76:19 85:4 87:21 88:22 89:5 92:13,21 97:3 114:20 120:6 120:8 134:12 135:18 139:9 154:21 157:5 158:16 163:8 164:5 165:2 needed 15:15 37:5 41:6 117:13 140:2 needing 70:9 needs 5:5 7:15 26:3 36:17 50:2 57:6,6 63:9 71:2 92:11 112:21 129:7 144:18 neglect 57:7 neighbors 31:7 neither 166:10 167:7 neonatology 20:6 nephrologist 19:20 nervous 32:2 network 12:12 70:4 neuroblastoma 126:14	neurocognitive 93:3 neurogenetic 49:15 neurologic 57:16 neurological 17:22 18:10 98:14 neurologists 115:9 neuromuscular 18:1 never 27:4 70:6 82:12 125:21 137:12 new 1:13 2:8 5:9 17:16 32:19 33:4 67:12 70:4 72:14 81:10 92:4 96:18 98:5 105:18 109:20 113:1 117:16 129:22 148:7 149:3,12 156:19 newborn 20:6 61:20 newest 94:11 newly 71:12 98:22 98:22 ni 158:12,13 niched 35:9 night 50:16 56:10 70:10,16 105:8 106:10,11,12 nih 152:16,19,20 153:2 nine 126:15 143:10 nonprofit 19:8 126:13,17 145:6 nonspeaking 74:18 nonverbal 49:22 nord 146:3,4 147:1
---	--	---	--

<p>nord's 147:6 normal 26:20 27:22,22 28:6 32:17,19 33:22 44:21 45:6 57:9 66:20 70:15 108:7 113:18 115:4 151:12 nose 82:8 104:18 notably 5:3 notary 1:16 166:1 166:19 note 165:4,7 notecard 14:20 notes 8:18 notice 20:17 114:18 142:1,11 noticeable 39:13 noticed 32:1 44:10 45:17 82:15 114:22 noticing 142:22 novel 7:22 november 71:19 nowadays 139:1 number 7:1 22:14 38:8 51:5,21 54:17 55:1,4 121:8 159:10 numbers 151:12 numbness 149:19 numerous 26:15 105:15 nurse 82:9,10 nursing 72:18</p>	<p>obstruction 131:1 131:5 obtain 7:16 149:13 obvious 121:22 obviously 53:11 138:14 occupational 56:19 occur 8:22 october 101:22 offered 108:2 offering 119:20 office 2:8,9,10,12 2:21,22 3:3 4:6 5:14,19 6:3,14,15 16:6 17:16 19:12 19:17,18 20:3,4 82:12 153:1 160:22 163:16 officer 2:18 12:3 15:6 80:3,8 81:13 86:12 166:2 offices 80:6 officially 33:19 offing 136:7 offset 53:21 oftentimes 46:4 ogden 152:9 ogden's 43:10 oh 25:16 34:3 48:14 51:18 52:21 94:9 104:21 107:11 109:22 110:4 116:3 123:9 124:18 125:7 ohio 17:20 oil 37:8 okay 24:14 27:8,8 30:15,20 35:1,19 37:20 39:3,16 40:13 42:2,15,15 42:16,18,22 43:1 44:6 47:18 49:6</p>	<p>52:10 54:6 58:16 59:2,2 62:9,14 64:10 66:7,21 74:10 76:20 79:12 95:2,12 99:6 101:2 104:7,8 114:11 116:3 118:7 124:19,22 126:8,8 134:19,22 135:12 138:4,9 141:3 159:18 old 23:20 25:4,8 26:6 34:22 49:14 55:22 70:1 71:14 97:17 98:12 104:13 105:2,16 105:22 107:1 108:7 109:1,1 142:17 older 25:2 36:18 64:1 77:8 78:4 oldest 98:10 onboard 121:11 once 16:3 39:8 63:11,11,11,11 64:2,4 72:2,17 122:18 oncologist 80:11 81:18 88:20 ones 24:17 47:21 68:2 71:22 121:20 132:11 150:11 158:18 ongoing 91:9 online 11:9,11 22:8,9 35:14,22 36:15 37:14,21 48:2,6 149:13 150:19,21 160:19 onset 35:2 opc 160:17 open 3:9 8:19 12:14 13:9 15:8 15:10,11,19,22</p>	<p>22:18 59:4,5 79:17 93:11 114:3 125:3 141:1,7 142:9 143:7 147:14 150:21 158:9 160:15 163:21 165:3 opened 48:21 opening 2:3 34:14 158:9 ophthalmologist 56:21 opinion 73:21 76:17 opinions 17:4 opioid 26:2 opioids 23:19 25:21 54:10 60:4 60:13 opportunities 5:10 opportunity 4:9 8:12 10:9 12:8 15:13 16:4 17:7 65:1 71:5 97:13 99:5,11 100:15,18 103:10 144:16 155:22 159:22 163:13 opposed 111:4 opposite 62:2 88:19 101:19 optimally 6:8 option 53:18 142:8 options 53:19 63:19 126:20 128:1,1 164:5 oral 63:7 order 22:13 70:13 84:14 145:14 oregon 91:2 organization 6:19 14:16 18:16 78:15</p>
<p>o</p>			
<p>o 4:1 o'boyle 74:3,3 oak 1:12 obesity 56:2 observational 35:10 91:13 observations 158:2</p>			

84:8 100:18 116:12,16 117:2,4 119:17 120:7 122:15 141:20 146:3 148:6 organizations 11:11 68:8 93:8 93:15 119:16,18 147:5 152:15 organized 117:15 organs 19:5 113:16 148:11 original 135:20 orphan 2:10,22 4:7 5:14,19 6:3,15 16:6 19:17 86:1 160:22 163:16 outburst 51:17 outcome 9:12 61:17 84:7 111:17 111:22 112:1,3 129:3 166:15 167:12 outcomes 67:5 85:10 88:4 outs 63:4 65:1 outside 10:10 11:22 25:6 outstanding 145:5 overall 32:15 38:2 85:2 88:6 overarching 156:10 overflow 13:1 14:19 overlapping 117:10 overproduction 97:1 oversee 80:4 overseeing 80:6 oversight 146:19 overview 2:4	oxygen 23:21 24:9 48:5 p p 4:1 p.m. 1:11 pa3156041 1:21 pad 101:12 page 2:2 125:3,3 137:5,5 paid 143:12,12 pain 23:17,18,20 24:1,16,18 25:1 25:17,19 26:17 29:12,12 42:11,14 46:9 48:8,9 55:3,3 60:1 149:19 158:4 162:3 painful 19:4 painkillers 60:13 paired 57:11 palliative 80:11 pancreas 103:8,11 113:17 panel 14:2,3 17:6 17:12 21:6 22:1 22:10 23:4,5 26:13 35:20 40:12 41:22 42:6,10,19 46:14 52:11 54:9 59:9 62:11 69:9 74:9 95:5,16 96:6 104:2 110:6 126:2 129:10,10 140:11 142:18 160:18 panelists 12:9 20:21 62:14 159:21 160:18 panels 13:21 paper 115:15 papers 125:4 137:1,13,13 parallel 120:5 parent 69:18 78:19,21 79:7,10	parents 44:22 57:8 58:12 70:18 76:16 78:11 137:17 152:13 park 74:21 parkinson's 18:13 32:3 part 8:5 41:10 42:14 43:17 61:19 67:19,20 68:4,6 70:19 81:19 85:19 87:9 89:21 93:18 102:1,4 103:13 109:13 111:19 118:10 148:13 159:13 participants 11:10 14:3,4 17:5,8,8 participate 11:9 15:14 29:18 35:7 35:9,10 81:9 102:8 103:10,19 125:15 131:8 134:6,21 143:5 157:21 participated 126:7 133:12 participating 20:21 102:16 134:18 160:16,19 participation 10:13 15:16 120:15 142:19 161:7 165:5 particular 28:3 35:5 111:21 particularly 19:10 61:9 81:20 149:7 parties 166:11,14 167:8,11 partner 147:19 partners 161:13 partnerships 144:19	parts 42:21 86:21 pass 14:21 passed 84:21 148:14 passing 32:9 passion 132:9 passionate 127:19 password 12:13 pathologist 136:18 patient 1:6 2:6,7 2:20 4:4 6:16 7:15 7:16 10:8,19,21 11:2,11 13:14 16:5 17:1,19 18:6 18:8 20:12 21:4 22:9 51:5 54:14 57:10 63:5,12 64:4 67:4,4,5 68:6 68:6,11,11,13,14 69:13 76:16 80:20 80:21,22 81:16 82:13 83:16 84:7 85:9,10,11,16 86:4,7 87:2 88:21 89:15 91:14,17 92:17,17 93:7,9 93:13,14,17 94:8 96:11 98:2 100:18 101:14,16 117:9 118:17 119:17 120:19 121:12 127:1 128:17 129:2 130:1,4,6 131:8 132:13 133:3 134:20 136:12,17 138:17 144:3,4,6 146:6,9 146:14 147:3,5,12 148:5 151:13 154:15,17 155:8 155:18,19 156:1,2 156:5,11 160:1,20 161:12,22 163:15
--	--	---	--

<p>patient's 7:7</p> <p>patientaffairs 17:2</p> <p>patiently 114:12</p> <p>patients 4:10,20 5:2,5,8 7:11,14 8:2,8,12 9:15,17 11:2,15 12:9 13:21,22 16:15 21:6 22:4,5 26:15 37:7 40:18 42:13 47:11 51:7,14 54:1 63:10 68:8 73:8,11,13,21 78:4 81:1,19,20 82:1,2 85:4 88:10 89:16,18 90:17 92:12 93:1,6 103:2 112:17 114:2 120:15 126:3 127:3 128:21,21 129:8 129:17 130:8,10 130:14 131:1,16 132:8,20 133:7 137:4,14 138:2 144:7 147:4 148:22 149:7,14 149:17,20 150:2,3 151:4,6,8,11,20 155:14 156:13,15 157:1,7,13 160:6 160:10 162:21 163:3</p> <p>patricia 46:1 94:10</p> <p>patrick 126:12</p> <p>pause 99:11</p> <p>payer 88:8</p> <p>pcori 68:7</p> <p>pediatric 2:9,21 6:14 19:20 20:3 40:15 56:20 69:13 106:4 107:3</p>	<p>126:14 140:8</p> <p>pediatrician 20:5 50:10 105:3,3</p> <p>pediatricians 115:9</p> <p>pediatrics 20:9 86:2,6</p> <p>pent 89:2</p> <p>people 4:22 8:21 8:22 9:19,21 18:16 19:9 23:1 29:10 30:11 32:18 35:6 36:7,12 37:6 37:9,17 41:22 42:18,22 43:2 45:18 47:15,19,20 48:3,8,22 49:3 50:7 54:12 58:18 59:1,4 61:5 62:6 64:5 70:17 78:16 79:4 84:2 96:2,13 103:22 104:20 105:9 116:13 121:11 123:12,19 124:5 125:6,20 127:1 129:19 133:16,22 134:2,4 134:14,16 136:22 137:20 139:21 140:1 144:21 153:11 158:14 159:6,8</p> <p>people's 33:4 147:22 159:1,11 159:12,14</p> <p>percentage 61:7</p> <p>perception 149:16</p> <p>perfect 31:10 73:6 78:3 94:19 127:3</p> <p>perfectly 27:10</p> <p>period 15:9,10,19 15:22 83:15 160:15</p>	<p>periodically 15:2</p> <p>peripheral 78:4</p> <p>peripherally 77:21</p> <p>peristalsis 58:3</p> <p>peritonei 129:18</p> <p>person 10:11 11:8 24:21 48:16 64:7 86:10 105:6 124:21 139:22 140:2 150:22</p> <p>person's 18:11 148:15</p> <p>personal 13:9 17:3 23:2 34:7 68:22 83:3,16 90:20 140:12,12</p> <p>personally 31:16 36:4 53:7,13 65:2 99:19 121:6 122:15 148:1</p> <p>persons 111:7</p> <p>perspective 6:20 23:12 36:19 63:5 64:1,20 81:16 85:16,17,17 87:3 92:8 95:6 140:20 149:14</p> <p>perspectives 1:6 4:4 7:17 10:21 67:5 68:8</p> <p>pertinent 72:6</p> <p>pervasive 50:12</p> <p>pfic 3:6</p> <p>pfic2 97:20 107:4 107:5 114:2</p> <p>ph 49:14 142:14</p> <p>pharmacy 47:11</p> <p>phase 59:22,22 60:1,2 63:1,2 64:21 108:2 126:16,16 127:6,6 127:7 135:16</p>	<p>phases 100:17</p> <p>phelan 74:4,4</p> <p>phelps 155:16</p> <p>phenomenal 117:19</p> <p>phenotypes 152:17</p> <p>phenotypic 157:3</p> <p>philadelphia 100:6 109:21 110:2</p> <p>phone 124:11,13 139:8 143:6</p> <p>physical 18:11 43:18 53:10 54:18 55:9,11,14 56:16 56:19 60:8</p> <p>physician 72:9 80:12 112:5 138:13 155:4 158:21</p> <p>physicians 41:3 67:18 159:2</p> <p>pick 65:7 132:7</p> <p>piece 84:21,22 88:11,18 94:11</p> <p>pieces 87:1</p> <p>pike 131:14</p> <p>pill 63:8</p> <p>pilot 103:10 117:1 120:12</p> <p>pioneers 80:17</p> <p>pipeline 62:22</p> <p>piper 114:22</p> <p>pitch 140:8</p> <p>pituitary 151:5</p> <p>place 28:15 29:5 40:18 62:1 84:8 143:7</p> <p>placebo 134:1 151:13,17,20</p> <p>placed 13:4</p> <p>places 84:15</p>
---	---	---	--

<p>plan 27:4 33:5 34:4 55:18 121:7 143:9 155:22 158:1 162:7 planet 123:20 planning 6:18 32:22 33:2 38:20 39:19 plasma 72:1 platform 37:21 144:18,20 platforms 36:15 37:14 platinum 55:18 play 36:2 plea 144:10,12 147:13 pleading 118:5 please 11:18 12:5 12:7,20,22 13:3,5 14:9,15,22 16:2,9 16:13 17:1,4 22:15,21,22 59:5 59:8 79:16 81:2 85:14 95:22 96:10 96:14 140:19 141:13,19 164:11 pleased 4:9 8:2 pleasure 155:22 pms 74:15 point 24:4 26:5,10 29:7 30:7,9,13 32:17 39:12 49:5 56:12 68:20 75:6 85:7 89:14 106:2 107:1,15 109:4 110:13 113:3 118:15 126:18 138:8 143:1 points 74:22 86:19 policy 85:22 120:3 120:3 146:2 152:5 pond 37:16</p>	<p>poor 31:6 population 24:6 37:8 51:5 74:21 75:8 121:12 125:17 portion 19:2 140:22 141:8 portland 91:2 portraits 9:16,18 9:20 10:10 pose 42:4 65:15 71:7 96:6 posing 22:1 positive 18:14 possibilities 102:19 possibility 30:1 possible 76:4 84:9 85:3 86:8,20 93:14 120:12 possibly 106:13 117:9 139:21 post 36:8 77:10 145:2 152:13 posted 125:6 151:2 potential 31:17 36:21 59:16,18 61:3 62:18 65:17 71:9 78:13 91:6 102:18 136:6 143:4 157:15 potentially 7:20 134:18 power 126:22 powerful 92:19 practically 123:9 prader 55:22 135:4 pray 122:2 praying 124:10 precise 38:14 preclinical 63:22 64:21 100:17</p>	<p>127:5 precluded 128:8 precursor 45:5 predict 92:5 predictable 28:7 prediction 27:15 preferences 67:4 67:13 112:12 premature 157:6 prenatal 82:17 prepared 29:4 167:3 prescribed 106:9 prescribes 29:12 present 3:7 6:22 117:6 presented 69:14 preserve 78:6 113:16 president 99:2 146:2 press 12:3 pretty 39:9 44:4 60:20 61:20,22 83:5 98:22 103:3 104:15,17 105:7 105:10 107:18,20 108:8 prevent 26:9 51:7 preventable 158:16 prevents 23:14 107:6 preying 37:7 primary 71:14 110:16,18,20 111:1 118:16,19 135:7 150:10 prime 90:21 principal 2:17 15:5 80:1,3 81:11 85:21 86:10 135:21</p>	<p>prior 155:17 166:5 priorities 150:12 prioritize 118:18 priority 80:5 159:11 private 48:17 privileged 132:5 probably 33:18 37:2 41:9 51:10 65:4 67:2 74:10 75:4 86:9 104:22 105:5 107:13 116:4 118:19 125:21 126:15,17 132:13 160:3 probe 160:9 problem 25:22 27:16 45:10 50:13 54:18 56:9 70:8 71:2 90:15 92:8 92:15 93:19 112:7 131:15,21 137:16 159:14 160:7 problematic 111:19 149:7 problems 18:3 19:3 24:7,10 29:9 39:14 44:18,22 60:14 84:3 98:20 99:1,2 112:6 116:10 132:1,20 137:8 proceeding 167:4 proceedings 166:3 166:4,6,8 167:6 process 59:20 65:18 69:8 85:1 85:14,18 89:13 116:6,19 119:14 146:15,16 151:18 processed 123:22 processes 86:15 86:22</p>
---	---	--	---

<p>processing 56:4 98:19 116:9 117:9</p> <p>produce 8:17</p> <p>produces 131:3</p> <p>producing 9:13</p> <p>product 5:13 6:8 6:12,13 7:5,20,21 9:5 10:14 13:12 14:18 85:2 88:2 141:22 163:5,11 164:7</p> <p>productive 20:22</p> <p>products 2:10,22 4:7,17 5:8,14,15 5:20,22 6:2,3,5,15 7:15 9:9 16:6 19:17 89:18 146:20 160:22 163:9,17</p> <p>professional 101:15 150:5 158:16</p> <p>professionally 155:6</p> <p>professionals 11:12 103:1</p> <p>professor 80:12</p> <p>profit 135:5</p> <p>program 9:11 17:16 117:1 147:2 147:3,4 155:20</p> <p>programs 6:5 85:12 120:12 146:8 147:8,10</p> <p>progress 16:21</p> <p>progressed 41:1</p> <p>progressing 79:5 114:19,20</p> <p>progression 79:6 91:3 157:13</p> <p>progressive 17:21 18:1 38:8 97:19 148:11 157:9</p>	<p>projects 145:2,3</p> <p>prolong 108:22 114:8</p> <p>prominent 27:19</p> <p>promise 5:17</p> <p>promising 5:22 6:2</p> <p>promote 4:16</p> <p>proof 139:5</p> <p>proper 153:13</p> <p>properties 159:12</p> <p>protect 4:16 34:12 159:11,12</p> <p>protections 29:5</p> <p>proteins 148:10</p> <p>protocol 61:21 100:9</p> <p>protocols 24:19 29:5 100:21 120:8</p> <p>proud 80:18</p> <p>proven 35:5 149:6</p> <p>provide 4:7 15:6 16:1 54:19 94:3 95:21 96:14 154:6 156:14 158:1,6,10</p> <p>provided 119:22</p> <p>provider 154:13</p> <p>providers 147:4 155:6</p> <p>provides 6:4</p> <p>providing 154:14</p> <p>pruritus 107:17 108:4 114:2,7</p> <p>pseudomyxoma 129:18</p> <p>psychiatric 31:3 32:6,12 53:14 57:6 65:5</p> <p>psychosocial 28:18</p> <p>psychs 115:9</p> <p>pt 55:2</p> <p>pten 93:1</p>	<p>public 1:2,16 3:9 4:4,17 5:12 10:21 12:13 15:9,10,11 15:19,22 80:10,20 141:1,7 153:21 160:15 164:10 166:1,19</p> <p>published 117:18 156:4</p> <p>pulpit 84:16</p> <p>pump 113:15</p> <p>pure 47:10</p> <p>purpose 93:10 101:20</p> <p>purposes 14:14 141:18</p> <p>push 145:12</p> <p>pushed 93:18</p> <p>put 9:1 10:2 57:20 61:1 68:9 72:21 89:8,9 92:13 105:9 122:8 123:11 124:7 127:9 138:18,21 139:11 146:14 151:6 154:7</p> <p>putting 88:2 106:17 111:14 124:3 129:2 155:12</p> <p>pws 56:1</p>	<p>53:18 59:14 65:15 66:22 69:15 71:7 77:5 79:3 92:20 111:5 119:3 123:3 123:7 130:6,9 138:15,19 154:20 160:7,11</p> <p>questionnaires 145:17</p> <p>questions 12:5 14:6 16:9 17:1,8 22:1,2,3 23:5 26:13 35:21 40:12 42:5,5 52:11 59:11 62:13 69:12 75:11,13 83:1,11 84:3 90:1,2,3 96:7 99:7,10 104:2,6 110:7 117:14 123:1 129:4 138:10 144:11 145:10 163:17</p> <p>quick 40:12,22 130:13</p> <p>quicker 91:20</p> <p>quickly 78:10 79:5 131:22</p> <p>quiet 48:16</p> <p>quieter 38:14</p> <p>quit 57:1 125:18</p> <p>quite 50:19 78:22 131:18,18</p>
		q	r
		<p>qualified 166:7</p> <p>qualify 135:10</p> <p>quality 29:6 32:15 38:2 116:8 145:2 147:5 149:16 151:15 157:12</p> <p>quarter 40:5</p> <p>quarterly 91:1</p> <p>queries 83:10</p> <p>question 29:17 40:22 48:3,9 52:13,15 53:3,6</p>	<p>r 4:1</p> <p>r35 152:20</p> <p>race 85:11</p> <p>rachel 2:12 3:3 19:11 69:11 145:22 146:1</p> <p>radiological 19:22</p> <p>raise 14:9 22:6 139:20 141:15 163:2</p>

<p>raising 119:21 155:7</p> <p>randomized 130:20</p> <p>randomizing 127:12,15</p> <p>range 14:7 108:6 115:4 151:12</p> <p>rare 1:2,6 4:5,12 4:19,20,21 5:1,3,5 5:6,8,11,13,18,22 6:5,7,8,12,22 7:3 7:6,10,13,17,19 8:1,9,14 9:9,15,17 9:20 10:2,14,17 10:22 13:11 14:18 17:15 18:7,10 19:15,21 20:8 27:1 30:3 32:13 36:21 37:15 42:14 43:9,13 44:9 45:7 46:20 49:14 51:4 57:19 58:7 65:11 69:13 70:3,16 81:17 86:1,5 87:3 90:16,16 91:10,11 91:18 92:9 93:2,7 94:3,17 97:12,21 103:4,7 113:7 116:17 117:2 123:21 129:18 140:7 141:21 144:14,15 146:3,5 146:8,20 147:2 148:10 150:1 152:3,8 153:4,10 153:22 154:3,16 154:22 156:2,13 156:20 157:5 161:21 162:8,16 163:5,8,11 164:7</p> <p>rarediseasefda 16:13</p>	<p>rarediseases.org 147:7</p> <p>rashes 72:4</p> <p>raskin 3:5 69:22 69:22 96:17,17 99:18 101:2 102:10 113:5</p> <p>reach 4:18</p> <p>reached 124:10</p> <p>reaction 90:9</p> <p>reactions 71:21</p> <p>read 9:7 107:12 107:12,14 137:13</p> <p>reading 107:22,22 117:12</p> <p>ready 94:20 95:14 122:4 147:18</p> <p>real 25:22 44:15 60:22 78:10 101:13 120:20 131:16,21 132:19 133:9 134:15 138:20,20 144:5</p> <p>realistic 122:8,12</p> <p>reality 132:8</p> <p>realize 36:11</p> <p>realized 24:2 84:14 116:6,17 117:11 123:17</p> <p>realizing 34:15 143:2</p> <p>really 16:18,21 18:17 25:10 27:1 27:13,13,20 34:2 36:11,16,19 37:22 38:12,20 39:9 40:3,6,16,17 43:18,21 48:21 49:3 50:16,19 60:1,1,8,10,19,21 61:5 63:12,18 64:8,16 66:13 71:16 72:6,7,15 72:21 74:17,18</p>	<p>77:6,7 78:8,20 79:10 81:22 82:7 83:14 84:1 86:2 89:1,3 94:2 97:6,6 101:8,13,17 102:15,22 103:4 103:14 104:19 105:3 106:3,5 109:8 110:9 111:3 113:13,20 118:14 128:6 129:22 132:16 134:5 139:3 141:5,6 146:9,14 153:3 154:20,20 155:5 155:13 160:6,22 161:1,21 163:1,9 163:19</p> <p>reason 55:10 75:22 84:18 127:18 132:19 164:12</p> <p>reasonable 76:4</p> <p>reasons 92:7 97:10 130:16,17 148:15</p> <p>recall 107:12 110:13</p> <p>receive 75:19 76:15,15 163:22</p> <p>recognize 5:4 7:7 21:15,17 23:1 45:12 50:7 140:14</p> <p>recognized 80:16</p> <p>recognizing 161:15</p> <p>recommended 41:9</p> <p>reconstructive 30:8</p> <p>record 28:4 140:18 166:9 167:5</p>	<p>recorded 20:15 166:6</p> <p>recording 12:16 166:8 167:4</p> <p>recovered 154:19</p> <p>recruiting 135:7</p> <p>red 18:22 82:7 142:5</p> <p>reduce 91:20</p> <p>reduced 166:6</p> <p>regarding 145:17</p> <p>regards 135:9</p> <p>regime 100:11</p> <p>regimen 29:12 133:20</p> <p>regional 128:5 132:2</p> <p>registered 15:15 139:3 141:9 142:11</p> <p>registrants 125:13</p> <p>registration 11:22 12:20 13:6 14:5 15:16 164:14,18</p> <p>registries 9:13 13:20 93:9 99:15 100:22 117:1 139:9 144:5,14,17 145:1,8,14,19</p> <p>registry 4:15 95:18 101:14 114:13 117:7 119:2 138:18,19 138:22 139:5,11 139:19 140:5 144:5 145:13 146:21 147:1,3</p> <p>regular 109:21 130:15</p> <p>regularly 104:15</p> <p>regulate 19:14</p> <p>regulation 80:6</p> <p>regulatory 130:2 146:2,16</p>
---	--	--	--

<p>reinvested 83:20 reiterate 58:22 79:14 relate 48:22 49:3 related 14:8 59:14 67:5,15 106:7 157:18 162:3,14 166:11 167:7 relating 162:12 relation 45:18 relationship 33:1 relationships 150:7 relative 166:13 167:10 reliable 83:17 relief 107:11 relieved 25:1 112:21,21 remain 14:11 142:9 163:21 165:3 remarks 2:3,17 3:10 4:8 15:7 16:1 17:10 142:6 remedies 35:14 remember 41:19 82:6 83:7 115:20 125:10 remind 59:4 88:20 104:3 reminder 46:11 142:8 reminders 95:20 remote 15:3 24:4 132:2 134:8 remotely 8:4 remove 121:21 removed 103:8 renal 2:11 20:1 replacement 91:7 report 74:12 85:10</p>	<p>reported 1:16 84:7 150:4,6 represent 92:22 146:5 representatives 6:13 represented 82:1 representing 14:13 71:12 96:12 required 55:14 rescind 27:21 research 10:5 17:17 30:12 68:18 68:20 72:14 77:2 78:14 94:5 99:3,4 125:15 128:16 129:16,16 135:15 146:9 157:22 161:13 researcher 80:17 152:14 researchers 23:22 24:2 32:11 78:9 93:12 100:16 101:16 118:4,11 researching 125:4 resonated 97:6 98:1 161:17,19 resource 9:8 resources 154:7 respect 20:9 146:19 respectful 17:4 22:22 87:11 respond 38:17 responding 22:15 response 25:12 33:8 responsibilities 85:22 responsibility 85:20 158:22 responsive 46:22</p>	<p>rest 82:4 restrictive 113:13 restrooms 12:1 result 23:19 108:17 112:3 131:2 143:18 158:19 results 35:11 117:21 131:20 retaining 120:15 retina 135:19 retrospective 41:15 review 101:14 reviewer 139:4 revolving 116:18 rhythm 70:20 right 12:2 23:17 23:17 25:2,17 30:20 34:20 38:9 39:11 51:15 56:7 69:2 72:6 84:10 85:4 86:5 87:17 90:8 94:9 104:13 105:20,20 106:16 106:18 110:13 113:4 114:8 117:22 119:9,10 120:9 121:7,9 122:19 123:9 125:9,22 130:11 141:14 151:10 risk 53:1 65:10 67:13,14,17 136:2 136:4,7 143:3 156:18 157:14 160:6 risks 62:18 64:13 78:13 risky 91:5 road 63:16,17 rob 159:14 robaxin 54:22</p>	<p>robert 46:18,18 47:3,9 robert's 47:8 robust 78:15 89:12 robyn 148:2,3 role 36:1 80:1 96:10 154:14 roll 137:22 romantic 33:1 room 1:14 8:22 10:11 11:3,10,20 11:22 12:12,21,22 13:1,22 14:9,19 16:17 17:9 21:5,7 21:15 22:4,20 45:20 46:4 49:9 51:18 62:6 69:5,6 71:6 79:15 93:19 95:17 96:3 127:18 133:17 138:7 141:14 160:4 164:20 rotberg 18:5,5 31:2 33:15 35:4 36:4 37:13 53:5 62:20 64:16 rothberg 2:16 round 19:1 55:2 route 157:20 rows 21:7 rules 16:14 run 46:8 152:5,16 running 27:11 79:13 117:3 147:8 rushed 106:19</p>
			s
			<p>s 4:1 sacrifices 128:10 safe 4:17 5:7 29:16 40:18 165:6 safety 27:15 127:6 153:13</p>

<p>samuel 1:16 166:2 166:18</p> <p>sandra 167:2,15</p> <p>sandy 12:3,4,7</p> <p>sarah 136:13</p> <p>sarascure.org. 136:12</p> <p>sarcoma 136:16 137:9,14,17</p> <p>sarcomas 137:12 137:15</p> <p>sat 82:12 133:2</p> <p>sates 147:9</p> <p>satisfying 106:17</p> <p>saturday 106:10 106:12</p> <p>save 126:20</p> <p>saw 65:7 105:4,15 108:11 136:10</p> <p>sawyer 98:10</p> <p>saying 44:2 61:12 109:19 111:15 115:16 162:10</p> <p>says 44:1,1</p> <p>scale 25:19 86:13 86:16,21</p> <p>scar 25:3</p> <p>scared 122:3</p> <p>scary 57:12 65:10 122:2</p> <p>schedule 28:7</p> <p>schizophrenia.c... 37:2</p> <p>school 26:18 27:7 27:11 38:18 42:21 51:8 66:13,19 71:1 87:16 94:16 116:21 157:8 162:12</p> <p>schools 10:5 94:5</p> <p>schoolwork 66:4</p> <p>science 91:20 103:13 116:22 144:2</p>	<p>scientific 5:9,20 6:1</p> <p>scientifically 145:17</p> <p>scientist 117:17</p> <p>scientists 101:16 118:5,11</p> <p>scoliosis 18:3 143:3</p> <p>score 152:19</p> <p>scratch 105:11</p> <p>scratched 105:8 105:14</p> <p>scratching 104:14</p> <p>screen 12:13 163:14</p> <p>screening 61:20</p> <p>scrubs 82:9</p> <p>sea 68:18</p> <p>search 124:8 127:22 132:6</p> <p>searching 109:10 126:19 133:8</p> <p>seat 14:20 164:9</p> <p>seats 13:4</p> <p>second 2:19 3:1 13:19 38:11 50:6 51:11 55:2 88:18 145:16</p> <p>secondary 110:15 135:9</p> <p>seconds 79:2 142:4</p> <p>secret 137:5</p> <p>secretary 153:1</p> <p>see 8:2 9:19,21,21 12:21 15:2 26:16 27:3 35:11,13 36:6,9,12 37:10 37:19 40:11 41:14 44:18 53:10,15 62:12 63:21 64:5 66:22 77:20 90:15 93:18 94:22 102:2</p>	<p>106:16 109:12 110:7,14,18 121:19,19 126:5 128:20 129:13 130:9 134:14,16 136:3,4 140:6 151:7 153:3 163:14</p> <p>seeing 33:9 37:18 47:19 74:11 93:6</p> <p>seeking 152:19</p> <p>seen 24:15 106:2 107:3 115:10 128:12 136:17 149:3 152:21 153:16</p> <p>seizure 45:13,15 50:8 74:15 75:1,7 75:7</p> <p>seizures 45:8,14 50:8 51:21 98:17 115:6 116:10 118:19 162:5</p> <p>seldomly 148:20</p> <p>selected 14:2,3 111:9</p> <p>selection 78:17 135:16</p> <p>sell 37:7</p> <p>sense 51:9 61:12 77:11 119:12 127:10 159:1</p> <p>sensed 41:8</p> <p>sensory 98:19 116:8 117:9</p> <p>sentences 96:15</p> <p>separate 145:1</p> <p>sequencing 46:19 55:17 131:15,17 131:20</p> <p>series 85:21</p> <p>serious 66:9,9 136:2</p>	<p>seriously 139:3</p> <p>serve 9:7</p> <p>served 15:17</p> <p>service 38:9 154:13 155:6</p> <p>services 50:3,4 146:9 150:10 154:9</p> <p>session 2:5,19 3:1 13:17,19,20 15:4 15:8,12 21:12,21 95:15,17</p> <p>set 15:11 37:1 118:4 130:20</p> <p>seth 2:16 18:5 30:16 44:19 52:14 62:15</p> <p>setting 51:15 85:14 92:3 121:1 145:1</p> <p>seven 33:19 73:10 73:21</p> <p>severe 46:8 47:4 97:2 157:2</p> <p>severity 157:4</p> <p>sex 78:17</p> <p>shaking 44:18</p> <p>shank 74:6</p> <p>shaped 19:1,2</p> <p>shapiro 2:14 18:19,19 23:13 24:18 25:16 26:21 28:5 29:1,21 40:14 59:21 68:1</p> <p>share 23:3 43:2 48:17 55:7 79:15 87:18 93:12 99:5 100:18 135:13 137:21 138:6 140:17 144:17 156:6,13</p> <p>shared 156:21</p> <p>sharing 7:8 8:5 14:14 15:3 17:5</p>
---	---	--	---

45:20 93:5 95:5 102:3 108:10 126:9 129:11 135:2 140:11 155:14 shazia 154:11,12 she'll 22:8 44:3 132:14 shelton 129:14,15 132:18 sher 145:22 146:1 146:1 shock 116:4 shocker 132:19 shooting 118:1 short 31:14 70:6 76:22 100:14 138:5 147:17 shortness 48:4 shot 116:20 shoulder 82:3 shout 147:11 show 42:12 75:4 111:17 126:7 134:20 139:10 showing 34:18 117:21 shown 35:5 shut 125:21 137:22 sick 61:13,15 72:3 72:7,7 94:17 sickle 2:14 18:21 18:21 19:2,9 23:9 26:16 29:15 40:16 40:18 61:22 62:1 side 31:21 45:21 53:2 59:17 62:18 64:14 66:8,10,12 72:20 74:16,19 109:6,8 118:2 122:1 128:17 133:21 162:20	sides 92:16 sign 11:21 12:5 15:15,15 signature 166:17 167:14 significant 5:2 14:17 39:9 47:12 141:21 161:21 162:20 significantly 149:22 signs 13:1 silence 11:19 silent 24:9 silver 1:15 silverstein 2:11 3:2 19:19,19 28:9 67:1 111:2 138:12 similar 47:21 49:8 84:3 111:12 114:18 similarly 9:16 41:2 simple 58:1 simply 31:11 58:10 67:20 sinai 106:20 107:2 sincerely 165:5 single 73:14,16,22 127:10 149:9 150:22 sir 77:5 90:3 sister 34:12 44:8 44:11 45:11,12 57:8 114:22 136:14 sister's 83:2 sit 16:16 18:14 82:13 98:3 sites 151:3 sits 86:5 sitting 26:22 82:3 83:7 87:12 114:21 116:3 122:4	situation 111:19 140:1 situations 92:11 141:7 six 77:12 124:9 130:2 size 85:4 skills 51:11 130:4 166:10 167:6 slavit 3:8 48:1 49:5 52:6 58:20 79:4 133:15 138:8 sleep 50:9,15,16 56:4,10,10 57:4,5 58:5 65:8 69:14 69:14,17,19 70:9 70:19 74:9 76:3,3 77:7,7 79:8 87:15 98:2,3,18 105:8 106:9 118:20 124:19 158:5 162:4 sleeping 52:9 70:13 105:10 sleeps 70:6 sleet 121:14 slept 105:17 slight 39:13 sloan 136:21 slots 15:20 158:9 slow 56:4 64:17 79:6 101:19 157:13 slowly 18:11 small 7:1 125:17 131:1,5 137:16 140:8 155:1 smaller 100:2 snake 37:8 snapshots 93:12 snow 121:14 snowballed 125:7 social 20:11 37:21 51:15 117:13	124:5 136:19 139:21,22 140:2 societal 154:5 societies 144:4 society 48:12 151:5 soft 137:9,12,15 software 69:2,3 80:8,15 solution 70:7 108:2,18 solve 92:11 93:19 solved 92:16 solving 92:7 somebody 51:17 69:3 76:9,9 88:9 126:4 139:12 somebody's 121:15 somewhat 102:20 son 46:18 57:15 57:21 70:1 71:13 71:18 72:17 77:5 77:8 99:19,22 100:7 102:1,11 103:6 117:11 124:17,17 126:13 128:15 son's 114:17 124:2 sons 77:6,19 soon 91:22 sooner 33:12 41:10 sorry 90:13 97:20 113:1 138:12 sort 22:11 23:12 23:15,16 25:21 33:8,10,11,12 36:1,2 39:18 41:4 41:6 52:17 59:12 59:14,19 64:11,13 79:13 82:3 84:9 97:7 101:10,12 109:9 114:14
---	---	--	--

126:10	speech 38:14	72:8 73:8 75:16	stopped 110:1
sound 140:18	43:12,21 51:12	78:5 90:14 95:15	stops 151:20
sounded 143:8	56:20 57:10,12	96:8 98:9 99:13	stories 16:20
sounds 44:1 110:8	58:21 143:3 158:4	100:8 117:14	87:18 88:15,16
150:20	speed 56:4	119:21 126:5,9	129:11 140:12
source 150:11	spell 45:14	started 23:3 43:19	141:4
sources 146:21	spelled 144:12	44:2 76:6 95:9,13	story 34:15 83:16
space 88:8 146:20	spencer 2:15	95:21 98:11 101:4	83:19 84:1,4,15
spaces 82:13	17:18,18 38:7	106:10 114:13,16	87:22 89:8,12,21
speak 12:20 14:10	39:5 40:1 41:7	116:12,14,14	92:6,19 114:17
16:5 48:6 53:7,8	48:13 65:19 66:11	119:6 123:7,14	123:6 125:19
66:20 67:2 68:2	spend 76:13 77:12	124:1,1,3 125:3,4	128:19
120:18 126:4	spending 21:12	125:7,19 142:12	strange 105:17
141:10 142:19	spent 47:8 81:19	147:1	stranger 48:17
148:4 158:14,17	spinal 63:8	starter 48:20	strategic 119:12
speaker 15:21	spite 39:1	starting 63:2	strategically
79:22 141:10,11	spoke 46:3 97:10	77:10,20 85:7	121:7
141:12 142:12,13	sponsors 5:21 6:4	93:8 100:17 108:1	streamline 69:7
143:21 145:22	9:8,10 154:14	starts 77:21 127:7	stress 27:19
148:1 150:16	155:6	startup 84:11	148:21
152:1 154:11	spouse 130:1	state 14:11,12	strong 127:14
155:10	132:3,8	55:12 73:4	struggle 60:9,19
speakers 22:14	spread 119:15	stated 157:21	62:7,7 98:18
141:9 161:6	120:4	statement 111:4	149:5
speaking 12:6	spreadsheet 101:4	154:20 155:5	struggled 149:18
16:12 23:1 36:4	spring 1:15	statements 12:11	160:3,5
41:20,21 42:2	staff 6:16 9:8	states 4:22 94:7	struggles 43:22
52:7 104:4 140:4	10:19 11:2 12:20	125:10 136:1	struggling 36:12
142:1,3	12:21 16:5 20:12	153:22	stuck 123:16
special 76:8 79:21	21:4 86:4 147:12	statistics 158:18	student 39:12
80:5 93:22	160:21,22 163:16	stay 16:2,7,8	studies 9:13 13:19
specialist 56:22	164:17	76:14 143:12	78:17 90:18,19
105:5 148:19	stage 63:22	stayed 124:11,13	95:18 102:7
specialists 67:19	stages 25:16,17	staying 40:1	103:18 104:11
106:3 115:8 132:6	stakeholder 10:17	steering 101:15	118:3,13 127:11
specific 8:11 75:17	145:8 154:15	stem 68:9,20	128:17 129:1
76:7 111:1 114:7	stakeholders 6:10	step 25:19 122:17	137:1 145:2,3
156:10 157:17	9:5 144:16 161:11	steps 34:5 66:1,2	study 35:11 90:20
specifically 5:14	stand 51:1,2 88:14	stimulants 56:8	90:22 91:1,2,9,12
109:6 131:12	147:18	stipends 119:22	100:21 103:11
154:15 160:11	standard 54:17	stock 138:22	111:18 118:8,8,9
specify 85:12	staring 45:14	stone 46:17,17	120:1,9 126:8,21
spectrum 88:6	start 17:13 23:5,7	stop 13:5 27:2	127:7 128:8 129:4
	27:2 34:17 59:13	93:21 110:4	135:16 138:17

<p>153:21 154:1 studying 103:2 stuff 22:7 36:10 69:1 91:12 107:4 subcutaneous 72:19 submissions 5:21 8:20 submit 12:15 79:16 140:19 142:9 145:12,16 163:20 submitted 14:5 144:8,13 subretinal 91:6 135:18 subsequent 83:22 subspecialty 19:21 20:5 succeeding 121:3 success 6:21 successful 137:12 143:19 161:2 successfully 6:6 145:6 suck 120:16 sudden 124:8 suffer 121:19,20 suffering 73:12,21 suffers 74:13 sufficient 73:1 sugar 97:2,3 113:9 113:16 sugars 70:11 suggest 160:9 suicidal 31:22 suicide 65:10 sum 53:6 summaries 14:5 summarize 156:5 summary 8:16 9:3 165:1 summer 44:3</p>	<p>sunday 106:12 supervise 158:22 supervision 50:17 supplements 35:16 54:11 support 6:8 7:21 10:14 36:3 134:8 137:16 150:11 supported 6:18 supporting 5:12 18:16 suppose 158:18 supposed 73:8 sure 27:3 35:21 37:6 46:13,16 52:16 55:13 59:6 62:10 67:22 70:11 76:4 78:20 86:6 89:7 95:7 99:11 99:18 101:1 104:4 104:12 108:8 112:19 121:1 123:4 126:12 138:11 139:9 158:6 surgeon 135:21 surgeries 94:15 100:10 surgery 122:5 135:17 survey 149:13,17 164:9,11,12,15,20 surveys 37:10 150:3 164:14 susan 2:6,9,21 13:13,14 20:2,10 21:1,3 67:14 susan's 28:9 susceptible 44:17 swallow 47:3 48:6 131:9 swings 31:9 33:17 52:19,21 65:9</p>	<p>switch 93:21 sword 56:18 57:2 sworn 166:5 symptom 4:13 13:17 31:9 38:11 57:17,18 58:12 71:19 73:16 112:20 114:8 118:18 151:8 157:3 162:14 symptomatic 32:7 73:14 symptoms 7:19 13:11 21:13,13 23:11 24:12,15 25:14 30:22 31:4 32:12 33:17 34:18 35:3 38:5,13 39:4 39:17,22 41:12 42:10 43:3 46:5 46:13,21 47:1,4 47:20 48:2 49:8 49:10,17 53:14 54:7,13 56:1,3,7 56:11 58:19 64:12 65:20 72:3 73:9 79:18 112:8 117:12 123:13 124:2 142:22 144:6 148:17 149:19,20 156:16 157:1,17,17 162:2 syndrome 44:10 46:2 49:15,15,20 49:21 52:8 54:15 55:22 74:4,5 93:1 93:2 94:14 135:4 syndromes 44:13 50:9 74:7,11 75:3 synergize 7:5 163:5 syngap 99:3 syngap1 3:4 57:16 98:13 115:16</p>	<p>117:8 118:10 124:8 125:12 synopsis 114:17 system 32:2 44:16 99:1 108:3 131:4 systems 83:17 84:6,7 156:22</p>
			t
			<p>table 11:22 13:6 15:16 62:12 99:9 104:6 123:1 138:9 164:14,18 tackle 78:20 take 8:15,16 10:12 13:6 22:11 31:18 38:16 54:4 63:10 63:14 65:22 66:2 72:1 76:20 81:13 82:18 83:19 86:15 114:7 122:4,11,16 127:4 135:19 139:3 147:17,22 151:13,17 taken 26:15 53:2 143:11 166:3,12 167:9 takers 159:18 takes 38:20 57:4 57:10 talents 10:4 talk 47:16 48:6,8 48:18 50:14 51:14 53:17 54:7 61:3 71:16 75:18 78:17 83:1 89:16 90:10 97:21 100:22 104:10,21 105:9 106:5 112:5 119:2 130:11,14 132:6 137:6,21 140:15 talked 49:7,11,18 52:9 97:6 112:11 134:4,8,14,17 157:7 162:1</p>

<p>talking 21:12 23:1 47:20 48:4 60:15 71:17 82:4,21 83:8 124:14 130:19 132:22 133:16 146:22</p> <p>tangible 39:10</p> <p>task 5:19</p> <p>taught 116:21</p> <p>taylor 98:10</p> <p>teach 63:3</p> <p>teaching 125:18 155:3</p> <p>team 28:14 29:10 41:3</p> <p>tear 104:18,18,19</p> <p>tech 84:11,12 92:17</p> <p>technical 92:8,10</p> <p>technology 80:14 86:18 144:17,20</p> <p>tell 34:11 74:20 76:5 81:14 88:14 93:16 99:16 104:9 105:6 114:14 125:22 132:3 133:6 137:19 158:16</p> <p>teller 167:2,15</p> <p>telling 44:20 125:19</p> <p>tells 128:19</p> <p>tenant 144:20</p> <p>tend 36:5</p> <p>tends 40:16</p> <p>tennessee 155:1</p> <p>term 31:14 148:9</p> <p>terminal 74:5</p> <p>terms 22:11 23:9 23:16 39:17 42:9 43:21 44:16 55:11 58:18 67:16 79:3 79:19 99:21 102:17 103:5</p>	<p>108:13 128:13 145:9 162:9,13</p> <p>tested 18:13 33:10 33:20 134:2</p> <p>testifying 166:5</p> <p>testing 33:14 34:6 34:7 68:16</p> <p>tethered 113:15</p> <p>texas 115:11 118:7 120:9,17</p> <p>thank 4:3 6:17 8:5 10:13,19 11:5,6 20:14,20 21:1 25:11 26:14 30:14 30:15 33:6 35:1 35:19 37:1 38:3 39:3 40:10,21 41:16 42:2 43:8 44:6 45:19 46:14 47:18 49:4,6 50:21 52:2,10 54:5,6 55:6 56:15 57:14 58:16 59:2 62:9,14,14 64:10 65:14 66:21 71:4 73:2 74:2 75:10 79:1,12 81:3,3,5 89:22 90:1,5 95:2 95:5,10 96:15 97:12,14 98:5,6 99:6 102:6 104:1 108:9,9 110:6 113:22 114:11,12 122:20 123:5 126:1 129:10,12 129:14,21 132:17 133:10,10 134:19 136:9 138:3 140:10,11,13,16 141:1,3 143:20,22 145:9,20,21 146:10,18 147:19 147:20,21 150:13 150:15 151:22</p>	<p>154:10 155:8,9,11 155:12 158:7,8,12 159:16,17,20 160:13,14,16,19 160:20 161:3,4,5 165:4,7</p> <p>thankful 152:14 153:8</p> <p>thankfully 154:18</p> <p>thanks 52:1 133:9</p> <p>theme 156:7</p> <p>themes 156:10 158:4</p> <p>therapeutic 91:13 164:5</p> <p>therapeutics 2:9 2:21 6:15 20:4</p> <p>therapies 2:13 3:3 5:6,10 19:13 29:20 30:8 47:12 91:21</p> <p>therapy 19:14 30:1,3,5,6 43:19 54:18 55:9,11,15 56:16,19,19,20 58:21 63:8 67:12 75:15 77:9 90:12 91:7,7 122:2,7 134:17</p> <p>thiamin 46:22 47:10</p> <p>thing 27:10 41:18 45:7 47:2 51:12 53:9 55:2,4 61:10 63:2 66:11 78:10 78:12 82:12 103:17 110:9 113:8 119:10,14 124:4 125:1 130:8 137:18</p> <p>things 8:22 20:15 22:16 24:4 25:13 26:4 31:15 32:22 33:3 37:3 39:20</p>	<p>41:5,12 42:19 43:11 44:14,15 45:17 54:9,16 55:1 58:6 60:14 60:21 66:15 77:22 78:1 79:19 82:15 84:14 85:8,18 87:5,17 89:1 92:14 94:17 99:17 107:13 108:12 113:12 115:1 116:10 117:20 118:21 121:4 122:13 126:21 128:12 129:3 133:16 140:15 145:18 150:20 153:19 155:19 158:4 160:2 162:10,11</p> <p>think 7:10 22:16 23:15,20 24:6 26:22 27:13,18 28:6 29:15 31:12 32:18,22 36:15 37:14,22 41:4,7 43:17 44:15,19 47:3 49:16 51:22 53:8,10,16 58:8 60:5,10 61:18 62:7,10,17,17 63:2,6 65:6 66:17 67:2,6 68:1,4,5,12 68:18,19 69:1,6 71:4,15 72:8 74:9 74:22 75:22 78:13 78:22 86:2 87:19 87:22 89:14,14,15 92:15,20 94:19 97:7,11 103:17,18 105:13 108:5 111:3,9,13 112:4 115:7,10,11 116:5 118:6,15 119:9,14</p>
--	---	---	---

119:16,18 120:7 121:4,8,10,11,12 121:20 122:8 124:11,15 125:11 128:7,19 135:8,12 138:16,18,21,22 141:4,5 151:18 160:6 161:2,12,13 161:16,16 162:16 163:7 164:1,4 thinking 30:21 32:10 33:10 34:4 34:20 59:17 62:18 65:16 66:8 71:8 76:11 84:11 87:13 89:17 106:15 113:10 145:19 146:16 159:4 162:9 163:4 third 42:15 49:18 50:9 77:4 90:14 152:22 thought 31:7 81:13 115:6 151:18 thoughts 31:22 65:12 140:17 thousand 92:12 three 23:11 24:12 27:6 30:22 34:11 35:12 38:5 39:5 42:9 49:16 50:16 52:17 63:15 65:3 69:15 73:11 77:10 97:17 98:10,11 109:1 110:2 111:5 116:14 124:14 125:1 thrive 114:3 throw 58:11 137:11 thrown 137:14 thursday 106:9	tie 120:21 tied 120:2 ties 55:19 tight 35:9,9 time 1:11 8:17 10:12 11:8 14:4 15:11,15,20 22:15 24:2,16 25:4 39:4 43:16 45:4 55:18 55:19 62:11 65:8 68:5,5 72:4,21 76:22 79:13 82:17 83:15 84:6 92:20 95:14 103:3,5 106:19 107:12,17 109:14 110:9 111:20 112:18 115:18 116:9,14 119:10 122:19 125:19 126:4 132:4 133:17 134:15 136:16 138:5 142:4,5,7 143:13 145:11 146:7 149:3 154:19 155:4 158:11,13 162:12 164:3,15 timely 4:18 41:5 timer 142:1,5 times 15:10 22:18 35:12 36:5 60:22 tired 38:15 tissue 2:12 3:3 19:12 25:3 68:21 137:9,12,15 148:11 tobacco 80:7 today 4:3 6:20 8:8 9:6 10:11 11:15 11:20 12:4,5 13:4 14:8 15:16 16:3 16:18 17:3 20:21 21:5 22:17 35:17	52:12 71:18 73:6 79:15 81:16 84:19 87:9 88:9,12,13 94:8 95:21 96:13 141:6,8 142:16,19 146:10 155:14 156:7,12 158:4 160:16,17,20 161:2,6,9,14,16 163:7,10 164:1,3 164:5 165:5 today's 4:18 6:11 6:19 8:7 9:15 10:13 16:13,15 145:9 told 61:20 76:2 90:6 106:20 109:5 133:3 136:14 tolerance 26:2 tolerate 47:15 64:14,15 156:18 157:14 tomorrow 140:3 ton 153:2 tone 57:22 top 38:4 65:12 topics 14:8 98:1 totality 87:22 88:17 89:12 touch 38:19 107:5 147:13 touched 32:16 touching 31:17 tough 35:13 53:17 toughest 144:19 town 82:10 track 124:1 traded 103:6 traffic 123:16,16 train 158:20 trained 28:20 training 40:2 130:3 155:4	trans 85:21 transcriber 167:1 transcript 8:18 12:18 20:17 164:21 167:3,5 transcriptionist 41:21 166:7 transition 25:8 32:20 41:18 42:1 transitioning 32:21 transparency 14:13 141:18 transplant 108:18 109:4 transplanted 109:2 transplants 30:2 61:6 travel 14:16 109:19 119:20,21 121:22 127:17 128:2,9 132:10 141:20 143:12 151:19 traveled 136:8 traveling 10:5 94:4 128:21 travels 165:6 treat 19:21 21:18 53:11 56:11 58:14 73:5 76:3 118:18 132:7 treated 50:8 52:20 53:2 72:22 77:8 treating 100:6 treatment 4:14 5:18 6:22 7:13 13:18 21:14 24:19 25:1 29:13 40:15 40:15 54:17 59:15 61:11 62:15 71:17 72:2,10,13,16 73:1 79:20 102:18
---	--	---	--

102:21 109:21 133:19,20 146:7 148:7 149:16 150:9 153:11,18 154:19 156:19 162:15,15,18,21 treatments 31:17 36:21 66:16,17 72:15 75:7,8 82:20 85:4 92:4 144:6 149:2,4,5 149:12 153:6 156:17 157:11 tremendous 45:10 71:3 155:13 trend 135:6 trends 117:7,13 trial 4:14 7:22 61:17 63:4 64:4 67:16,18,19 68:7 68:11,15 75:16,20 76:1,7,11,12,15 78:5 103:10,21 108:1,5,11,14 109:14 110:10,11 111:14 112:1,6,9 112:10,16 113:3,4 117:22 120:13,22 126:8,20 127:22 128:1,13,20 129:1 132:15,21 134:3 134:10,11,13,21 143:5 160:4 trials 19:14 29:18 29:19 30:5 35:8 35:10 36:20 61:5 61:13 62:22 64:21 65:1 67:7 68:10 68:13 75:15 77:3 85:9 88:1 90:13 99:15,21 100:1,3 100:20 107:16 109:10 114:5 119:6 120:14	126:16,18 127:2 128:4,15 129:2 130:20 131:6,11 131:13,19 133:1 133:12 134:17 135:6,11 137:8,11 142:20 143:16 144:15 151:9,21 153:7 160:13 163:1 trick 70:12 tried 54:21,21,21 54:22,22 57:8 74:15 104:16 trip 110:2 trips 143:10 trouble 44:19 159:9 true 153:21 162:10 166:9 167:5 truly 30:5 33:22 89:11 120:2 155:15 trusted 103:4 try 19:3 31:18 32:11 34:12 35:12 53:6,8 63:9,12 65:6 75:17 76:6 76:15 95:9 101:20 109:4 112:14,15 120:8 122:15 137:13,20 139:20 140:3 151:3,5 trying 32:14 35:15 35:17 36:10,16 37:7 40:8 47:8 62:3 63:3 64:22 65:2 67:14 75:16 78:8 82:18 83:15 86:2 111:16,17 112:9 119:6 121:5 125:16 130:3 160:4 162:11	tube 47:5,5 94:15 tumor 93:1 131:13 tumors 131:3 turn 10:18 21:1 22:4 40:11 42:3 59:9,11 62:12 83:17 84:10 96:7 140:21 141:12 142:3,5 turns 22:11 91:3 tweet 16:12 twenty 105:22 twice 40:2 43:19 57:21,22 twin 114:22 twins 98:11,12,12 twitter 16:11,12 two 13:13 15:21 23:10,20 30:21 38:5 42:9 44:8,13 49:16,17 50:16 53:15 65:22 69:15 71:12,13 76:1 77:3,6,19 79:4 81:11 86:7,22 90:12,22 91:2,8 96:19 100:9 104:12 105:2 107:1 109:1 115:9 116:6 117:3 124:13 125:8 129:19 138:16 141:9 145:10,18 147:17 149:3 157:1 158:9,10 160:1 type 14:22 37:20 54:15 92:10 106:8 108:21 158:15 types 25:13 115:19 117:20 127:11 157:17 typewriting 166:7	typical 51:9 typically 47:14 73:9 152:10 typing 83:8
u			
ubc 154:13,13 ucla 143:7 ultimately 84:7 85:2,13 86:12 87:16 93:18 107:22 ultra 90:16 91:11 91:18 123:21 unable 149:20 uncommon 148:18 undergo 77:16 undergrad 39:12 underlying 83:17 understand 11:7 30:19 36:16 63:9 63:12 64:22 70:15 87:20,21 92:6 99:14 106:3 112:16 122:14 149:15 151:14 understanding 88:1 101:9 understands 45:10 understood 33:22 127:14 underway 90:13 unexplained 72:5 unfortunately 53:7 54:2 72:13 114:5 130:12 unique 6:20,22 7:8 8:11 50:19 87:19 156:9 157:16 united 4:22 62:8 94:7 125:10 135:22 153:22			

university 39:11	various 9:4 28:15	36:11 40:9,10	waterproof 121:1
unknown 148:15	112:8 147:9	42:3 43:1 45:16	way 21:13 36:16
unlock 83:16	vascular 25:4	46:12 50:13 52:10	48:13 82:3 84:13
unmet 5:5 157:5	vector 135:20	53:8 54:6,11	86:7 88:15 91:1
unpredictable	versus 36:18,18	58:17 59:4,9	91:16 94:18 96:9
162:6	61:8 64:2 78:13	61:10,11 63:18	102:15 109:4
unreasonable	127:12	67:16 70:12 71:16	114:19,21 117:15
108:20	vice 146:2	75:10 79:14,21	119:1 122:6
unveil 94:11,13	video 20:18	87:4,16 89:3,6	123:17 127:3
unveiling 95:3	views 17:3	94:17 95:7,13	139:20 140:20
upcoming 62:22	visibly 53:9	100:21 103:22	ways 21:19 62:5
upset 31:11	vision 77:14 78:2	104:3 106:8	70:21 82:1 83:15
136:22	78:3,4,7 136:3	111:20 112:19	84:18
urgent 12:19	143:3 148:6	118:18 120:11	we've 23:3 26:6
usable 76:17	visits 54:20	121:19,19 122:22	47:10,22 51:16
use 16:13 17:9	vitamin 47:12	126:2 127:4 128:7	54:8 57:20 60:14
27:22 35:15 38:9	vitamins 47:10,13	129:10 133:11	68:2 69:1,5 86:16
39:6 43:5 71:21	54:11 82:17	134:16 135:13	89:2 90:11 115:10
83:18 85:8 88:11	voice 22:9 38:14	137:6,11 140:11	119:22 126:17
89:2,9,13 95:14	68:6 81:6 85:10	140:21 145:14	131:16 133:15
130:4 140:3	86:7 88:12,13,14	146:10 147:11,18	137:2,3 146:22
144:22 147:4	89:3,8 92:19	151:12,16 154:12	149:3 153:16
160:12 163:4	120:19 127:1	156:6 159:20	159:15 163:7
useful 112:10	128:17 146:14	160:20 164:10	wear 50:11
139:14	156:4 161:18	wanted 27:21	wearing 12:21
user 69:5,6 87:15	voices 81:1 158:14	30:16 36:14 40:11	web 3:8 8:4 9:1
uses 47:5	164:4	40:14,19 43:11	22:5,20 42:8
utilize 22:19	vomiting 72:5	47:16 51:22 52:6	46:15 47:19 52:3
v	w	52:14 53:11 55:8	52:3 58:17 71:6
vacation 27:6	wait 63:14	57:16 58:11,22	76:21 79:3,16
valentine 155:10	waiting 35:11	72:21 75:5 89:22	81:8 88:13 95:7
155:11,16 160:1	105:18 114:12	90:9 95:5 101:13	95:17 96:1,2
validated 145:17	waiver 47:9	111:2 131:8 132:7	104:5 133:12
valuable 9:4,10	walk 13:7 38:15	134:21 150:18	138:6 140:14
11:16 37:14	40:5 43:16 48:18	163:12	161:7 164:19
value 138:22	65:21 74:21 115:3	wanting 34:12,13	webcast 8:21 11:7
140:6	walked 39:6	48:17 65:8 134:14	12:16 14:1,22
variability 157:3	walker 39:7	warriors 60:5	17:9 20:15
variable 158:19	walking 18:2 38:9	washington 152:4	webpage 14:6
variants 125:12	40:4 41:8 43:20	152:6	website 20:16
varied 148:17	51:13 55:10	watch 105:11	147:6
variety 8:1,9	walsh 12:3,7	watching 117:11	wedding 106:11
113:12	want 11:17 16:2,7	water 121:14	week 12:17 35:12
	16:21 20:20 26:21		40:3 43:19 57:22

63:11 72:2,17,20 98:12 117:19 weekly 58:15 weeks 27:6 144:9 weigh 59:15,16 62:3 66:12,18 78:12 weighs 77:14 weight 27:18 weird 70:20 90:9 welcome 4:3 10:20 11:2 81:2,5 weldon 3:4 57:15 57:15 98:7,7 114:16 119:9 123:14 wellbeing 60:7,8 150:6,7,13 welt 45:22 46:1 welton 94:10,12 94:22 wendy 3:8 22:6,6 42:7 47:18 49:4 52:3 58:16 79:1 133:11 138:5 went 61:16 101:22 103:8 104:15 105:2,16 106:4 115:7,7 125:18 whatnot 133:8 wheelchairs 43:17 whispering 51:18 white 1:12 whitepaper 144:13 wi 12:12 wife 97:16 willi 55:22 135:4 willing 64:13,14 67:17 109:13,16 136:2 145:16 156:18 157:14,21 willingness 156:12	winds 107:7 winning 117:1 wise 93:8 wish 36:13 165:6 witness 166:4 witten 2:12 3:3 19:11,11 29:17 30:14 69:11,11,21 75:14 123:3,5 wobbly 31:6 woman 46:7 82:16 women 46:6 wonder 45:5 wonderful 159:21 wondering 36:1 39:19 46:7 86:9 99:15 woods 136:11,11 word 27:22 wore 82:9 work 10:15,16 19:13,22 20:11 21:4 42:21 53:22 54:2 61:7 70:21 78:8 83:21 85:19 86:3,13 87:3 89:13 96:9,18 100:13,15,19 101:17 105:10 130:5,7 132:11 147:10,16 150:5 153:9 157:9 159:22 160:21 162:12 165:1 worked 80:13 83:14 84:5 144:3 151:11 152:22 155:17 worker 20:11 working 6:21 7:14 39:10 58:4 75:2,8 92:14 119:5 122:7 132:12 144:15 154:14 155:7	161:1 164:6 works 85:3 88:2 world 10:4 19:7 62:1 84:17 86:10 100:5 101:17 111:8 113:8 119:16 120:20 121:10 123:17 130:1 138:20,21 140:4 144:5 152:18 worldwide 18:17 151:8 worry 35:17 worse 45:6 52:21 78:22 106:1 worst 107:18 worth 77:14,15 wound 106:16 wounds 114:4 wow 116:3 wrapped 95:3 write 8:16 14:20 writing 116:20 written 115:15,16 137:1 wrong 61:16 105:6 115:3	108:7 115:6 116:16 143:10 years 19:6,8 23:20 25:4 26:6 32:8,9 33:19,20 34:11 39:6,11 40:3 47:8 63:16,16 68:3 83:22 90:12 91:3 91:8 96:21 97:17 100:13 101:18,18 101:18 107:1 108:6 109:1,1 116:21 117:3 137:4 138:21 139:19 140:6 142:17,21 144:3 149:18 152:5 155:21 yellow 106:13 107:18 142:4 york 98:5 109:20 113:1 young 18:16 24:17 24:19,20,21,21 32:18 33:3 36:18 46:6 61:5 63:22 96:19 114:19 158:12,12,13 younger 78:6,14 96:20 youngest 152:7 youth 18:15
		x	younger 78:6,14 96:20
		x 2:1 152:11	youngest 152:7
		y	youth 18:15
		yeah 22:21 28:5,5 28:8,9 30:13 34:3 37:13 66:20 109:22 113:10,21 124:19 133:15 138:12 year 25:8 26:1,1,1 34:22 43:19 49:14 55:15,22 63:11 70:1 71:14 73:11 77:10,22 90:22 98:12 107:21	