









































































































































1       been on a new medication and it has improved my  
2       life tremendously. Just dealing with Hereditary  
3       Angioedema since 18 months, it's really been hell,  
4       so I've been through it all. I think it's very  
5       vital that we continue to do the research, because  
6       it's needed. Thank you.

7                   MS. FRENCH: Hello. I'm Cheryl. I am a  
8       Hereditary Angioedema patient as well as a  
9       caregiver, because both of my daughters have  
10      Angioedema as well.

11                   The FDA is a data driven bank of  
12      information. I would like to share with you some  
13      of my data. I was

14                   when I started swelling. I waited 16  
15      years for a diagnosis. I'm celebrating my 20th  
16      anniversary of having a diagnosis, but I've only  
17      had five years where I had treatment where I could  
18      continue a normal life, if "normal" is a word that  
19      we can even use in this family.

20                   In one year I was admitted in the  
21      hospital 184 days. A school year -- I'm a  
22      teacher. A school year is only 180 days long, so

1 184 days admitted in the hospital. That's not  
2 including clinic days, going back and having test  
3 results, CT scans, abdominal sonograms, biopsies,  
4 the report after they did my surgery and took my  
5 appendix out, because I was diagnosed with  
6 appendicitis.

7 I've lost one child due to abdominal  
8 swelling so severely throughout the pregnancy. I  
9 have lost 14 jobs because of this disease. I have  
10 had three deaths in my extended family because of  
11 laryngeal attacks. In one month, I incurred  
12 \$384,000 of medical debt. This has affected my  
13 entire life and this is a disease that I carry  
14 physically in my body, but I physically also carry  
15 emotional. It's like I've been diseased  
16 emotionally as well, because of all the things  
17 that this has impacted in my life. Another thing  
18 I carry as a parent is guilt, because now it's my  
19 babies.

20 I'm here today for two, that's my big  
21 number today is two. Because of my two daughters,  
22 I need more. I'm begging you to go with those to

1 continue this fight, because I've truly only lived  
2 ten percent of my life. Only 10 percent of my  
3 life has been somewhat normal.

4 MS. LIPSCOMB: Thank you. I'm going to  
5 jump in here and I'm going to sound -- we have a  
6 lot to ask, so we're going to try to keep the  
7 discussion points on what the questions are. I  
8 think there will be times to hear all of your  
9 experiences, so please don't feel like I'm cutting  
10 you. We're going to hear one more person and then  
11 we're going to go to our next discussion question.  
12 I'm sure there will be a time for you to be able  
13 to do that.

14 MR. EDWARDS: Thank you. My name is  
15 Miles. My wife has HAE. As a teacher, I have  
16 discovered a couple of students with it. One case  
17 in particular I know absolutely it was HAE.  
18 Trying to get assistance for that family, trying  
19 to get the family to understand what's going on  
20 was next to impossible. Educating the school  
21 nurse was next to impossible. When she did figure  
22 it out, did the research she was like, there are



1 more kids out there that we need to discover and  
2 we need to discover the kids in the school system,  
3 because the monster effect that was pointed  
4 out is crippling so many kids, because they swell  
5 up, they feel like they're monsters, and they  
6 don't need that. So please help us find and  
7 discover these kids, because there's a lot more  
8 out there than what we have numbers on right now.

9 MS. LIPSCOMB: Thank you. I don't even  
10 know what to say. Your stories and experiences  
11 are so moving. Let's get some more questions,  
12 facilitated questions, and we can get some more  
13 information from you.

14 So have you experienced one or more  
15 vomit attacks involving your throat, yes or no?

16 Chris, can you -- wow, 89 percent. What  
17 is the web numbers?

18 DR. PIERCE: We have just four  
19 responders, three said yes, one said no.

20 MS. LIPSCOMB: Thank you. Let's go to  
21 the next question, because I think it leads into  
22 this. If you answered yes to the previous

1 question, was a breathing tube inserted into your  
2 windpipe.

3 So 29 percent did, 71 percent of you did  
4 not need -- does someone want to talk more -- who  
5 would like to share their experience with --

6 MS. LONG: Hi, I'm Janet Long. I just  
7 want to point out that the question we have to  
8 also understand does not cover folks who  
9 experienced a tracheostomy instead of a breathing  
10 tube or intubation.

11 It also does not cover those who may  
12 have been undiagnosed and did not even know that  
13 they had the option of going and having that take  
14 place and were fortunate to actually not have  
15 their throat close all the way. So it is good  
16 information, but you also need to know there are  
17 other factors.

18 MS. LIPSCOMB: We'll add that to our  
19 conversation as well.

20 MS. PEREZ: Hi, my name is Brittany  
21 Perez. I have HAE. I'm a patient. I had my  
22 first swell when I was seven. My main issue is --

1 I have issues with urination, because the swelling  
2 and doctors don't seem to understand that.

3 So when you go to the hospital and you  
4 try to explain that to a doctor, they don't --  
5 because of issues, you start to throw up and your  
6 stomach starts swelling and it causes other issues  
7 with your HAE.

8 So they stick a catheter in you. A  
9 catheter, they tell you to relax. They tell you,  
10 well, you're worrying, relax, you're making it  
11 difficult. You're tensing up, and and it really  
12 hurts.

13 When you try to tell them it's not that,  
14 they tell you you're lying, it's not HAE, it's  
15 something else. My one experience, the nurse just  
16 shoved it in and it -- he's like, well, I can't  
17 get it in. He's like, you're making it really  
18 difficult. So you got someone else and it took  
19 them three attempts. By the third attempt, it  
20 just felt like a hot dagger just going in.

21 When they did get in they didn't get it  
22 in correctly, so they had to keep playing with it

1       just to get the urine out and then they said, well  
2       -- they kept asking me what HAE is. I explained  
3       it to them. They wouldn't give me my medicine,  
4       which they had on hand at the hospital. Instead  
5       they did sonograms and they found out there was  
6       all this urine retention. They said, well, I'm  
7       just holding it and --

8                   MS. LIPSCOMB: I'm sorry.

9                   MS. PEREZ: -- it was such an argument.  
10       By the time they got the urine out, they sent me  
11       up to Albany thinking it was because of my back.  
12       Albany told me, well, that I came up for no  
13       reason, I wasted their time. Because there was no  
14       urine, (inaudible) sent me.

15                   When they took the catheter out, I was  
16       bleeding. I was just so bad. I had -- quite  
17       often, I swell from the HAE and this one gets so  
18       bad I can't pee for days at a time sometimes, even  
19       with medicine.

20                   MS. LIPSCOMB: Thank you for sharing  
21       that experience. Thank you very much.

22                   You had your hand up.

1 MS. BRAHEN: Yes. This is for the  
2 swelling in the throat. I never had had it  
3 before, and so I didn't know what it was. I'm  
4 lucky that I did have Firazyr on hand. I thought  
5 my throat was sore. Usually -- I'm lucky, because  
6 so far my attacks have started slow and gone slow.  
7 I thought maybe I was getting a sore throat and  
8 usually the sore throat turns into a cold.

9 After about half a day, it didn't turn  
10 into a cold. I said, well, I'm always -- let me  
11 just try Firazyr and see what happens. I'll be  
12 darned, within -- Firazyr works for me within five  
13 to 15 minutes. Within 15 minutes, it's like I  
14 found out it wasn't a sore throat. My throat was  
15 starting to swell, so that really opened my eyes.

16 If I hadn't have had the Firazyr or the  
17 options available, then it would have continued up  
18 and slowly would have closed off. I knew I had  
19 HAE, but again the problem is convincing these  
20 doctors and convincing the hospitals and stuff,  
21 because they don't want to hear it.

22 Anyway, it can be slow, but you can --

1 at least I can control it with the Firazyr, but  
2 you have to recognize what it was. I didn't. I  
3 thought it was a sore throat turning into a cold.

4 MS. LIPSCOMB: Thank you for that. Did  
5 you have something you want to share?

6 MS. SANTEE: Hi, my name is Tina and I  
7 have HAE with normal C1 inhibitor. I've been  
8 intubated three times. The very first time they  
9 actually had to resuscitate me, because they had  
10 trouble getting the tube down. I stayed in the  
11 medical ICU for three days, and this is  
12 pre-diagnosis properly. I've spoken with John's  
13 mother and we felt that I had it, but the testing  
14 came back negative.

15 The second time I was intubated, I  
16 almost lost my life from a secondary infection of  
17 staph pneumonia. This was all before medications  
18 came to market.

19 The very last attack that I had was just  
20 three years ago. I did have acute medicine,  
21 rescue medicine, available. However, because I  
22 just recently had throat surgery and was still

1       numb, I was a little late in administering the  
2       medication.

3                 That's why I'm here today. It is very  
4       crucial that the FDA continue to fund our  
5       research, because for me and the type that I have,  
6       I only can respond to my attacks after the fact.

7                 So I too want to be able to have a  
8       little bit more freedom. Since the medicines came  
9       to market, I have had a little bit more autonomy,  
10      but I do fear that I will have an attack that I  
11      won't be able to respond in time for.

12                The very first one I mentioned, the only  
13      way that I'm here today speaking to you is because  
14      I had an alarm that woke me up and I had just five  
15      minutes to get to the hospital, so thank you.

16                SPEAKER: Donna, I have someone.

17                MS. LIPSCOMB: Okay.

18                MS. WHITAKER: Hi, my name is Diane and  
19      I have HAE 1. I began really feeling symptoms  
20      when I was in probably fifth and sixth grade. I  
21      know in sixth grade I missed 65 or 70 days of  
22      school, and it was due stomach pains. They would

1 be so bad, I would just -- would crunch over.

2 When it first started, the doctor gave  
3 me phenobarbital; then another time, the next  
4 year, I was on Librium, next year it was Diazepam,  
5 or Valium, and the pain just continued, continued,  
6 continued.

7 I didn't get diagnosed really until I  
8 was 40. But when I was 18, I had a  
9 hemorrhoidectomy, which is not common for an 18  
10 year old. So about five years ago, I was having  
11 problems with my sphincter, and she's talking  
12 about genital and I'm talking more rectal.

13 I have a Medtronic device now in my  
14 back. Because of all the swelling in that area  
15 with my sphincter, it would go out -- it lost its  
16 control and the Medtronic device now does, so I  
17 can go to the bathroom as a normal person.

18 But we need to spend so much more time  
19 in trying to find other therapeutic ways to help  
20 people, because there is no -- when you're having  
21 these stomach attacks and when you -- you almost  
22 feel like a guinea pig, because it's -- it seems



1       like it's always something, always something.

2                    Like this last week, I had an ultrasound  
3       of the stomach. They wanted to do a -- I feel  
4       like there's knives in me at different times. It  
5       happened in the middle of the night. They want to  
6       -- the doctors don't understand.

7                    I'm a huge advocate. I'm going around  
8       to as many hospitals, colleges, especially  
9       anesthesiologists. I had an anesthesiologist once  
10      -- I was going in for something minor and the  
11      anesthesiologist said, I'm not treating -- I could  
12      hear. I'm not treating that HAE patient. Why  
13      didn't anybody tell me. And I stayed calm. He  
14      came, I'm giving you FFP and steroids. I said,  
15      no, you're not, sir. I said the order is for me  
16      to have the therapy before surgery. I don't want  
17      to. I said, but if you look at the order -- I  
18      stay calm. I've learned -- I try to stay as calm  
19      as I can. They don't.

20                   Then when he went to infuse me, this is  
21      a professional, he goes A is for after death, B is  
22      for burial, C is for cremation.

1                   I said, okay, I guess I'll join in. D  
2           is for death, E is for eternity, and -- a lot of  
3           patients might not take it that way, but I had to  
4           in order to keep myself calm. We just need to  
5           really be able to reach out and educate as many  
6           people in the professional world as possible.

7                   MS. LIPSCOMB: Thank you. I think I saw  
8           a hand over here. Go ahead.

9                   MR. WILLIAMSON: I'd just like to add a  
10          little bit on the breathing tubes. I spent a  
11          majority of my childhood communicating with my  
12          mother on a dry erase board, because she was  
13          constantly intubated, more intubations than I can  
14          count.

15                   I think we all know here that there's  
16          something extremely terrifying about having to  
17          find that right position that you can hold your  
18          head just so that you can get enough air in while  
19          you're waiting to get to the emergency room.  
20          That's it, thank you.

21                   MS. LIPSCOMB: Thank you.

22                   MR. ARDITO: My first experience with

1 HAE was when I was seven years old and my  
2 stepfather had a throat attack. He was put into a  
3 coma for almost two weeks. So I guess as a seven  
4 year old, it was terrifying. Because he had been  
5 in my life for a couple years now at that point  
6 and suddenly he was taken away from me, and I  
7 didn't know if he was going to live to see the  
8 next day, if I would ever be able to talk with him  
9 again. Thank you.

10 MS. LIPSCOMB: Thank you.

11 MS. EDWARDS: I'm Carol. About a year  
12 after being diagnosed with HAE, I had a crown done  
13 at the dentist. After going to the dentist I went  
14 to target to buy some wine, because I was going on  
15 a cruise. I'm not feeling too good.

16 I'm going no, no, this can't be a throat  
17 attack. I thought I was immune to it, because I  
18 only had the abdominal kind. We're not immune to  
19 it, so I picked out my wine. I said, well, I'm  
20 not going to an ER, they'll never believe me. I  
21 went home and that prompted me to be able to go to  
22 the doctor and say, maybe I need some meds in case

1 I have a problem. He said, well, did you go to  
2 the ER after you had your throat swell? I said,  
3 no, I wasn't going to go. He said, you were  
4 really stupid.

5 So I do admit that I can have laryngeal  
6 swells and I'm not immune to it, and that takes a  
7 lot for someone like me, so anything can happen  
8 with this disease.

9 MS. LIPSCOMB: Thank you so much. This  
10 will be our last one, then we'll move on to our  
11 next question.

12 MR. VENTURELLA: My name is Steve and I  
13 am a caregiver, I'm not a patient. Our son -- is  
14 not the patient, it's my wife -- is on the Autism  
15 spectrum. Every time something like this would  
16 happen, and it happened a number of times  
17 throughout his childhood, he thought his mom was  
18 going to die. So this has always been something  
19 that we have been dealing with. Even as an adult,  
20 he still struggles with it.

21 I just want to echo what so many others  
22 have said. This opportunity for research through

1 the FDA, please continue. Please advocate through  
2 your local communities and hospitals and  
3 physicians. It's really critical. Our son has  
4 turned out quite well, but it impacts more than  
5 just the patient. It impacts the entire family.  
6 I think it's really important that we all are  
7 aware of that and that we continue advocacy.

8 MS. LIPSCOMB: Thank you so much. I  
9 want to give people on the web a chance. Are  
10 there any comments that were written that you want  
11 to --

12 DR. PIERCE: We're not getting any  
13 comments.

14 MS. LIPSCOMB: Web, what's up? This is  
15 me talking to the web, so my back's not to you  
16 guys.

17 If you're on the web and you are having  
18 issues, please log out and then log back in and  
19 that should help. We do want to hear your  
20 comments, if you have any, on the web, so please,  
21 please, please go ahead and feel free to write  
22 comments.

1                   We're going to go to our next question:  
2           Have you ever had an attack that was treated in  
3           the hospital?

4                   (Indistinct chatter)

5                   MS. LIPSCOMB:   So 95 percent of you  
6           have.  I'm going to ask the second question, then  
7           I'll come to you guys.

8                   The second question is:  For those 95  
9           percent of you if you answered yes, how many times  
10          over the past year have you been in the hospital,  
11          one time, two to five, or more than five times?

12                   (Indistinct chatter)

13                   MS. LIPSCOMB:  That was for if you  
14          answered yes to the last question.

15                   (Indistinct chatter)

16                   MS. LIPSCOMB:  Was it ever -- okay.  In  
17          my mind, I will do a show of hands for zero, how  
18          about that.  These slides make so much sense when  
19          you are talking about them and not living them, so  
20          I apologize for that.  Thank you for bringing that  
21          up.

22                   We'll give those answering -- well, I

1 think that tells us the answer there with the 13  
2 people responding.

3 Chris, can you go ahead. For those of  
4 you who were, 38 percent, one time; 38 percent,  
5 more than five times. Wow. How does the web --  
6 did we have any responses?

7 DR. PIERCE: So three out of four for  
8 the Question 9 had been treated at some point in  
9 the hospital. For the four responders to Question  
10 10, they all had been hospitalized between two and  
11 five times in the past one year.

12 MS. LIPSCOMB: Thank you. I'm  
13 presuming, but I don't want to do that, we all  
14 know that cute little acronym.

15 How many of you have not been in the  
16 last year but previously, right, okay, thank you.

17 Well, I want to know if anyone wants to  
18 talk about their experience -- well, sometimes I  
19 just think it's silly for me to ask the question.  
20 I just should say, who wants to put their hand up.

21 MS. FRENCH: Well, between Question 9  
22 and Question 10 and because of the work that we

1       have all done together, our lives have improved so  
2       much in the last five years, that Question 9  
3       really doesn't apply to my life anymore, and I'm  
4       grateful for that.

5                Because as a patient that was 184 days  
6       in the hospital in one year, it has now been five  
7       years since I've been admitted to the hospital,  
8       and that's because of the new treatments, the new  
9       medications, an excellent doctor that works with  
10      our family, a diagnosis, and finally getting to  
11      live that life. So Question 9 and Question 10  
12      thankfully apply to the old me.

13               MS. LIPSCOMB: Thank you. I appreciate  
14      that. Kind of clarification. That's good for us  
15      to know.

16               MS. URBANIAK: Well, my name is Sally  
17      and I was just going to -- kind of to your point,  
18      when people ask my how do you live with HAE, it's  
19      like it's two different worlds. There's like one  
20      before therapy and then one after.

21               So I would say the same thing. Since  
22      therapy, I have not been to an ER or hospital.



1 Before that, totally different story.

2 MS. LIPSCOMB: Thank you. Let's go to  
3 someone who hasn't spoken. We'll get back to you.

4 MS. BREADY: Hi, my name is Regina. I  
5 have Hereditary Angioedema Type II. I was  
6 diagnosed at 35. Nobody in my family has it. I'm  
7 the only one.

8 But I just want to say the impact of  
9 research for the way hormones affect our attacks,  
10 I am going through menopause right now and I've  
11 been going through hot flashes. Since September  
12 2nd, I had ten attacks, three in my throat, three  
13 in my face, and other parts of my body.

14 With the therapies that we have now, we  
15 need more therapies. Because when a therapy gets  
16 stuck in a place and we can't get another therapy,  
17 it's important we have access to things that are  
18 going to help us.

19 I'm on a waiting list right now, so I  
20 can't even get preventive medicine right now  
21 because of the backup. So it's so important that  
22 we keep doing this research and finding out better

1 ways to help us, especially when we're going  
2 through different changes of our life, so thank  
3 you so much.

4 MS. LIPSCOMB: I'm going to jump behind  
5 you and I promise you you are next.

6 MS. YODEN: Yes, my name is Denise and  
7 my father had HAE and suffered terribly with it  
8 for years. I watched him suffer in bed and  
9 agonize so badly that if anybody even sat on the  
10 bed, it just -- he was in excruciating pain just  
11 from the small movement of somebody else sitting  
12 on the bed next to him.

13 They told him that he it was all in his  
14 head. They opened him up, did exploratory  
15 surgery, sewed him back up only to have his  
16 stitches burst after he swelled, because of the  
17 trauma from the surgery.

18 My sister and I are the only two  
19 children my father had and we both have HAE. My  
20 oldest daughter, I have three girls, she has it  
21 and she has two boys and her youngest son has it.

22 As a child, I mainly had it on my outer

1        extremities.  If I would go swimming, snorkeling,  
2        just going into the lower depths of the pool, the  
3        pressure, wearing a snorkel and a mask, the  
4        pinching, my lip between the snorkel and the mask  
5        would cause my face to swell.

6                    I would mow the grass, my hands would  
7        swell, that sort of thing.  When I started having  
8        my children, I started having attacks in my  
9        stomach.  Of course you can't take any medication.  
10       I couldn't take the Danazol, the Danocrine at the  
11       time when I bearing children.

12                   So when I finished nursing my youngest  
13       daughter, I got on the Danazine, Danocrine,  
14       Danazol, and it changed my life.  So I was on it  
15       for 32 years, had a wonderful life, could manage,  
16       and then here recently I went to the doctor and he  
17       said that my cholesterol was a problem, an issue,  
18       and that I would have to get on cholesterol meds.

19                   I didn't want to get on cholesterol  
20       meds, so I said, can I get on the Berinert, so I  
21       got on the Berinert and I've been on it for about  
22       three months now.  I've given myself the IV and

1       it's going very successfully.

2                   But when we were at the summit, I heard  
3       about the HAEGARDA and I'm real excited about  
4       that, because it's subq and I'm just so thankful  
5       for all the new options that are out there for us.

6                   I'm so thankful for the opportunity to  
7       be here today and to plead our case. I hope that  
8       you will listen to us and have sympathy for us and  
9       for our needs. I just am so privileged to be  
10      here. Thank you.

11                  MS. LIPSCOMB: Don't want to go back on  
12      a promise.

13                  MS. EDWARDS: I've never been accused of  
14      talking too much, trust me. When I see these two  
15      questions, Question 9 and 10, and talking about  
16      being treated in the hospital, what kind -- what  
17      do we mean by "treated"? Were we treated with the  
18      proper medications, with something that's not  
19      going to work, and was it in a timely manner, and  
20      I think it's no for a lot of us.

21                  So being treated with the proper way  
22      really means a lot. I wish on these -- the rescue

1        meds, or whatever, for HAE that they put in "needs  
2        to be administered in a timely manner, otherwise  
3        it's really not that effective", because you just  
4        can't get that across to the medical  
5        professionals. I'm a nurse and you just can't  
6        tell them. They don't care.

7                    MS. LIPSCOMB: Thank you. We're going  
8        to take one more comment and then we'll go to our  
9        next discussion question.

10                   MR. CASTALDO: Thank you. I would dare  
11        say, though, from some of the comments we have,  
12        but even some of the research that's been done,  
13        notwithstanding, we'll get into this I guess when  
14        we talk about treatments.

15                   Notwithstanding the availability of  
16        current therapies, we still do see a fairly  
17        significant burden of illness for the reasons that  
18        folks have talked about before.

19                   Non-demand patient still has distress  
20        associated with whether or not they're going to  
21        have an attack, whether or not they're going to be  
22        able to treat it in a timely manner. I thought it

1 was very articulate some of the folks on the panel  
2 talking about if you wake up in the morning, will  
3 you wake up, will you have a laryngeal attack.

4 So I just want to make sure that, yes,  
5 we do have therapies and we'll talk about those.  
6 Certainly it's changed many of our lives, but  
7 there is still a significant burden of illness out  
8 there. I don't want that to be eliminated from  
9 our discussion.

10 MS. LIPSCOMB: Absolutely. In fact, we  
11 are actually running ahead of time, so it seems to  
12 me that some of you would like to talk about  
13 either treatment -- I mean, not treatments,  
14 because that's this afternoon, treatment's this  
15 afternoon, but symptoms that maybe we've not  
16 talked about or issues.

17 I think I've seen your hand. Let me get  
18 you, then we'll come over here.

19 MS. THOMPSON: Hi, my name is Dakota and  
20 actually five years ago today I was diagnosed with  
21 HAE. It took me about six years to be diagnosed.  
22 Through all of this, the other most debilitating

1 symptom is actually mental health. I suffer with  
2 depression, I suffer with anxiety, and it sucks.

3 It's not a traditional symptom, but  
4 we're afraid of when our next attack will be.  
5 We're afraid of how we're going to be treated.

6 I remember before I was diagnosed, I  
7 didn't even want to go to the hospital. My pain  
8 was ten out of ten. I didn't want to go. They  
9 couldn't do anything and they were just going to  
10 accuse me of drug seeking. Even now I've been  
11 diagnosed for five years and I have a really great  
12 doctor, and I still don't want to go to the  
13 hospital, because I'm afraid of what they're going  
14 to say to me. I'm afraid that they're going to  
15 say no and, like so many others, die from a throat  
16 swell, because the doctors don't believe what we  
17 have.

18 On a day-to-day basis, I have no social  
19 life, because I've lost friends who think that I  
20 just want to blow them off. I don't. I want to  
21 go out. I'm 25. I want to go to the club. I  
22 want to go hang out. I can't, because I'm just

1       either in an excruciating amount of pain or I have  
2       fatigue. Fatigue has followed me everywhere since  
3       I was 14, and I don't have the energy to go out  
4       even for lunch or Starbucks, so I have no friends.

5                It took me -- I failed out of college,  
6       because I couldn't make it to class. I had to  
7       quit my job, because I couldn't hold anything. My  
8       hands would swell up too much. And working at a  
9       fast food restaurant, you need your hands for  
10      every aspect.

11              It's followed me throughout this whole  
12      thing. I'm happy that we have better medications,  
13      but now I don't know what I'm going to do with my  
14      future, because I'm still so afraid that I'm going  
15      to go back to swelling twice a week, every week  
16      for two months straight, having to go to the  
17      emergency room twice a week every week for two  
18      months straight, and it's terrifying.

19              This is the only other symptom besides  
20      the abdominal pain and the nausea that has hit me  
21      the hardest. Anxiety and depression are real.  
22      The mental health aspect needs to be addressed at



1       least. Thank you.

2                   MS. LIPSCOMB: Thank you, Dakota. Do we  
3       have someone over here? Then we're going to go to  
4       the web.

5                   MS. FOX: My name is Debbie. I think  
6       one issue that is very common for women is that  
7       the disease is often triggered because of hormonal  
8       changes. When you are in your teens, you often  
9       have your first really bad episodes. For me  
10      pregnancy -- I was not diagnosed until I was past  
11      all my childbearing years. It was almost 40 years  
12      before I had a diagnosis, so I went through four  
13      pregnancies extremely sick and all kinds of  
14      medications to help with nausea that never worked.

15                   My last pregnancy, my two year old went  
16      and lived with my mother for three months because  
17      I could not care for her, because I was so sick.

18                   It was that same two year old when she  
19      turned 16 and began to have extreme episodes every  
20      month that said, momma, I'm not going to live to  
21      see what you have lived and thrived (inaudible).

22                   We finally got diagnosis, so I would

1       like to see a lot more research about -- I guess  
2       about the hormonal impacts and how you can adjust  
3       medications and things based on where you are in  
4       your life hormonally, menopause, all those  
5       different aspects of your life as a woman that  
6       severely affect the disease.

7                   MS. LIPSCOMB: Thank you. We're going  
8       to go to the web and hear some of those comments,  
9       please. Stacey.

10                               (Indistinct chatter)

11                   MS. CHINN: So Beth on the web has  
12       echoed similar comments that have been presented  
13       here in the room, that prior to new medications  
14       becoming available, she was in and out of the ER  
15       four to seven times a month and this was a big  
16       burden on her life.

17                   As well we have a comment from Crystal  
18       who has shared a story about being in the ICU for  
19       laryngeal swelling. Upon being transferred to the  
20       floor, her C1 inhibitor was not continued. After  
21       a two-and-a-half hour delay in getting the  
22       medication, the nurse ignoring her, she wasn't

1       able to speak and was worried that she wouldn't  
2       live to see her daughter's birthday, which was  
3       just ten days away.

4                So I think has shared similar stories to  
5       all of you who have just realized that there is a  
6       lack of understanding sometimes in the medical  
7       community. It takes too long to get the  
8       medication you know you need.

9                MS. LIPSCOMB: Let me get to you.

10               MS. RAMSEY: Adina again, sorry for  
11       hogging the mike. Something that hasn't been  
12       addressed yet is the relevance of using ports or  
13       maintaining vein health whenever you're  
14       administering medicine. I was very fortunate to  
15       have started a prophylactic treatment in 2009  
16       after my laryngeal episode, and I had a portacath  
17       implanted.

18               That port malfunctioned and had to be  
19       taken out. I had a PICC line implanted, that PICC  
20       line came out. I'm not on my second portacath,  
21       and there are other factors to consider when it  
22       comes to treating HAE.

1                   One thing that could happen is  
2           development of blood clots, and I'm sure all of  
3           you are aware, but I think trying to be aware of  
4           the method of medication being administered.  
5           Obviously subq -- having a pill a day would be  
6           fantastic. Subq is a nice compromise and IV is  
7           necessary, so I guess trying to aware of other  
8           things that go into method of treatment.

9                   MS. LIPSCOMB: Thanks again. We will be  
10          talking treatment much more exclusively in the  
11          afternoon.

12                  MS. BEITER: Hi, my name is Angelica. I  
13          just wanted to sort of go off of what she said too  
14          as far as veins and stuff like that.

15                  When I was diagnosed, they wanted to  
16          teach my mom how to start an IV on me, and it's a  
17          burden on a health care -- for the caregivers and  
18          stuff like that. But when a registered nurse  
19          can't get an IV in, they're poking you six to  
20          seven times for one IV, it's so discouraging to be  
21          spending four hours of your every two days to get  
22          this IV put in.

1           I was attending college for a while with  
2       IVs in the back of my hand and in my arm, because  
3       they were so scared to remove it because they  
4       couldn't find another one the next time I needed  
5       treatment.

6           They finally decided to put a PICC line  
7       in, but being 19 and not being able to shower  
8       normally or swim or play sports or really do  
9       anything, lifting, anything like that, because  
10      some of us can't tolerate ports and stuff like  
11      that. Different doctors think different things  
12      don't work.

13          For everyone to be on the same page  
14      would be nice, but it's definitely a burden to be  
15      19 and not able to do things because I can't get  
16      my right arm wet. To know that -- like there's no  
17      medications coming out that are subq, but some of  
18      us aren't approved for it. I know a lot of people  
19      too not every medication works for them.

20          So it's important that we continue to  
21      look for different ways to administer the  
22      medication as well as being able to still live

1       life, because at 19 and trying to explain to  
2       people I have a tube hanging out of your arm is  
3       really sort of an awkward conversation to have,  
4       that's for sure.

5                But it changes everyone's life and  
6       everyone has to cope with it differently, because  
7       a lot of times doctors won't treat you for other  
8       things you have going on because they're scared to  
9       interact the medications, because they are not  
10      very well known.

11              So when you go to see a doctor because  
12      you think you have rheumatological issues as well,  
13      they say, well, we don't really want to kill you,  
14      that's really scary.

15              I think a lot of us in the room can say  
16      that maybe HAE isn't our only thing we have going  
17      on medically. But to get a diagnosis, a lot of  
18      times doctors just stick every symptom under the  
19      umbrella of HAE because there is so much lacking  
20      as far as knowing what symptoms can stem from HAE.

21              I know me personally I have so many  
22      problems with infections and my white blood cells

1 don't elevate, but they don't know -- they can't  
2 figure out what's wrong. I can't control my body  
3 temperature and there's so many things that I've  
4 seen -- that I've talked to other patients that we  
5 have similar, but it's not considered a symptom  
6 because it may not be researched yet, so thank  
7 you.

8 MS. LIPSCOMB: Thank you.

9 MS. CLASEN-KELLY: Good morning. My  
10 name is Liz. I have HAE Type I. I had my first  
11 attack when I was nine and I was finally diagnosed  
12 at 34 after some unnecessary surgery, many  
13 hospitalizations, and much of my life thinking I  
14 was crazy. Actually I knew I wasn't crazy, but  
15 everybody else thought I was.

16 So the symptom I want to talk about or  
17 the word I want to talk about is "potential". So  
18 thank you, FDA, for having this. It's so powerful  
19 to get patients in a room. I hope you just get a  
20 taste of what an amazing group of patients we are.

21 So much of the disease for me has been  
22 about not being able to live out my potential. So

1       when I was

2                       -- and I was straight A student. I  
3 missed a ton of school. I always made up my  
4 stuff. I was -- got accepted into some great  
5 colleges. When I was 18, my doctor told me he  
6 didn't think I should go to college because I  
7 couldn't handle the stress, because my body  
8 couldn't handle the stress, which just made me  
9 really angry and work all the harder. I proudly  
10 have my master's degree from Duke University.

11                    At every kind of stage of better  
12 treatment, so once I got my diagnosis, once I got  
13 on the modern therapies, now on a drug study, what  
14 I've been able to give back to the world at every  
15 level is just enhanced. So as I get healthier,  
16 there's so much I can give back.

17                    I'm now proudly the executive director  
18 of one of the largest emergency shelters in the  
19 southeast. We provide emergency shelter and help  
20 350 men every night get out of homelessness. I  
21 could never have dreamed of doing this job ten  
22 years ago, because now with the modern therapies



1 and thankfully being able to be on a clinical  
2 trial, I can lean into my potential and I don't  
3 have to miss those big moments as I did throughout  
4 life.

5 And I -- just get to know the amazing  
6 patients in this room and just know the more  
7 access we have, the more we're going to give back  
8 to this community and to this world, so thank you.

9 MS. LIPSCOMB: Thank you.

10 MS. RENDON: My name is Amy. This is my  
11 daughter. I'm going to read what I wrote, because  
12 I'm not good at holding it together.

13 With a newborn, they tell you about  
14 sudden infant death syndrome. For the first six  
15 months of her life, she slept on the couch with my  
16 hand on her back, new mom, you know how it is,  
17 just to make sure she was breathing.

18 No one told me that 25 years later, I  
19 would worry every time she sleeps too late in the  
20 morning. The fear of what I might find opening  
21 her bedroom door and wondering if she had an  
22 attack, wondering if I lost her in the middle of

1 the night.

2 Throat swells and losing her is a great  
3 fear, but there's everyday pain of watching what  
4 she goes through, the emotional toll and the parts  
5 of her life that have been taken.

6 We almost lost her last year, not to  
7 HAE, but to an infection. She became septic from  
8 the port that she needed to be able to access the  
9 medicine. The multitude of ways that we can lose  
10 our loved ones and the many ways HAE takes part of  
11 their life from them is vast.

12 We're fortunate that she was able to get  
13 on to a clinical trial and it is making a huge  
14 difference in her life, but there's drugs in the  
15 pipeline that can make an even bigger difference  
16 not only for her, but for all the others.

17 As a mom, I don't have HAE myself. I  
18 don't know what my daughter goes through. I just  
19 know the fear of losing her and wanting to do  
20 everything possible to keep that from happening to  
21 her, to everybody in this room. Thank you.

22 MS. LIPSCOMB: Thank you.

1 MS. KLINGER: Hi. Lydia again. I just  
2 want to say first of all what you said about  
3 potential I think is something that our entire  
4 country should hear when we're debating health  
5 care and access to health care. Because while it  
6 seems like just a greater expense, it's truly an  
7 investment in our country and the people of our  
8 country.

9 Moving on, I would like to emphasize  
10 what my friend over here said about mental health,  
11 because I think I've seen -- I have Hereditary  
12 Angioedema, my mother has it, my brother and  
13 sister who are in their early 20s have it, my kids  
14 probably have it, thankfully no symptoms yet, and  
15 they're six and seven.

16 But I think that the constant anxiety of  
17 not knowing what to expect from your body impacts  
18 us probably more than all of the other lists, just  
19 because you really don't ever know what to expect.  
20 You don't know what's going to make you swell, you  
21 don't know how you're going to feel from day to  
22 day.

1                   Yesterday I stopped at Nordstrom Rack  
2                   and spent way too much money on shoes and this  
3                   morning my hands swelled from carrying all of my  
4                   purchases in the plastic bag. So was it worth it,  
5                   yes.

6                   But when you're in a constant state of  
7                   anxiety, it impacts not just what you can do from  
8                   day to day, but how you feel about other things in  
9                   your life. When something else pops up that's  
10                  unpredictable, you've already stacked that anxiety  
11                  on top of the anxiety you have about just  
12                  existing.

13                  So I think while the disease itself can  
14                  cause anxiety and probably depression as well,  
15                  it's also being at that heightened state of  
16                  awareness and anxiety that makes us even more  
17                  prone to adding to that problem. So I think  
18                  that's one of the biggest impacts in my life  
19                  anyway.

20                  MS. LIPSCOMB: Thank you. What I'd like  
21                  to do though actually is go to the next question,  
22                  because I think it's going to piggyback on this

1 and I think some of the comments you have might  
2 feed that, keeping in mind we might not have  
3 included everything that you think we should and  
4 we'll hear about that, I'm happy to say.

5 When you have an attack, what  
6 limitations in the activities of your daily life  
7 do you experience? Please choose all that apply  
8 and know that one of the -- that they're going to  
9 come back. I want you to think about it, mull it  
10 around a little bit.

11 We have a story to talk about.

12 MS. CHINN: So Jennifer on the web also  
13 has Hereditary Angioedema with normal C1  
14 inhibitor, as was mentioned by a woman earlier, it  
15 took a while for her to be diagnosed and she has  
16 had many unnecessary eye surgeries because of  
17 this.

18 She also wanted to echo sentiments about  
19 the social impact of her disease and how it  
20 impacts her relationships in life and she can feel  
21 irritability and other symptoms like that when her  
22 attacks are coming on.

1                   She also shared one other story about  
2                   going to surgery for unnecessary eye surgery  
3                   during a swelling attack and the nurse would not  
4                   get her Firazyr out of her bag, because she  
5                   thought she was drug seeking. So, again, similar  
6                   themes running throughout everyone's experiences.

7                   MS. LIPSCOMB: Thanks. I actually have  
8                   this slide, so I'm going to read you what your  
9                   choices are.

10                  So the first choice -- so this is all  
11                  that can apply. A, I cannot go to school or work;  
12                  B, I cannot participate in family and social  
13                  activities -- oh, it's not online.

14                  MR. NGUYEN: What happened was the power  
15                  wasn't plugged, so --

16                  MS. LIPSCOMB: Let's do this, let's make  
17                  the best use of your hands. A, who can't go to  
18                  work -- when you're having an attack, what  
19                  limitations do you experience, so if this happened  
20                  to you before: Can't go to work or school, cannot  
21                  participate in family activities, social  
22                  activities, cannot participate in sports

1 activities?

2 I would raise my hand, just because I'm  
3 not very good at sports. I'm unable to care for  
4 myself, eating, dressing, pulling up our pants, as  
5 we found out, that was never talked about before.

6 (Indistinct chatter)

7 MS. LIPSCOMB: I'm able to care for my  
8 children, I feel left out. What else do we have?  
9 All of -- well, you can pick everyone.

10 Is there something that's not on this  
11 list?

12 MR. CASTALDO: Just a quick comment and  
13 I'll add something to the list. I think the sum  
14 total of all we've heard so far this morning, and  
15 these stories are so compelling, is that there is  
16 significant anxiety.

17 Lydia, you made the case and many others  
18 have about the significant amount of anxiety  
19 associated with HAE, that's even now. I would  
20 dare say that there's -- researchers have looked  
21 preliminarily at sort of the broad spectrum of  
22 stress associated with HAE. I think there is --

1 probably eventually we're going to see a link  
2 between PTSD and HAE. You can see why as you  
3 listen to the stories that we have here.

4 There's another piece of this that maybe  
5 somebody might want to comment and it comes up  
6 from time to time and that is that people also  
7 fear passing the gene on to their family members.  
8 As a result, some folks might be hesitant to have  
9 children and that's been something that we've  
10 heard about quite a bit in the anxiety spectrum.

11 MS. LIPSCOMB: Thank you.

12 MS. SANTEE: Just to piggyback on what  
13 Mr. Castaldo said. I'm a single mom and my first  
14 attack that I spoke about earlier -- I'm Tina  
15 again.

16 My son was only four, so he's 15 today.  
17 While I do suffer from anxiety and I do believe  
18 post traumatic stress probably would be a better  
19 suited diagnosis for our feelings, my son also has  
20 anxiety.

21 I believe some of that has come from  
22 seeing his mom, his only caregiver in and out of



1 the hospital and me not sometimes being able to be  
2 that stronger person for him to say, I'm okay,  
3 because I'm also scared.

4 It's heart breaking to see him get  
5 worried as a child when I sleep in sometimes or if  
6 my eye swells and my Firazyr is taking a little  
7 time to work, mom, do we have to go to the  
8 hospital, do we have to go, where should I go.

9 So that has been very hard on the family  
10 and I do believe that everyone has said that, but  
11 my son doesn't have HAE, so it affects our family  
12 if they have it or if they don't.

13 Again one of the things that has been  
14 somewhat of a relief to me is having a rescue  
15 medication where I can give myself Firazyr and  
16 stay home, so I don't have to find a babysitter or  
17 sometimes it requires that my dad comes from out  
18 of state and stay with me, because that trip to  
19 the hospital for treatment became intubation or  
20 overnight observation that went from one night to  
21 five nights.

22 So I just thank you guys for having us

1 here to talk about it, but again it's not just us,  
2 as the people in the back of the room, our  
3 caregivers, our family members, and even my future  
4 husband. I would like to meet him one day without  
5 being (inaudible), so please give us some medicine  
6 so I won't have so much anxiety. Thank you.

7 MS. WHITAKER: Diane again. I just  
8 wanted to, one, thank the FDA for this, but I want  
9 to tell you my entire biological family are all  
10 deceased, but everyone here is my swell family.

11 I don't think in any other rare disease,  
12 you will find a group of people that will be so  
13 supportive and so motivated to not only help each  
14 other but work with you and you work with us. I'm  
15 sure if you call on anyone in this room, we will  
16 do whatever it takes to help get solutions.

17 MS. LIPSCOMB: Thank you.

18 MR. SELSOR: I think one of the things  
19 that nobody's touched on as far as activities that  
20 people don't participate in when they've got HAE,  
21 a lot of times I think people forego other  
22 necessary medical treatment because they're afraid

1       that will trigger an HAE attack. One of the  
2       things I can think of specifically is dental work.  
3       I've run into all sorts of people with this  
4       disorder that they're terrified to get necessary  
5       dental work done, because they're afraid it's  
6       going to trigger a laryngeal attack.

7                I know personally once I started having  
8       airway events, I put off dental work to the point  
9       where I had a gigantic loose filling on one side  
10      of -- in a big molar. I would just chew on the  
11      other side of my mouth.

12              I had a friend say, when are you going  
13      to get it fixed? I said, well, I can chew on the  
14      left side. Well, what happens if something  
15      happens to the left side? I said, I'll eat soup.

16              But I know when I finally got treatment  
17      and even after that, and I knew the treatment  
18      worked well and -- even in the past, I never had  
19      dental work trigger a problem, but just making  
20      that first denial appointment afterwards to get  
21      everything taken care of, I got off the phone with  
22      the clinic and I was just shaking from, I don't

1 know, stress, terror, worried about what was going  
2 to happen when I actually went to get this stuff  
3 done.

4 Everything turned out okay, but I know a  
5 lot of people that I've talked to are in the same  
6 boat. They're terrified to get other things that  
7 are medically necessary done, because they're  
8 afraid of triggering some sort of event.

9 MS. NEHRING: I just wanted to comment  
10 on the sports and activities thing. I was  
11 involved in competitive dance for almost my entire  
12 life, 16 to 17 years.

13 When I was diagnosed with HAE, the  
14 reason I wasn't able to partake wasn't because of  
15 swelling. I actually felt better when I was  
16 exercising, it was because my mom was like you're  
17 not going to school, you're not going to dance.  
18 My parents are both in education, so that was  
19 something that we -- I struggled to understand  
20 from them, but I get it now.

21 When I finally got on a treatment plan  
22 and got to college, I tried out for the dance team

1 at my school and I made it and practiced with them  
2 for four years -- for four months. After that,  
3 the team physician told me that I couldn't  
4 participate, because I was a liability to the  
5 university.

6 So I just want everyone to keep in mind  
7 that sometimes it's not the symptoms of HAE that  
8 limit participation, it's the other people in the  
9 environment that you're in.

10 MS. LIPSCOMB: Thank you.

11 MS. TUMA: Hello. My name is Stephanie  
12 and I have Type III, or the normal C1 S G  
13 inhibitor protein. No one in my family has it.

14 This question is very interesting: When  
15 you have an attack of Angioedema, what limitations  
16 in the activities of daily life do you experience?

17 What some of guys have touched upon is  
18 like it impacts your life regardless of whether  
19 you're having an attack or not. For the dental  
20 work, like yeah, I definitely put that off, like,  
21 no, I don't want to go, maybe I have a cavity, I  
22 don't know.

1                   But things like that, scheduling  
2           different things, that all impacts you, it limits  
3           my ability to procrastinate like a normal student.  
4           I always try to get all of my assignments done as  
5           soon as I can, as soon as they're posted, so that  
6           just in case I have an attack, I'm prepared.

7                   A lot of other things, that's just one  
8           example. But it limits your life when you have an  
9           attack or when you're not having an attack. The  
10          anxiety is real and I know a lot of you feel that  
11          way.

12                   Any time I get a cold, the flu, it's not  
13          just your normal I have a sore throat, stuffy  
14          nose. I have all that and now it's walking  
15          pneumonia and I have throat attacks and I have  
16          everything else that goes on with that, and I know  
17          a lot of patients relate to that as well. So it  
18          definitely affects your -- all aspects of your  
19          life. Thank you.

20                   MS. LIPSCOMB: Thank you. I think we  
21          have one more.

22                   MS. FRENCH: One thing that none of the

1 patients have touched on yet, and I'm going to be  
2 a little brave here, physical intimacy is also  
3 affected.

4 We talk about whether it's your kidneys  
5 or your hands or whatever else, but when your  
6 partner and you and your relationship are also  
7 affected by it and you're afraid to have a  
8 relationship, relationship, with your partner for  
9 fear of swelling shut, and then that leads to a  
10 yeast infection or another trip to the doctor or  
11 possibly an awkward pap smear just because I love  
12 my husband, it's hard to put that into words and  
13 try to explain it.

14 In a way this disease has turned me into  
15 a liar. It was easier to say that I had been  
16 stung by something then to try to explain this or  
17 to say that maybe I had the stomach flu instead of  
18 explaining HAE or to say I had bronchitis or come  
19 up with any other thing to explain that sounded  
20 normal that other people had heard of, because we  
21 don't look sick.

22 If you were not having a facial swell or

1 if they couldn't see the swell, I didn't seem  
2 sick. So I would lie about what was happening to  
3 my body to make it okay for everyone else around  
4 me so they could deal with it. I don't know if  
5 other patients did that, but that's one of the  
6 things that goes with our disease.

7 Another thing I never thought I would  
8 have to face is my two year old -- well, at that  
9 point two and thank the lord she is seven, we've  
10 lived through five laryngeal attacks already.  
11 When she was two, she sat with us through training  
12 to learn how to do an IV. When your two year old  
13 says, yeah, it's red in the line we got a good  
14 one, what two year old should have to live like  
15 that. But she also realized that that red in the  
16 line, yeah, we got a good one, could save her life  
17 and when you celebrate that in her tiny little  
18 veins you got a good one.

19 The other thing is that you swing the  
20 pendulum. As a parent that has children with HAE,  
21 you swing in this pendulum from absolute dread of  
22 next attack. And then when they've been diagnosed



1 and they don't have an attack, I have a friend who  
2 lives in dread every day thinking when will the  
3 first one occur.

4 I've lived through the point now that I  
5 celebrated when my children did have an attack,  
6 because I knew that they knew their bodies could  
7 tell me what was happening. Now I have witnessed  
8 my child who is 13 advocating for herself in a  
9 doctor's -- in the emergency room actually and  
10 being able to stand up for herself at 13 and say,  
11 that is not my treatment. I will not take  
12 steroids. This is my treatment, and here's the  
13 telephone number for my doctor.

14 Then she has the wherewithal at 13 years  
15 old to say, I am not doubting you as a physician,  
16 i am doubting your knowledge of my disease. This  
17 is my treatment and you will do what my doctor  
18 says.

19 MS. LIPSCOMB: Thank you. It's getting  
20 close to our break for the first half. FDA panel,  
21 do you have any questions that you'd like to ask  
22 of any of the participants?

1 MS. CHALASANI: First off I want to  
2 thank everyone, all you who are in the room, for  
3 traveling all the way out to White Oak and sharing  
4 such personal stories. It is very valuable  
5 information. I know I speak on behalf of all my  
6 colleagues that we really do appreciate it.

7 We've heard from several folks about  
8 your triggers. We heard about the Nordstrom  
9 shopping spree, we also heard about hormones, the  
10 dental visits, but I think we would be interested  
11 to hear from folks if there are several other  
12 triggers that we may not have already talked about  
13 already this morning. I think I see several hands  
14 going up.

15 MS. THOMPSON: So one of the other  
16 things that's a trigger for -- I've seen in a lot  
17 of people is anxiety or stress creates this big  
18 whole runaround that never ends. The other one  
19 that I have found for myself is the change of  
20 weather. If the barometric pressure changes, I  
21 swell and I'm in bed. I'm down for the count, I  
22 can't get out, I have no energy.

1                   When we did a summit in Denver a lot of  
2                   us were swelling and having difficulties, because  
3                   the barometric pressure was different than the  
4                   other 49 states, so those are two that I know of.

5                   MS. BOMAR: Hello. Someone had  
6                   mentioned about pap smears -- I'm sorry, my name  
7                   is Fran Bomar from Alpharetta, Georgia. I'm not  
8                   embarrassed to have that on the web.

9                   We talked about having pap smear and  
10                  that is -- it's traumatic just to think about it.  
11                  But unless the physician is skilled, you can leave  
12                  and know that you're going to have an attack. The  
13                  other is a mammogram, better known as the breast  
14                  press, because it is so painful.

15                  My husband, Ken, had asked me one time  
16                  what was so bad about a mammogram. When I  
17                  explained to him, it a whole different matter. So  
18                  I have had an attack from having a mammogram.  
19                  When your chest swells up, that's not a good thing  
20                  and you can't breathe.

21                  So those are the kinds of things, along  
22                  with everything everybody else has said about

1 anxiety and even having commitments. I'm long  
2 retired. At this point, people say, well, why  
3 don't you volunteer for this and volunteer for  
4 that, I don't want to do it, because they can't  
5 count on me, even though I'm on treatment and I  
6 have -- I do have breakthrough attacks. Sometimes  
7 I'm just not in the mood to do it, I just don't  
8 have the energy to do it.

9 So there are other factors out there  
10 too, so I agree with everybody else. Yes, I'm  
11 missing parts as well, appendix and other things  
12 that people decided to take, because they didn't  
13 know what was going on. So thank you very much.

14 MS. LIPSCOMB: So we'll let Lonny's  
15 person go first.

16 MS. BRAHEN: My name is Peggy. It's not  
17 just stress and anxiety, but it's any -- it can  
18 also be happy things, like you're so excited about  
19 something, you're surprised about something, it's  
20 emotions.

21 If I'm really happy about something or  
22 if I'm really mad about something, it can -- they

1       used to call it Angioneurotic Hereditary  
2       Angioedema, because it was all in your mind and  
3       that's -- a lot of people they have -- and it is.  
4       This disease is bridge between Western and Eastern  
5       Medicine in a way. The mind can very much affect  
6       the physical symptoms.

7                   I don't think sometimes the drug  
8       companies and everything get that it's -- when we  
9       smile, there's chemicals that go on that do  
10      things. So it's just not stress and anxiety,  
11      which are a great part, but it's also the opposite  
12      spectrum too.

13                   MS. PERRY: Louis Perry; Fresno,  
14      California. One of the things to remember too  
15      growing up I had this same problem, everybody  
16      would ask why did you swell. Sometimes we don't  
17      know.

18                   The fact that I don't have enough  
19      working or functional C1 inhibitor is enough to  
20      make me swell. A lot of times I have no idea, and  
21      that was part of the stigma. Especially since my  
22      dad died so young, my mom always wanted to know

1       what happened, what happened. You don't always  
2       have an answer, but you swell.

3               MS. LIPSCOMB: Thank you. We're going  
4       to take about two more, because then -- it's 11:31  
5       now.

6               MS. BEITER: One of the things that I  
7       definitely wanted to touch on was I know for me  
8       infection is a huge trigger. The second I get any  
9       type of -- even viral or anything, it triggers  
10      something to happen.

11              That was actually how I was diagnosed.  
12      When I was in my senior year of high school, I was  
13      homeschooled for six months because I had a sinus  
14      infection. To tell someone you're homeschooled  
15      because you have a sinus infection, you sound  
16      absolutely awful. It's just -- you sound like a  
17      baby.

18              Every time I would -- the infection  
19      would flare up, my face would swell. Then the  
20      doctors thought it was such a bad infection that  
21      they started doing swelling, because they thought  
22      the swelling was from the infection.

1           A lot of times I know that the triggers  
2           sound simple, but it can create an awful cycle of  
3           like hormones and then you end up stressed,  
4           because you don't feel well and then you swell and  
5           then you're stressed because you're swelled.

6           I think a lot of us get in a pattern of  
7           infections and then doctors trying to treat it  
8           with medications. I know there's some people that  
9           have problems with certain antibiotics that cause  
10          -- is a trigger.

11          Like she said sometimes people are like,  
12          well, why did you swell? You're like, I don't  
13          know, maybe because the sky's blue. You really  
14          can't explain what is going on in your body,  
15          because it just happens when it wants to.

16          MS. LIPSCOMB: Thank you.

17          MS. KLINGER: Hi, Lydia again. Just to  
18          kind of clarify on the Nordstrom shopping trip,  
19          what that trigger was is soft tissue trauma.  
20          Which was not a large trauma, but any little thing  
21          for me, like to my body, that is traumatic to my  
22          soft tissue can make me swell.

1                   For example, I don't know how many  
2           people with small children have ever been face  
3           bopped by your kid coming up when you're going  
4           down to kiss them, I've had numerous facial swells  
5           because of that, just getting little tiny conks in  
6           the face from my kids.

7                   If I am gardening or something, if I'm  
8           pulling weeds for too long, that always makes my  
9           hands swell. Holding a rake is not possible. I  
10          can hold it, but there's no raking. My husband  
11          still thinks I'm just trying to get out of  
12          something.

13                   But dental -- oral surgery is a huge  
14          trigger for me, when I was in college just always  
15          around exam time I would swell from that emotional  
16          stress. After college I thought that I needed to  
17          have two full-time jobs, and that was a bad idea,  
18          that caused swells, basically the fatigue. So it  
19          can be any number of things.

20                   MS. LIPSCOMB: We're going to have one  
21          more and then we're going to cut.

22                   MS. CONKLIN: Hi, I'm Katie. One of the



1 things that can happen is just repetitive motion,  
2 so just walking, and usually I can control it by  
3 wearing sneakers. I've gotten to where even if I  
4 know I'm going to be doing a lot of walking  
5 wearing sneakers, within a couple of hours I can  
6 start an attack, whether in my feet or in my knees  
7 or in my hip just from the repetitive motion of  
8 walking.

9 MS. LIPSCOMB: Thank you, everybody. I  
10 know there's so much more -- so many more triggers  
11 that we could hear -- okay. Ross, go ahead. No  
12 lunch for you.

13 DR. PIERCE: Along the lines of  
14 repetitive motion, one of the web participants  
15 mentioned if they were driving a car over a road  
16 that had been resurfaced where it was graded.

17 Also one participant mentioned textures  
18 of food and also things that are very salty or  
19 acidic foods like tomatoes or vinegar based.

20 MS. LIPSCOMB: Thank you. I feel like  
21 we covered so much. I hope I didn't cut off any  
22 of you guys; right. We're going to ask for you to

1       come back at what was going to be 12:30, but I'll  
2       give you to 12:34. We're going to start right on  
3       time. In the afternoon, we're going to hear about  
4       your perspectives on treatment and clinical  
5       trials.

6                   I think we'll probably continue the line  
7       like what we've been talking about. Again, thank  
8       everybody on the panel so much for sharing your  
9       experiences. Thank you for being so willing to  
10      share. We are so thankful.

11                   I don't promise that lunch isn't great,  
12      but I love it, so that's all I'm saying. That  
13      might say more about me than you. We'll see you  
14      in about an hour.

15                                   (Recess)

16                   MS. LIPSCOMB: I, once again, would like  
17      to direct your attention to the FDA panel. We  
18      have a couple of new people sitting on the panel.  
19      I'm going to go ahead and let you and Stacy  
20      introduce yourselves.

21                   MS. CHINN: Hi, I'm Stacy Chinn, I'm an  
22      allergist, immunologist in the Office of New Drugs

1 in the Center for Drug Evaluation and Research.

2 MS. MUELLER: I'm Christine Mueller from  
3 the Office of Product Development.

4 MS. EGGERS: I'm Sara Eggers from CBER's  
5 Office of Strategic Programs.

6 Dr. PUROHIT-SHETH: I'm Tejashri  
7 Purohit-Sheth, division director for Division of  
8 Clinical Evaluation in pharm talks in OTAT CBER.

9 MS. MALONEY: Hi, I'm Diane Maloney,  
10 associate director for policy in CBER.

11 Dr. GOLDSMITH: Jonathan Goldsmith. I'm  
12 the associate director of the (inaudible) program  
13 in the Office of New Drugs, CBER.

14 MS. LIPSCOMB: Thank you. Thanks  
15 everybody for getting back. I hope you got your  
16 lunches without any kind of hiccups. It seemed  
17 to be going pretty smoothly. This afternoon, the  
18 first topic is about current approaches to  
19 treatment. I'm going to invite our panelists,  
20 Joyce, Janet, Karen and Anthony to come up please.  
21 What we've asked this time for discussion, and  
22 we'll leave this up so everyone can see it is,

1        what treatments are you currently using, how well  
2        do the treatments work, what are the most  
3        significant advantages and disadvantages,  
4        complications of the treatments, how has your  
5        treatment regimen changed over time and why. We  
6        heard a little bit about that earlier. What  
7        aspects of your condition are not improved by your  
8        current regimen and what treatment has the most  
9        positive impact on your quality of life. As we  
10       found this morning, if somehow these questions  
11       need to be tweaked by you, we certainly  
12       understand. I'm going to go ahead and invite you  
13       to start speaking and we'll go down this way  
14       please. Make sure you put your mouth close to it.

15                    MS. PERRY: My name is Lois Perry and  
16       I'm grateful to be here and have the opportunity  
17       to talk in front of the FDA about hereditary  
18       angioedema and the current approaches to  
19       treatment. Not a lot was known about HAE in my  
20       early lifetime. Over the years, I was relegated  
21       to medieval HAE treatments that simply didn't  
22       work. I'm fortunate during a bad throat attack, a

1 doctor at my local hospital had heard about the  
2 NIH and their studies that they were doing and  
3 suggested that I went to NIH. That was in 1976  
4 and that was the start of my journey. Finally, in  
5 participating in HAE clinical trials in the search  
6 for a better life. I participated in the first  
7 clinical trial at the age of 17 at NIH. I've been  
8 in two clinical trials since then which were  
9 targeted directly towards being able to allow  
10 patients to live a normal life by treating and  
11 replacing the missing protein in my blood.  
12 Clinical trials aren't easy, it is a double blind  
13 placebo portion which means you have to go off  
14 your medicine and go on a placebo and suffer  
15 attacks. I was allowed rescue therapies for the  
16 trials but just knowing I had to give up a therapy  
17 that worked well for me to try to find something  
18 better had a significant emotion toll during the  
19 trials.

20 For me, the clinical trial site is a 3  
21 hour drive one way so it is a challenge but it is  
22 well worth it. I treat every attack regardless of

1 location due to not knowing when those attacks can  
2 move from hand to stomach to face to throat. I  
3 currently use a sub q version of the C1 inhibitor.  
4 The current treatment has changed my life  
5 drastically. Back in the day when I was first  
6 diagnosed, all there was, was nothing at first and  
7 then Danazol, Stanizol, Oxzandrin. Going on those  
8 therapies for 30 years, I had a heart attack when  
9 I was 45 years old. While they did keep my alive  
10 and I am grateful to having had those therapies,  
11 it's not optimum. So, I'm really happy to see the  
12 therapies that we do have now. I've witnesses  
13 many milestones living at a young age with no  
14 therapy and being sick constantly in and out of  
15 the hospital, missing school, work, activities  
16 just like everyone said. Of course, I'm 59 years  
17 old, I admit that, and therapy has been only  
18 approved since 2008. So, there were many, many  
19 dark days that I had been prescribed everything  
20 that they ever thought would be working for  
21 swelling. Today's modern therapies are wonderful  
22 and life changing as you have heard already many

1 times today. But I still have to remember not to  
2 miss a dose and I'm always aware of any little  
3 thing that used to bring on an attack. All my  
4 attacks are well controlled now, it's always in  
5 the back of my mind that I could have an attack  
6 anytime, anywhere. So, I have to always remember  
7 to take my therapy wherever I am. It's very  
8 critical to have that care plan in place.

9 In a perfect world, longer lasting  
10 therapies would help me live as if I didn't have  
11 HAE at all. The therapy that could soon ward off  
12 attacks for long periods of time would allow me  
13 to almost forget that I have HAE. Therapies even  
14 with easier methods of administration are  
15 something that I am greatly looking forward to and  
16 hopeful to see progress in my lifetime. Would I  
17 do clinical trials again, of course. Because one  
18 day I hope to live in a time when HAE is something  
19 that I have that doesn't have me.

20 MS. WILMOT: My name is Joyce Wilmot and  
21 I have HAE type 1. I started having recurring  
22 stomach attacks when I was in the early 1990s

1 while I was at college. Everyone attributed the  
2 stomach issues to ulcers, college stress, stomach  
3 flu's et cetera. I was getting frustrated since  
4 no one was able to figure out what was wrong.  
5 Coincidentally, my older sister who was in medical  
6 school at the time, also started having similar  
7 symptoms. So, she dug into her medical books and  
8 was able to come up with a diagnosis for both of  
9 us. So, in that way, I was very lucky that it  
10 took a little less than a year to get a diagnosis.  
11 After I finished college, I pretty much limped  
12 along. I was fortunate that I only had 50 to 10  
13 attacks a year, most years I was able to limp  
14 along. Any time I had an attack, I would lose  
15 three to four days out of work, out of life, in  
16 and out of the hospitals. I remember those days  
17 curled up on my bed waiting for an attack to end.  
18 I participated when the clinical trials came  
19 around, starting with the Baxter. I was  
20 participating in the trial. I remember I was  
21 pregnant with my twin girls when the Baxter trial  
22 was going on. There was one point where the trial



1 was discontinued and I remember in my bedroom just  
2 crying because the trial was pretty much keeping  
3 my babies healthy at that point because I was  
4 getting an attack almost every week while I was  
5 pregnant. When the clinical trials came around, I  
6 participated pretty much in all the ones I could.  
7 Currently, I am not on prophylaxis. I have rescue  
8 medicines. My doctor started me on Berinert when  
9 it was approved. That takes care of my attacks  
10 pretty well as long as I take it early during the  
11 attack. If I take it too late, I would still have  
12 to deal with the residual swelling for another day  
13 or two. For the most part, that works really well  
14 but I soon realized that I needed something else.  
15 I was in the middle of a camping trip with my  
16 daughters for a girl scout troop in the middle of  
17 nowhere and I had a full blown attack. I realized  
18 I had no access to clean water, antibacterial soap  
19 or any kind of clean surface to do my prepping for  
20 an infusion. It was at that point that I realized  
21 I probably needed something else. So, when  
22 Firazyr was approved, I spoke to my doctor and we

1 added that to our tool box of how to handle my HAE  
2 attacks.

3 So, unfortunately, the HAE meds work  
4 differently for all of us. Firazyr for me will  
5 stop the attacks pretty quickly, the progression  
6 of the attacks but there are times when I would  
7 get a rebound attack the day after. So, even  
8 though it is a lot more convenient than my  
9 Berinert at the time, I still have to rely on a C1  
10 inhibitor some of the time to fully get rid of the  
11 attack. So, I'm just thankful these days that the  
12 physicians have several medications to choose from  
13 because the treatment plan has to be customized  
14 for each individual.

15 My daughter, who just turned 15, has  
16 recently started getting abdominal swells. So, I  
17 have learned to infuse her. She's someone who is  
18 awfully terrified of needles. When she was six,  
19 she would hide under a chair to keep the doctors  
20 from giving her her shots. So, it's been a  
21 challenge for her. I'm looking forward to the day  
22 when there is a treatment that is easier to

1 administer. I remember a couple of months ago,  
2 she had an attack. She was dehydrated at the time  
3 so I had a hard time finding a vein to do the  
4 infusion. I tried three or four times, I still  
5 couldn't get one and so I started calling urgent  
6 cares and emergency rooms hoping that I would get  
7 quick help in infusing her. It was then that I  
8 realized that we still have a long way in  
9 educating doctors and emergency rooms as how to  
10 treat HAE. The two or three urgent cares near our  
11 house pretty much refused our request for help.  
12 They said I couldn't bring the medication in.  
13 They just didn't feel comfortable giving her the  
14 medication. I called a couple of emergency rooms  
15 and I wasn't getting a definite answer whether  
16 they would do it or not. Thankfully that night, I  
17 was able to infuse her and everything was okay but  
18 I still have concerns over the next time she has  
19 an attack and I can't get vein access for her.

20 I just want to stress the idea that we  
21 still do need better medications. Our pharmacy  
22 ships two doses at a time for us. I'm just

1 fearful that a disruption in the supply line will  
2 take the medications away from us. I cannot  
3 imagine going back to the dark ages when we don't  
4 have medicine. I'm just thankful for this  
5 opportunity to air our concerns and hopefully the  
6 FDA will see the need to keep the funds going in  
7 to HAE research. Thank you.

8 MS. LONG: Hi, my name is Janet Long.  
9 I'm also very grateful to the FDA for this  
10 opportunity to speak with you today. My story is  
11 not very unsimilar from those you've heard but it  
12 illustrates life without therapy so that's where  
13 I'd like to start. I was 7 when I experienced my  
14 first HAE attacks as far as I can remember. To  
15 this day, I'm haunted by the look of helplessness  
16 on my mother's face when she could only offer me a  
17 hot water bottle and a couple of baby aspirin.  
18 Treatment, we both knew, would do nothing to ease  
19 my suffering. As a teenager, each monthly period  
20 meant excruciating pain and days missed from  
21 school due to severe HAE abdominal attacks. Sleep  
22 overs with girlfriends meant a constant worry that

1 I would need to call my mom to take me home  
2 because I was the one too sick to be a normal  
3 teenage girl at a sleepover. At 21, I experienced  
4 an abdominal attack so severe it caused internal  
5 bleeding and I underwent an unnecessary  
6 exploratory laparotomy and spent a week in the  
7 ICU. Despite the innumerable tests I went through,  
8 no one could figure out what was wrong with me and  
9 the ensuing years brought nothing but scores and  
10 scores of doctors who either admitted to being  
11 totally baffled or offered theories from sinus  
12 drainage to chronic colitis. I knew none of these  
13 guesses were the answer.

14 Over the years, I continued to suffer  
15 mainly abdominal attacks. I was tired of showing  
16 up at the ER only to be sent home. Every  
17 physician told me nothing could be done for me and  
18 I would just have to learn to live with the pain.  
19 I vividly remember my first throat attack. My  
20 general practitioner had told me it was all in my  
21 head and that I was imagining my throat closing so  
22 I took two Advil and went to sleep and by all

1       rights, I should not be here today. I should have  
2       died that night except for a spontaneous remitting  
3       of the swelling. My abdominal attacks used to  
4       last for three days but with some time in between  
5       attacks. With hormone replacement therapy, my  
6       attacks started to come one right after the other.  
7       Three days of nausea, vomiting and diarrhea  
8       followed by three more and three more and three  
9       more. The toll on my body was so unbearable, I  
10      was convinced I was going to die. I faced what I  
11      believe was the very real possibility that my  
12      three beautiful young daughters would be left  
13      motherless. I told my husband, if I don't make it  
14      through the night one night, please tell the girls  
15      that I love them.

16                After 40 years of suffering, a brilliant  
17      gastroenterologist unraveled the mystery of my  
18      life and diagnosed me with HAE. I know she saved  
19      my life because throat attacks are coming once a  
20      week and one would surely have killed me. One of  
21      my three daughters inherited HAE for me. She was  
22      fortunate to be able to participate in clinical

1 trials in middle and high school. She suffered  
2 tongue and throat attacks which is not surprising  
3 in the teen years when stress is high and we know  
4 that HAE is exacerbated by stress. Without access  
5 to clinical trials, she would have died on more  
6 than one occasion. I am so grateful for the  
7 trials for all of the now FDA approved therapies.

8 Today, my own HAE attacks are so severe  
9 and frequent, that I need prophylactic therapy but  
10 I keep an acute medicine with me at all times,  
11 according to the HAE's medical advisory board  
12 guidelines. This just makes good sense with a  
13 disease that is so unpredictable. Not all  
14 therapies work for all patients or even in the  
15 same way during all periods of your life. We are  
16 so fortunate to have more than one choice to treat  
17 HAE attacks.

18 FDA approved treatments meant I had an  
19 alternative to attenuated androgens and their  
20 debilitating side effects which were my only  
21 option when diagnosed 18 years ago. My HAE  
22 physician and I agree that it is important to make

1 my therapy choices according to my needs and to  
2 live a normal life. I'm grateful for the HAE  
3 experts that we have working alongside us who have  
4 also made possible these FDA approved medicines.

5 My grandmother had HAE though no one  
6 knew it. Of course, in those long ago days, near  
7 the end of her life in the late 1970's, doctors  
8 did not know what to do about the pain and  
9 swelling in her face. So, they cut all the nerves  
10 in her face. Current and newly developed HAE  
11 therapies mean we've come a long way but we still  
12 have a long way to go. I hope that my daughter  
13 will never have to suffer as I did. Of course, the  
14 ultimate goal is a cure or a treatment that is in  
15 essence, a cure. But there is not a day that goes  
16 by that I am not more than thankful to still be  
17 alive, to see the advances in HAE drug development  
18 already achieved and still to come. Thank you so  
19 much.

20 MS. BAIRD: My name is Karen Baird and I  
21 reside in Houston, Texas. I also want to thank  
22 the FDA, the panel that's here today, so much for



1       your time. I want to thank Donna Lipscomb, you're  
2       just a joy, your sense of humor. I called you the  
3       comic relief in the hallway but you're so  
4       compassionate too and it is just such a pleasure  
5       to be here today. When I talked to Donna on the  
6       phone, we discussed a little bit and she wanted me  
7       to share about the mother's heart. I feel that  
8       that's really the caregivers heart, not just a  
9       mother's. I want, for just a moment today, to  
10      talk to you about the mother's heart, the  
11      caregivers heart but also the perspective so we  
12      don't get off track on the therapies that my  
13      children are using.

14                    I have two children who suffer with HAE.  
15      My son, Kyle, showed his first symptoms at age 2  
16      and he is now 33. My daughter, Ava, showed her  
17      first symptoms at age 15 and she's now 29. My  
18      husband, Sandy, is the carrier of HAE. He's 58  
19      and has only swelled two times in his life which  
20      occurred in his 40s. I feel he is sort of a  
21      marvel. I've spent the past  
22                    years pleading the cause of my children.

1 I became my sons mother in 1984 and I became his  
2 caregiver in 1986. HAE has affected every aspect  
3 of his physical life as Kyle has an attack every  
4 four days. The first 17 years of his life were  
5 filled with attacks, pain in his body, tears and  
6 anxiety with no treatment. Of course, as a mother  
7 this caused tears, pain and anxiety in my heart.  
8 I felt that I was groping blindly in the dark. I  
9 was reaching out for anything I could touch to  
10 find any kind of stability of our family, all the  
11 while knowing that the worse could happen and that  
12 would be a laryngeal swell.

13 As with all of us, I could not find a  
14 physician that could help me, that could explain  
15 to me or how to even treat it. Our family  
16 history, there is 50 percent of us in the Baird  
17 family that have this disease and they all knew  
18 very little about it. So, for over the past four  
19 generations that we can count back to my son Kyle  
20 appears to have the most extreme battle with HAE.  
21 He seems to carry the greatest burden. It has  
22 affected his daily activities through all the

1 chapters of his life. Attendance in school from  
2 elementary to graduate school, participation in  
3 sports, family vacations, holidays, birthdays.  
4 Someone mentioned earlier about just the  
5 excitement. I can remember every birthday, my son  
6 spent his entire time in the bathroom with  
7 diarrhea, even as a little boy, to where he didn't  
8 want to have a birthday because he associated his  
9 birthday with being sick. All it was, was he was  
10 just excited about his birthday party. It was very  
11 sad. And then going on to college, all of us  
12 know, the dorm life, the dating. My family, we  
13 work in Africa and our children work with us so  
14 that was an added difficulty for us of leaving the  
15 borders of the country with both of my children  
16 having this disease.

17 My son is a professional now. He's a  
18 history teacher, a football coach but he's now at  
19 a place in life where his wife is the one working  
20 and he's the stay at home dad because it really is  
21 the right thing for him right now because he  
22 struggles so much even with therapy. He just

1 generally feels ill all the time. So, despite his  
2 fortitude and his graciousness in having this  
3 disease and his faith and hope, he struggles on a  
4 daily basis.

5 We're so grateful for the day that we  
6 were introduced to HAEA. So grateful to Tony  
7 Castaldo, so grateful to so many people that  
8 really have changed our lives that we feel that  
9 we're part of something. After Kyle was about 17,  
10 he started on Stanazolol, an androgen and after  
11 five years on that, he started having heart  
12 palpitations. He made the choice to take himself  
13 off of it which was a very dark day for me because  
14 for five years I really felt that I could have a  
15 little bit of breathing space. I knew that the  
16 androgen was helping him and as a mom, I just took  
17 a big deep sigh. So, the day he went off of it,  
18 it was terrible for me to say, no Kyle don't do  
19 that, I want you to stay on it. I knew he didn't  
20 need to be on it but I wanted him on it. He went  
21 off of it and his swelling began again.

22 In 2011, Kyle began to infuse with

1 Berinert and it worked very, very well for him.  
2 And then he went, because of insurance purposes,  
3 he switched from that to Cinryze and it has worked  
4 well but not as well from his testimonial to it as  
5 Berinert. As we all know now that the production  
6 of Cinryze seems to have taken a temporary halt,  
7 hopefully -- Kyle found himself last week with  
8 nothing. Once again for himself, our family and  
9 myself as his caregiver even at 33, that dark  
10 cloud comes back over me because I realize that my  
11 son, once again, needs help. Ruconest has come to  
12 the front for us in a very quick and timely  
13 fashion and now he will be starting on Ruconest  
14 this week. So, we're very excited and grateful for  
15 that.

16 In 2003, my daughter Ava at age 15, had  
17 spent the weekend surfing. On Monday, when I  
18 picked her up from school, her hand was swollen. I  
19 think that was one of the most difficult days of  
20 my life back then because I drove back in the car  
21 trying to have a smile on my face, realizing that  
22 15 years into her life, it never occurred to me

1       that Ava would have it as well. And then to  
2       realize that both of my children have it. So, I  
3       found myself as a caregiver in a position that all  
4       my people have it, everyone in my house.

5               Since 2004, I've worked in 35 countries  
6       rescuing children. Tony and I had had a meeting  
7       with Tom Delay. I remember sitting there telling  
8       Congressman Delay is that one of the most  
9       disheartening things in my life as a mother is to  
10      come back to the United States and not even be  
11      able to rescue my own children. Again, there was  
12      a bright light as Ava began therapy treatment with  
13      Berinert in 2011. The quality of her life has  
14      greatly improved. Ava is different from Kyle in  
15      the sense that she swells three to four times a  
16      year but it is always laryngeal. So, for me, I  
17      consider her to be the more extreme of the two of  
18      my children.

19              One would look at my children and see  
20      two beautiful adults now who appear to be  
21      completely healthy. They are both married, they're  
22      parents, they're productive, they work all over

1 the world. Their therapies have changed their  
2 lives. Their therapies have given them security  
3 and given them freedom and we're so grateful. But  
4 I go back in my mind to Christmas 2016. My family  
5 was gathered at my table for dinner, it was  
6 Christmas Day and Kyle was sitting beside me and  
7 he began to act strange saying that he felt his  
8 food wasn't going down the right way. Within  
9 seconds, Kyle collapsed over on me. And at that  
10 moment, as reality soaked in, I thought it's  
11 Christmas Day and I've lost my son. He was  
12 swelling and we were immediately able to infuse  
13 him with Cinryze which saved his life. I remember  
14 my two year old grandson Beckket crawling up on  
15 his daddy's chest and crying, even at two. He  
16 knew enough to know that something was really  
17 wrong with his daddy. Needless to say, it was  
18 really hard that night to carry on and open all of  
19 our gifts with the sobering reminder of this  
20 disease and how quickly it can change our lives.  
21 That night when I went to bed, here's what I  
22 thought. I thought to myself, if Kyle dies from

1       HAE, he'll be in heaven and there will be no more  
2       suffering and that seemed to be my comfort.

3               Now I realize in my children's lifetime  
4       that there really could be a cure with the  
5       timeless research of our physicians, our  
6       scientists, the vision of a cure has begun to  
7       appear on the horizon within our region. I'm  
8       beginning to realize that HAE could actually be a  
9       memory in my children's life. It would be  
10      something in their past and not something in their  
11      future. So, I'm not ready for my children to go  
12      to heaven so that their suffering can end. I'm  
13      ready for my children to have their heaven on  
14      earth.

15              MR. COSTALDO: Good afternoon, I'm Tony  
16      Castaldo. My HAE story is kind of boring. I was  
17      diagnosed at the NIH a long time ago. I'm one of  
18      these people that actually did really well on  
19      androgens. I could get a relatively low dose of  
20      androgens and have some breakthrough attacks but  
21      pretty much my story is very boring. 35 years on  
22      androgens, I tell everybody that all of this is



1       because of androgens, my doctor says no, you eat  
2       too much. We'll go with whatever the story might  
3       be. I would like to share the sentiments of the  
4       panel here and thank the FDA for conducting this  
5       patient focused drug development meeting. I think  
6       this really does show that the Agency has a  
7       commitment to hearing the patient's voice and  
8       hopefully we'll see that translated into the  
9       regulatory decisions as well. I'm also very happy  
10      that we have somebody from CDER here. You'll be  
11      having a bunch of products up for review, I think  
12      you have one now and we would like to make sure  
13      that the message here from the patient gets  
14      percolated throughout the division. Hopefully Dr.  
15      Chowdhury will get a chance to look at the  
16      transcript as well and we're glad everybody is  
17      here today.

18                So, being that my story is boring, what  
19      wasn't boring, however, was that of my daughter.  
20      Age 5, weekly abdominal attacks, horrific.  
21      Covered with erythema marginatum which is the rash  
22      about 25 percent of us get. This was a really,

1 really sick kid. We had an intractable situation  
2 with her and fast forward, we worked really hard  
3 to try to figure out a solution for this beautiful  
4 young child. Three days a week at Georgetown  
5 Hematology. We were frequent flyers there for  
6 fresh frozen plasma which really kind of worked  
7 but I'm not quite sure. I'm a compassionate dad,  
8 I have the disease. I'll never forget one time on  
9 the way to Georgetown, my daughter looked at me  
10 and said, dad all I ever really wanted was just to  
11 go to school. I'm a perennial C student and I  
12 said what, but then I got it. This was a kid who  
13 wasn't going to give up, all she really ever  
14 wanted to do was live a normal life and she looked  
15 at me and said can you help me. That's where it  
16 began.

17 That's where the advocacy you see in  
18 front of us today. We have here in this audience,  
19 some incredible patient advocates. People who  
20 have given up their day to come here all to be  
21 part of a cause and that's the HAE cause. We've  
22 heard the stories today from each on the

1 individuals, each one of these advocates here  
2 today. The passion and their concerns for  
3 themselves, for their children and amongst all of  
4 that is their children's children as well. So, I  
5 just wanted to give you guys a hand for being here  
6 today. Thank you, HAE advocates, for your  
7 participation. You make a difference. Why do you  
8 make a difference, well think about the dark days  
9 and everybody has talked about the dark days.  
10 Some of you might remember that we had a program  
11 back before had access to medicines where we  
12 actually imported medicines from overseas sources  
13 and the Agency was actually very helpful and the  
14 enabled us to do a program where we would bring  
15 the medicines in and we met certain provisions.  
16 Mary Marlarkey at the time, was the head of  
17 compliance, and that program saved a lot of lives.  
18 But that motivated us further as a  
19 patient community to get organized, to work  
20 together. We've heard testimonials today of how  
21 that's worked. Well, that has resulted in  
22 something really special at this juncture. There

1 are many other disease states out there that don't  
2 have the kind of advocates that are sitting in  
3 this room today. Don't have the kind of  
4 physicians that are also sitting in this room  
5 today and also the cooperation from the  
6 pharmaceutical companies. HAE now has six  
7 approved products to treat the disease. That is  
8 quite extraordinary given the limited size. Why  
9 did that happen? That has happened because of the  
10 people sitting in this room. We have a galvanized  
11 patient community and we'll talk about this a  
12 little later when we talk about clinical trials.  
13 There has never been an instant where HAE patients  
14 haven't been willing to participate in clinical  
15 trials and some of them are pretty difficult,  
16 quite frankly, a require a big commitment. But  
17 this community, the united and galvanized  
18 community has never blinched from taking it on the  
19 chin and participating in clinical trials.

20 We also have an incredible cadre of  
21 physician researchers, quite unique for a disease  
22 state like ours given that this really an

1 ultra-orphan rare disease and some of them are  
2 here today. They work selflessly, they care about  
3 the patients and they understand the disease, they  
4 understand the devastation that we've all heard  
5 about today about what this can do to people's  
6 lives. And these physicians have been willing to  
7 participate in clinical trials, participate in  
8 patient care, participate in research and do the  
9 things that are necessary and that's part of it.

10           And then we also have had industry and I  
11 think we've all forged a great relationship. I  
12 think we've forged an excellent relationship with  
13 industry and thank goodness for their investment  
14 in these products and that's where we are today.  
15 However, and this is a huge however, ladies and  
16 gentlemen, I'm here to tell you that the game is  
17 not over by any means. The game is not over by  
18 any means. Dr. Pierce, who've I'd have the  
19 pleasure of interacting with in the past, who has  
20 been a CBER reviewer and knows the disease quite  
21 well, he said something very key this morning when  
22 he made his talk talking about Hereditary

1       Angioedema. He said, no proved therapy eliminates  
2       all attacks. Think about that for a second. So  
3       really, where are we right now. Yes, we finally  
4       through the grace and goodness of this community,  
5       the physicians, the patients, pharmaceutical  
6       companies working together to get things done, we  
7       now have products where lives have been  
8       transformed.

9                    But if you look at some of the studies  
10       that we do, we're not quite there yet. I'll just  
11       give you a couple of quick statistics. We  
12       actually did a quick study of 980 patients not too  
13       long ago. If anybody wants to think that the game  
14       is over for HAE, listen to just a snippet of some  
15       of these stats. 74 percent of the patients that  
16       we polled in our 980 patient sample said they had  
17       more than one attack a month.

18                   percent of that sample said they had  
19       more than one ER visit in the preceding six  
20       months. 50 percent said that they were somewhat  
21       to not at all satisfied with their available  
22       therapy. Basically, we also found that 50 percent

1 of the patients we polled either had used or were  
2 currently using and indwelling port.

3 So, that's the message here today.  
4 We've heard about the stories. We've heard even  
5 with therapy there is still a high level of  
6 anxiety among patients. There is still a fear  
7 that one day we might not wake up. So, I think  
8 it's really important that the agency hears these  
9 messages and when products come in front of you  
10 for review, it's important that you understand  
11 that there can't be any complacency. Obviously,  
12 as regulators, you are entrusted first to protect  
13 the public health and safety, I think we all agree  
14 with that. We think that's paramount, paramount  
15 importance. However, within the confines of that,  
16 we would just ask you to work closely with  
17 industry, with expert physicians who can come in  
18 and speak to you about what is going on because we  
19 still need and have a need for better therapies  
20 and ultimately a cure. Thank you.

21 MS. LIPSCOMB: Well thank you to all of  
22 our panel, thank you very much. How many of you

1 in those conversations recognize your treatment  
2 stories? Does anybody want to talk specifically  
3 about any particular treatment? Let's go and do  
4 our next question please. So, which of the  
5 following medications do you currently take to  
6 prevent an attack? I would then to read these but  
7 then you would have reason to laugh at me. We're  
8 going to read this one. Well, we're going to go  
9 back to hand raising. I know for some of you, if  
10 you're using them, raise your hand for each and  
11 every one that we're doing. How many of you are  
12 using, A is Danazol or a similar steroid based  
13 medication. B is Cinryze, C Haegarda, D other, E  
14 I do not take any medications. Let's vote. That  
15 seems to track like your hand raising. I'm glad  
16 you weren't telling me stories. So, what about  
17 medicines -- Ross what was the web like?

18 MR. PIERCE: So, like in the audience  
19 here, the most popular answer was other and that  
20 was twice as frequent as collectively, Cinryze and  
21 Haegarda which were the other popular choices.  
22 There was only one participant from the web who



1 was taking Danazol and everybody was taking  
2 something, nobody chose choice E.

3 MS. LIPSCOMB: Okay. What about, let's  
4 talk about medicines that are used for treatments  
5 and attacks? Chris, can you hit the next one.  
6 Which medications do you receive from your  
7 healthcare provider to treat acute attacks and  
8 pick all that apply. I think we heard a couple of  
9 you talk about how helpful Firazyr has been.  
10 We're going to ask one more medication question  
11 and then I'm going to let you guys have a chance  
12 to talk to me about it. Chris, I'll check with  
13 you guys about the web. How was twelve?

14 MR. PIERCE: Firazyr Icatibant was the  
15 most popular choice followed by Ruconest and  
16 Kalbitor, Berinert was after that.

17 MS. LIPSCOMB: Okay, so very similar.  
18 Let's talk about the medications you're using on  
19 the results. Especially for people who wrote  
20 other in this one, what are those treatments that  
21 you use?

22 MS. YODER: I think I already mentioned

1 earlier that I was on the Danazol for 33 years and  
2 just got off of it three months ago and started on  
3 the Berinert because of the cholesterol issues.  
4 It's a prophylactic now. I started that, I did  
5 have it for catastrophic attack but now I'm taking  
6 it as a prophylactic.

7 MS. LIPSCOMB: Okay thank you. Anybody  
8 else?

9 MS. BRAHEN-GRESSENBACK: Yes, I was on  
10 from 1974 until 2011 I was on Danazol and I  
11 actually switched from Danazol for the last five  
12 years to Oxandrolone because it was less affecting  
13 me because it is less masculinization. And then I  
14 hit menopause and the Oxandrolone was messing me  
15 up so I went off that and I had 53 attacks in one  
16 year. In 2011, I found HAEA and met a doctor and  
17 he mentioned Firazyr for me because that was  
18 available. I started using that, it cut down my  
19 attacks from 53 to about 25 the next year. But  
20 then I was starting to have rebound attacks. So,  
21 then I went on Cinryze and I was on Cinryze but  
22 then I started again menopause having hot flashes

1       so I went on a real low, low, low dose 0.25 of  
2       bioidentical estrogen because hot flashes every 15  
3       minutes, the quality of life, I don't care if you  
4       have angioedema or not, you have to balance  
5       quality of life with everything else happening.  
6       So, the Cinryze I was breaking through a little  
7       bit and then it became unavailable in 2016. So,  
8       in 2016 I switched to Berinert and then that's  
9       weight based and I haven't had any problems except  
10      for real excitement or something with  
11      breakthroughs and then I use Firazyr and then I  
12      follow up after Firazyr with Berinert because of  
13      the 24 hour rebound that I have. So, I guess I'm  
14      of all these therapies that are available, I'm  
15      almost used all of them. As life changes, as your  
16      experience changes, for women especially who have  
17      hormonal changes, you have to switch and use  
18      different things. Also, in this case, it's just  
19      not the hormones it is actually companies. When  
20      the companies change and they can't provide the  
21      drug, there has to be something else out there  
22      that we can go to. Because if I didn't have, I was

1 in a clinical trial for subcutaneous and I got the  
2 saline unfortunately and I started attacking every  
3 two or three days and so I had to actually drop  
4 out of this particular clinical trial because it  
5 was too dangerous for me. So, I guess what I'm  
6 saying you have to have different drugs to go back  
7 and forth to.

8 MS. LIPSCOMB: Thank you. Did anybody  
9 else have other meds you wanted to mention?

10 DR. BUSSEY: I wasn't going to mention  
11 about the treatments, I'm a physician. My name is  
12 Paula Bussey and I take care of a large group of  
13 patients with HAE and I just want to talk on the  
14 physician's side. It's wonderful now to be able  
15 to provide patients with medications but yet there  
16 are several frustrations that we have and I would  
17 like you to be aware of them. One, there is a lot  
18 of paperwork that's involved in making the  
19 prescriptions and sometimes very frustrating  
20 things. For example, if I have had patients that  
21 haven't had their medicines filled because for  
22 example, they have to prove they have HAE. I have

1 bloodwork from several years ago that proves they  
2 have HAE but I'll get calls back from the  
3 insurance company saying, I need recent blood  
4 work. Well, this is a genetic disease, it doesn't  
5 change. So, patients that have a lapse in their  
6 therapy which is not good and extremely  
7 frustrating for myself.

8 Another thing I think is important for  
9 physicians and everyone to be aware of is the  
10 proper use of the medications and the proper  
11 prescription patterns. Make sure that the patient  
12 really has HAE or has hereditary angioedema because  
13 with the shortages that we do have sometimes, when  
14 medications are not prescribed properly, the  
15 patients who need it may not have it. Those are  
16 some of my frustrations.

17 MS. LIPSCOMB: Thank you.

18 MS. EDWARDS: I'm Carol. Before I was  
19 diagnosed with HAE, I started taking testosterone  
20 for libido which worked very nicely. But I  
21 noticed that same week, I was getting an HAE on my  
22 way to work and it was like half as bad and I was

1     like hey, just give me a couple of hours, I can  
2     continue on with work. That was the first time  
3     since I was 10 years old that there was any  
4     deviation into an attack not being as bad. When I  
5     was diagnosed with HAE probably about six months  
6     later, my HAE doctor actually prescribed a  
7     testosterone for me for another six months because  
8     my attacks were so much less severe. That was the  
9     other thing I used and it helped me. I'm not on  
10    it anymore. My husband enjoyed it but I couldn't  
11    take it anymore.

12           MS. LIPSCOMB: Let me ask the next  
13    question real quick.

14           MS. LONG: I just wanted to mention, a  
15    lot of women have mentioned the role of hormones.  
16    Progesterone only therapy can also be used  
17    sometimes. My daughter chose that route when  
18    there was no therapy currently approved by FDA and  
19    it works for her. It doesn't work for everyone to  
20    our point that not everything works for everyone.  
21    But sometimes progesterone only can be affective  
22    for HAE.

1 MS. LIPSCOMB: Thank you for adding  
2 that. We've heard in our conversation that when  
3 an attack is coming, you or your caregiver at home  
4 administer treatment. So, different people may  
5 feel different symptoms as harbingers of an  
6 upcoming attack. Our next polling question is  
7 about when you feel a treatment is needed. I  
8 think a couple of you have talked about that. A,  
9 no symptoms appear but you can feel attack coming  
10 on. Once symptoms interfere with activity, once  
11 pain or discomfort from swelling becomes  
12 intolerable. That seems to be the most, C and A.  
13 What about the web?

14 MS. BOUCHKOUJ: Similar responses, C and  
15 A.

16 MS. LIPSCOMB: Okay thank you. We would  
17 appreciate if some of you could share your  
18 experiences about this phase.

19 MS. STARR: For me over the years, I've  
20 learned that effective treatment is to get it  
21 right away when the attack starts. I've learned  
22 my prodromes like symptoms that start before an

1 actual attack starts is when I treat. Because if  
2 I don't, then I'm already in pain, the swelling  
3 has already started and it takes longer to  
4 resolve. So, I've learned how to do it that way.

5 MS. LIPSCOMB: Thank you.

6 MR. CASTALDO: So, just to comment here  
7 about this data here is quite remarkable and not  
8 in a good context, quite frankly. Because I invite  
9 anybody who is a non patient to think about how  
10 you would feel if you had to get sick to the point  
11 where pain and discomfort becomes intolerable  
12 before you could treat. That's not an acceptable  
13 way to look at it. Now, recognizing there are  
14 certain situations where you can't get to the  
15 treatment soon enough. This is something that I  
16 think our medical advisors have always stressed  
17 and it is so important that for those patients  
18 that are on, on demand therapy, the earlier you  
19 treat the better. Because you can stop whatever  
20 is going on biochemically that is causing the  
21 swelling. You can stop that pretty quick with the  
22 available treatments. If you don't stop it and you



1 let the swelling get into your tissues, you are  
2 sick and then it is up to your body to reabsorb  
3 those fluids and you'll be sick until it does  
4 that.

5 And let me just make one other point  
6 that I think is very clear as we've talked about  
7 the array of acute therapies that we have  
8 available for us. It is very important that  
9 everyone understands, there is variability in  
10 effect and we hear this a lot from our patient  
11 community. There was a lot of variability in how  
12 various therapies work for various patients.  
13 Those were valid concerns. One of the things  
14 we're blessed with at this juncture is that we  
15 have therapeutic options. That's a good thing  
16 because what we find on that is that not  
17 everything works for everybody in the same way.

18 MS. URBONIUKI: I want to say as a  
19 patient, it's really important to treat early as  
20 all of us know to just shut that pathway down.  
21 You're going to feel a lot better sooner. In  
22 talking to some patients, I've heard before, well

1 I'm just going to deal with it if it's like an  
2 attack on my hand or my foot. I'm not sure how a  
3 lot of people are but I know for me it's never  
4 just my hand. And you never know, it could travel  
5 to various places, abdominal, even laryngeal.  
6 It's just really important to treat every attack  
7 as soon as possible.

8 MS. LIPSCOMB: Thank you.

9 MS. EDWARDS: For me, I need an F on  
10 there because I have to wait for my symptoms to  
11 appear but I cannot take them until they are  
12 intolerable. As soon as they appear and I'm sure  
13 it's an attack, I want to treat right then but my  
14 symptoms have to appear otherwise I don't know  
15 it's an attack.

16 MS. CLASEN: Hello, I'm Liz, again. I  
17 think there is two sides of the coin for many of  
18 us who have gone so long without diagnosis. One  
19 of the positives is I know those warning symptoms,  
20 I know them really well because I suffered for so  
21 long and I learned my body so well. The flip side  
22 of that is you begin to think suffering is

1       supposed to be part of your life, so I had this  
2       weird human psychology around, oh it's just a hand  
3       attack and this is my lot in life. So, I really  
4       want to say a huge thanks to HAEA because I think  
5       very loudly and frequently say, treat attacks  
6       early because it is more effective and treat every  
7       attack because it is your right. It's your right  
8       and we have that benefit because we have these  
9       therapies not to have to suffer. There is still  
10      this weird human psychology that it's important  
11      that my husband and that my dad has heard that so  
12      they can remind me when I have an attack like, oh  
13      yeah I should do this, because sometimes I need  
14      that extra voice because suffering had become so  
15      my normal.

16               MS. BREADY: I was always told from my  
17      doctors, because I take an acute therapy, that is  
18      I would have swelling in my face or my throat or  
19      stomach, to take the medication right away but not  
20      to take it for my hands or my feet. So, I'm just  
21      like recently like I just deal with a foot or a  
22      hand swell. It is very interruptive and I think

1 I'm going to start taking for my hands and feet.  
2 I just wanted to make a comment too on some of the  
3 questions here. Sometimes I'll wake up in the  
4 middle of the night too with a throat swell. It's  
5 not like I'm thinking, oh I'm starting to feel,  
6 you're sleeping and you're waking up at 3 in the  
7 morning and your face is swelling or your throat  
8 is swelling and you're like, oh no is this real  
9 and then you treat.

10 MS. LIPSCOMB: Thanks, we're going to  
11 take two more.

12 MS. CONKLIN: I want to speak to what  
13 Liz said. My name is Katie. So, you say to treat  
14 when you start to have an attack and I know from  
15 experience. If I start to have an attack, if I  
16 take that medication immediately, I feel better  
17 and that usually stops the attack. However, with  
18 the shortage of medication most recently, my last  
19 dose of Cinryze was on September 10th. Three days  
20 later, I began to have attacks. I had an attack  
21 for 11 days. I'm lucky that I had Firazyr on  
22 hand. However, Firazyr did not stop the attack.

1 I ran out of Firazyr and it was a battle to get  
2 Firazyr. So, I'm always hesitant to treat a hand  
3 or a foot attack when I am low on medication  
4 because what if I had that laryngeal attack and by  
5 goodness, I'd rather suffer through a hand and  
6 foot attack then to have a laryngeal attack. My  
7 children watched me leave my house when they were  
8 3 and 5 years old on Christmas Day. I'll never  
9 get that back but I was having severe attacks.  
10 Every time I leave my house to go to the ER my  
11 children are terrified mommy is not coming home.  
12 Like Tony, I'm a lucky one. My story is very  
13 boring but I have many members of my family that  
14 have this disease and not having access to  
15 medication is detrimental to our health.

16 MS. BEITER: I think something that is  
17 really important about what is up here is that we  
18 wait until there is pain or discomfort that is  
19 intolerable is that I know for me, my story  
20 doesn't go nearly as long as a lot of people in  
21 the room. I had so many years where doctors  
22 chalked it up to really weird things or just wrote

1 me off. So, a lot of times I convince myself that  
2 maybe it's not an attack until it becomes  
3 intolerable because then you're like, well I guess  
4 this is what it actually is. So, I think that 43  
5 percent sort of holds that true to a lot of feel  
6 that like we can say, oh maybe I have a cold or  
7 maybe it's just a headache or maybe I just don't  
8 feel great this morning. And then four hours  
9 later, we're in that intolerable discomfort. I  
10 think a lot of us do that as well. I've heard  
11 people say that they wait too long because they  
12 think maybe it is not necessarily all know exactly  
13 what it really is.

14 MS. LIPSCOMB: Thank you. Was there  
15 anybody on the web?

16 MR. PIERCE: Just one web participant,  
17 David, mentioned that he treats when symptoms are  
18 recognized, he does not wait until they interfere  
19 with his activity or become intolerable.

20 MS. BOUCHKOUJ: Also, Jennifer from the  
21 web is echoing what Ross just said. If they don't  
22 treat the first attack it's really hard for them

1 to get a hand on taking care of the rest of the  
2 attack.

3 MS. LIPSCOMB: Thank you guys. So,  
4 let's talk about your decisions of choosing  
5 different treatments or how you choose one  
6 treatment over the other. Aside from the cure  
7 when considering a new treatment for your  
8 condition, which benefits would you consider the  
9 most meaningful, and you can choose up to two.  
10 So, reduction in attack, frequency, reduction in  
11 severity, rapid response to treatment of acute  
12 attacks and completeness of response to treatment  
13 out of acute attacks. So, we hear we should have  
14 said all that apply. My new obsession is Hamilton  
15 so I feel like we could say you should have been  
16 in the room when it happened. Can we see? So, for  
17 us is reduction in attack frequency and you kind  
18 of did answer more than once considering B and C  
19 are almost a statistical tie. What does the web  
20 look like?

21 MR. PIERCE: So, reduction in attack  
22 frequency and rapidity of response are getting the

1 highest responses but just by a small margin.  
2 Next is reduction in attack severity and lastly  
3 completeness of the response to treatment of acute  
4 attacks.

5 MS. LIPSCOMB: Okay. Do we want to talk  
6 about the two choices that they picked? I didn't  
7 talk to her last time so I'm going to pick her.

8 MS. NEHRING: For me, being in college  
9 it's important for me to be able to get back into  
10 the swing of things quickly. When I miss, I have  
11 one class that's three hours so if I miss that  
12 class once, I miss a whole week of material. But  
13 I also think it's important to mention that some  
14 people don't have a choice in their medications.  
15 So, the beginning for me because I was a patient  
16 with normal C1, I was given two options for acute  
17 attacks. I didn't get to pick which medications I  
18 was on, I didn't get to try different ones so some  
19 patients don't have that option.

20 MS. LIPSCOMB: Thank you.

21 MS. SANTEE: Well, to piggyback, on what  
22 Kelsie said, we have the same type and rarely can



1       you participate in the acute side of things.  
2       However, I was diagnosed a little earlier so I was  
3       able to try the prophylactic even though we  
4       thought it may fail, it did. I was hoping and  
5       praying that it would work for me and that was  
6       Cinryze. So then after that, I had to get back on  
7       those dreaded androgens and yes, it did blow me up  
8       so I do understand. But then the acute attacks  
9       came, the acute rescue medicine came. The first  
10      was Kalbitor. Unfortunately for me, as I told you  
11      earlier, I had a young son I had to take care of  
12      and he also had health issues. So, having to have  
13      that administrated in the hospital was not a good  
14      fit for me. So, I went to Firazyr when that  
15      finally came aboard and that has given me a little  
16      bit more autonomy. However, I'm here today  
17      because there are new medications that perhaps are  
18      on the same vein of our acute medications that we  
19      have, may provide prophylactics. I think that I  
20      answered A and B and I'm just hoping that A and B  
21      can really be preventing attacks and not even B  
22      being an issue because I won't have an attack to

1 have severity. But research is so crucial for some  
2 of us who don't have options to flip flop to and I  
3 just thank you for having us here. We definitely  
4 have to continue, like they said, there is not an  
5 option for everyone. We all have variability in  
6 how we respond to certain attacks. I just really  
7 hope that we can get a prophylactic for people who  
8 only have the rescue medication.

9 MS. LIPSCOMB: Would you like to talk  
10 about the treatments?

11 MR. COSTALDO: So, the good news is  
12 about the HAE with normal C1 inhibitors, there is  
13 significant amount of research being done. As a  
14 matter of fact, down at the angioedema center at  
15 the University of California San Diego, they  
16 probably have seen more normal C1 inhibitor  
17 patients than just about any center in the United  
18 States. They are taking the blood samples and  
19 they're really thinking it through. We have some  
20 really incredible scientific minds that are  
21 looking at it and I wouldn't be surprised, if at  
22 some point, they're able to come up with a

1        biomarker which simply means that they can then  
2        better look at what the cause is and then  
3        determine what an appropriate therapeutic regimen  
4        might be.

5                    So, normal C1 inhibitor right now, HAE  
6        with normal C1 inhibitor is still a brave world,  
7        if you will. There are lots of elements of it  
8        that we just don't understand but we're very  
9        excited about the work that's going on at the  
10       angioedema center and their focus and the  
11       Hereditary Angioedema Association has really been  
12       very active in making sure that that research is  
13       being funded. The Angioedema Center also apropos  
14       some of the things we've talked about here with  
15       the treatments, they're looking towards this  
16       notion of precision medicine. This has nothing to  
17       do with the regulatory side of things because our  
18       wonderful friends at the FDA, they are responsible  
19       for reviewing candidate medicines and approving  
20       them for license. But there are other types of  
21       research being done that can actually look at a  
22       current medicine and find maybe what is the right

1       dose, the right incidence of taking the disease  
2       and so forth.

3                   One other point I want to make and I  
4       think is important for all of us here sitting in  
5       this room and that is as we get better preventive  
6       therapies and if you look at what is being thought  
7       about in the pipeline. Currently there is  
8       Lanadelumib is in the clinic. Haegarda was just  
9       approved. There are probably going to be clinical  
10      trials with the kallikrein inhibitor pill form  
11      probably next year, if I read the press releases  
12      correctly. There are two other companies that  
13      have pill forms, kallikrein inhibitors that are  
14      looking at it. There is also a trial going on  
15      with a pill form for acute. I can tell you also  
16      that two other companies have been in touch with  
17      the HAE Association that are looking at gene  
18      therapy solutions for this disease. So, there is  
19      a lot going on out there right now. So, just keep  
20      in mind that all that is happening because we also  
21      want to make sure that everybody is willing and  
22      continues to be willing to go and participate in

1 clinical trials as we go forward. So, stay tuned  
2 folks, there is a lot in the hopper.

3 MS. LIPSCOMB: Well, since he's led us  
4 to the clinical trials question, we're going to go  
5 to our next question which is the precursor to the  
6 clinical trials question. So, which of the  
7 following factors, of the following factors, which  
8 three would you rank as most important to your  
9 decisions about using treatments to treat your  
10 condition. Again, use up to three. How the  
11 medication is administered, how frequently the  
12 medication is administered, access to treatment,  
13 possibility of common and non severe side effects,  
14 possibility of infrequent but serious severe side  
15 effects, previous improvement in response to a  
16 similar treatment, previous lack of improvement  
17 from another treatment.

18 MS. BEITER: can you explain the G?.

19 MS. LIPSCOMB: I can and I can explain  
20 it by walking over to Larissa and letting her.

21 DR. LAPTEVA: So, I guess it's the G  
22 that needed to be explained. If you've previously

1       used some type of treatment and it didn't work for  
2       you, would you choose that treatment or category  
3       of treatment again or would you choose something  
4       else? You would obviously choose something else.  
5       So, that's something that would influence your  
6       decision to choose your next treatment and that's  
7       the G. Did that help?

8                   MS. LIPSCOMB: Thank you. Let's go  
9       ahead and close this poll. So, in looking at the  
10      top three factors, the first one, how the  
11      medication is administered, is the most often  
12      cited followed by access to treatment, cost  
13      insurance coverage. And then almost a tie between  
14      B and E really. How frequently it is administered  
15      or the possibility of infrequent but serious and  
16      severe side effects. How does the web pair up to  
17      that?

18                   MR. PIERCE: It really looks very  
19      similar.

20                   MS. LIPSCOMB: Okay thank you. So, it  
21      looks like to me that really, and I think we've  
22      heard about PICC lines and ports and sterile

1 environments that there is a lot to go in when you  
2 think about what medications you want to use. Is  
3 there anything else about a treatment that you're  
4 thinking about before we go and ask the questions?

5 MS. TUMA: My name is Stephanie and I'm  
6 concerned also about like long term effects of  
7 these medications. Like I'm 25 years old now, if  
8 I'm still taking this medicine at 75 years old,  
9 through the next 50 years if I'm on the same  
10 treatment, what are the side effects going to be  
11 for that?

12 MS. LIPSCOMB: Okay. Anybody else want  
13 to comment?

14 MS. BRAHEN-GRISSENBACK: Peggy. I  
15 didn't get a chance to vote for all of these but  
16 it depends on each of these becomes important in  
17 different situations. Like in travel or my  
18 husband helps me infuse. If he has a migraine or  
19 something or he's away, how the medication, if I  
20 can use subcutaneous. And then the other one is  
21 like again, I'm older now, I'm 62 years old so  
22 that's something I was thinking about for long

1 term effects. It's like okay it's going to help  
2 me now but it's going to take 30 years for it to  
3 damage my liver. Well, okay if it's 30 years to  
4 damage my liver, I probably don't have 30 years to  
5 live so maybe I'll do that one as opposed to  
6 somebody that is 20. They really have to think  
7 about that. So, I think, again the different  
8 situations you have and the different age and how  
9 some people's attacks come within 10 minutes, some  
10 people's come within a day. So, again it switches  
11 back and forth. And then insurance, I have good  
12 insurance. Other people, they can't the  
13 treatment, they don't have a choice because of  
14 insurance companies.

15 MS. LIPSCOMB: We'll take one more and  
16 then I'm going to ask the FDA panel if you have  
17 any follow up questions.

18 MS. FRENCH: There are so many decisions  
19 we have to make on a personal basis about all of  
20 those. One of the decisions we don't get to make  
21 in some cases is C. Because what the FDA does and  
22 all the hard work they put in about how the



1 medication should be given and the quantity per  
2 day because of the data that we have given them,  
3 what is your insurance company balks and say  
4 you're supposed to be able to take three doses per  
5 day but your medical insurance says well I'm only  
6 going to give you three boxes a month. What do we  
7 do then for the other 20 something days and have  
8 an attack when you in your wisdom and us in our  
9 hard work have proven otherwise? So, sometimes C  
10 is taken out of our hands and is not even a  
11 choice.

12 MS. LIPSCOMB: Thank you. The panel, do  
13 you have any questions?

14 MS. PUROHIT-SHETH: Hi, I'm Tejashri  
15 Purohit-Sheth and I want to go back to the  
16 question that was asked of you regarding the  
17 prophylactic treatment. So, many of you picked  
18 other. I was very interested in learning what  
19 other therapies for prophylaxis have you been  
20 using outside of Danazol, Cinryze or Haegarda.  
21 Thank you.

22 MS. RAMSEY: I have been using the

1       Cinryze and with the recent manufacturing problem,  
2       I was out. I was lucky enough to have access to  
3       Ruconest. Unfortunately, I'm having small  
4       episodes start after I do a dose. So, three or  
5       four days past and I start to have another  
6       episode. So, I'm practically on the same  
7       prophylactic schedule, I'm just experiencing that  
8       kind of lack of C1 is triggering episodes for me.  
9       So, it's practically prophylactic for me right  
10      now. I know it's off label so that's why I was  
11      reluctant to raise my hand earlier but that's the  
12      situation I'm in. I responded very well to the  
13      Cinryze and it was a literal life changer. The  
14      Ruconest has been great but if I try to go  
15      without, I end up having another episode start. I  
16      know we talked about the importance of treating  
17      when we see the first signs.

18               MR. MALLORY: I'm Mike from Ohio. I've  
19      been treating prophylactically with a study  
20      medication that has been working very well for me.

21               MS. LIPSCOMB: Thank you. Anybody else?  
22      I'll get you, Dakota.

1 MS. THOMPSON: Thankfully, I have been  
2 able to actually get on the clinical trial for  
3 Lanadelumib so I'm no longer actually taking a  
4 prophylactic but instead, just taking part of a  
5 research trial.

6 MS. LIPSCOMB: Okay thank you. Anybody  
7 else on the panel?

8 MS. PUROHIT-SHETH: I have one more  
9 question. Many of you mentioned that you have  
10 some warning symptoms before your swelling  
11 actually starts. I was interested in  
12 understanding what some of these warning symptoms  
13 felt like.

14 MS. FOX: I'm Debbie. I get the rash the  
15 rash and also just extreme fatigue like you can't  
16 go another step.

17 MR. SELSOR: I get that rash too and  
18 before an abdominal attack I'll get a specific  
19 vague headache. It's the only time I'll get it is  
20 the day before.

21 MS. STARR: I get very dizzy,  
22 lightheaded and that's one of my first signals.

1 MS. NEHRING: Fatigue is a big one for  
2 me but also severe dehydration to the point where  
3 I'm drinking water and it is not helping resolve  
4 the dehydration and the cotton mouth.

5 MS. RAMSEY: I'm Adina. For me, I'm  
6 fortunate that most of my episodes are on my  
7 extremities which is kind of a downfall because it  
8 is easy to overlook those. I'll feel a tightness  
9 or an ache. My knees are really bad about it and  
10 I'll try to wait to see if it is and then it  
11 starts to show that red area so I know and I  
12 infuse.

13 MS. EDWARDS: I'll get abdominal swells  
14 and I can't recognize it unless I have cramping  
15 before until my stomach has already cut everything  
16 off and it is just these putrid burps. And at  
17 that point in time, even taking Berinert right  
18 then, I still have like a two day attack.  
19 Everything has got to go through and up and out  
20 but it's not as severe as it used to be which  
21 would be days and days.

22 MS. SANTEE: I have a lot of peripheral

1 limb swelling as well. Even on my face I get  
2 tingling or a little itching. It's not itching  
3 like a normal itch but a sensation. Hours later,  
4 that area typically will swell.

5 MS. BOMAR: My name is Fran. I have  
6 many of the pre symptoms that a lot of these folks  
7 have talked about, fatigue and so on. One of the  
8 things that I think is interesting is I feel like  
9 I'm an out of focus picture. I can't keep moving  
10 and I just don't feel right. The other thing,  
11 also my white eye gets so blood shot and painful I  
12 can't even look at me, it just makes me cringe.  
13 As soon as the attack comes on, the redness goes  
14 away.

15 MS. RENDON: My name is Amy. I don't  
16 have HAE, Dakota does. Prior to her being on a  
17 prophylactic, I used to be able to tell her within  
18 12 to 24 hours when she would have an attack  
19 because she would get what I dubbed, HAE PMS. She  
20 would get cranky and short tempered and just not  
21 happy. So, there was an emotional side to it that  
22 she also gets the rash. At one point, a surgeon

1 had called her telling her he wasn't going to put  
2 in her port. He was on the phone with her and I  
3 literally watched the rash crawl across the her  
4 neck. It scared me to death. I took the phone  
5 from her and would not let the surgeon talk to her  
6 any longer. What he was saying, literally, I  
7 watched him send her into an attack. But there is  
8 a HAE PMS, I'm telling you.

9 MS. LIPSCOMB: I think we have some --

10 MS. KASS: Donna, I have one more.

11 MS. LIPSCOMB: Okay let me talk to the  
12 people on the web first and then we'll get there.

13 MR. PIERCE: Diane on the web says, that  
14 she feels like she's done too many sit ups and  
15 then the swelling because obvious afterwards. Her  
16 waist circumference goes from 37 inches to over 40  
17 inches during the attacks. So, some people think  
18 she looks like she's pregnant when she's  
19 experiencing an attack.

20 MS. BOUCHKOUJ: Also, we have some other  
21 comments that some of these symptoms include bad  
22 breath and foul smelling gas. So, that can happen

1 just before the attacks.

2 MS. LIPSCOMB: We have one more.

3 MS. BARNES: I'm just going to reiterate  
4 what Amy said, she kind of talk my line. Jim,  
5 when he was 5, I could always see an episode  
6 coming because he was moody. We didn't  
7 necessarily call it PMS. It's putting up with  
8 Momma. He had a lot of the behavior and the  
9 irritability, I could see within a day or two and  
10 then he'd sleep a lot. And then after the  
11 episode, it was the opposite swing of the  
12 emotional pendulum. He would be real sappy and  
13 sweet and overly affectionate. So, that was like  
14 a rebound for him but I could always tell when he  
15 was getting ready to have one with the rash and  
16 everything too.

17 MS. LIPSCOMB: Okay, thank you. Any  
18 other questions? Okay thank you. So, I think  
19 that's an easy lead into our next discussion  
20 topic. We're going to go to topic three which is  
21 the possibility of clinical trial participation.  
22 Now, I'm pretty sure I heard a couple of you say

1       you've been on clinical trials, you believe in  
2       them. I heard a cheerleader back there so I think  
3       this will be an interesting conversation for us.  
4       So, these are really kind of what I want you to  
5       think about when you're answering the questions.  
6       So, if you have the opportunity to consider  
7       participating in a clinical trial studying  
8       experimental treatments, what aspects would you  
9       consider when decided whether or not to  
10      participate. If you have previously participated  
11      in clinical trials, discuss your own experience  
12      whether favorable or unfavorable and explain why  
13      you chose to participate. So, if you had the  
14      opportunity to participate in a clinical trial  
15      with investigational treatment, which of the  
16      following best describes your thoughts. Yes, I  
17      would consider participating, no I would decline  
18      the offer to participate and maybe depending on  
19      various factors. And you know we're going to talk  
20      about those various factors. So, only 5 percent  
21      said no but 65 is a resounding yes and 30 percent  
22      maybe depending on various factors. How did the



1 web look on that?

2 MS. BOUCHKOUJ: No one said no, so they  
3 would all participate in a trial. Some of them it  
4 depends on various factors.

5 MS. LIPSCOMB: Okay great. And although  
6 several products have been made available -- I see  
7 a hand up, tell us about your decision.

8 MS. THOMPSON: My name is Dakota again.  
9 Like my mother mentioned in the first half, I  
10 became septic and nearly died last year. I went  
11 to, ended up getting my port removed, got my PICC  
12 put in and I went to go talk to my specialist  
13 about new medications like what to do from there.  
14 He did not trust the research trial if there was  
15 going to be a placebo in it. I swelled way too  
16 much, way too often and way too severe to even  
17 consider taking a placebo. But I was able to join  
18 the current trial because it's open label and I  
19 know I'm getting the medication daily. So, the  
20 factor is that I need to make sure I don't end up  
21 in the hospital constantly because of my attacks.

22 MS. LIPSCOMB: Thanks. Anyone else want

1 to talk about their experience?

2 MR. MALLORY: Hi, I'm Mike from Ohio. I  
3 chose to be involved in as many clinical trials as  
4 I could when my wife and I were having our first  
5 child because I didn't want my child to suffer the  
6 way that I have. We've seen a lot of great  
7 medications come along and out of my three  
8 children, my youngest daughter is the only one  
9 that is currently diagnosed with this disease. I  
10 want to have better treatments for her if she ever  
11 does start presenting with this. So, I  
12 participate as much as I can in hopes that she  
13 never has to suffer.

14 MS. LIPSCOMB: Thank you.

15 MS. BRAHEN-GRISSENBACK: I participated  
16 in one of the clinical trials but it was either  
17 you got the drug or you didn't get the drug and  
18 there was no escape clause in terms of, I  
19 unfortunately got the saline because I had to drop  
20 out because I would ended up in the hospital  
21 because almost every day I was attacking. So, I  
22 guess when the clinical trials are brought up,

1       there has to be some way to, since it is all so  
2       stressful and mental, to allow the people to know  
3       that you can escape or get the real drug or open  
4       label if it's not working for you and you're  
5       seriously suffering.

6                   MS. LIPSCOMB: Thank you.

7                   SPEAKER: So, Dakota brought up a really  
8       good point, both speakers brought up a good point.  
9       And that is, at what point does an institution  
10      review board determine that maybe a placebo is not  
11      appropriate. I don't know the answer to that. I  
12      think that's something though that as current  
13      treatments get approved and are more effective or  
14      are affective, particularly the prophylactic  
15      treatments, at what point do IRB's or even  
16      patients begin to wonder, can I afford to  
17      participate, do I want to get sick if I've not  
18      been sick before. That is an ethical and  
19      regulatory decision going forward that I think is  
20      going to be interesting.

21                   MS. LIPSCOMB: Thanks. I think the next  
22      question --

1                   MR. GOLDSMITH: I just wanted to talk  
2 back to the issue about open label. No trial  
3 should have less than the standard of care. You  
4 either get the approved therapy, you have lots of  
5 them, that's the standard of care that has to be  
6 the comparator for a licensure trial. You can't  
7 get less than that, that wouldn't be an ethical  
8 trial. So, if it's an open label trial often it's  
9 because they've already finished the testing phase  
10 of the drug and they've enlarged the access  
11 because they have promising data. They have a  
12 treatment entity and they let other people come in  
13 the trial and get the drug. They get additional  
14 safety and efficacy information from that group.  
15 If they are approved therapies, that's the  
16 standard of care. You can't get less than the  
17 standard of care.

18                   MS. KLINGER: So, are you saying in a  
19 phase one trial for an angioedema drug, the  
20 placebo would be an approved therapy not a  
21 placebo?

22                   MR. GOLDSMITH: It's a phase one trial

1       so a phase one trial is really a safety trial.  
2       It's a first look in humans of the use of that  
3       drug. So, it's important to have a true placebo  
4       to understand what the adverse effects are that  
5       you can attribute to the drug versus what you  
6       might attribute to getting the placebo.

7               MS. KLINGER: I guess that's what I'm  
8       asking because you just said it wouldn't be  
9       ethical to have the standard of care --

10              MR. GOLDSMITH: In a treatment trial  
11       right but that's a safety trial.

12              MS. KLINGER: Right, I actually work in  
13       clinical trials in an academic medical center in  
14       clinical trials administration. So, I do think  
15       that that's a problem not just for hereditary  
16       angioedema but for other serious rare diseases.  
17       As you've heard today, going with a placebo is  
18       life threatening for us. So, I've participated in  
19       a clinical trial for the same reason as Mike. I  
20       have two kids, I don't want them to go through  
21       what I and my family have been through. I  
22       understand the importance of the first in human's

1 information and data but maybe there's a  
2 discussion that needs to happen about what is the  
3 difference. If you can blind the treatment and  
4 know that one treatment is an approved therapy and  
5 one is the first in humans, then why is that data  
6 any worse than the other. I know with the placebo  
7 you risk. If you want to talk about SAE's, death  
8 is certainly the worst of all of them and we  
9 wouldn't want to put people through that  
10 possibility.

11 MR. GOLDSMITH: Right I'm not arguing  
12 about that but most of these are like single dose.  
13 It is a placebo controlled trial but it is a  
14 single dose or it is multiple doses and it won't  
15 go on terribly long, those studies. They might be  
16 two week studies, four week studies just to get an  
17 idea. Because if there is some terrible adverse  
18 event with a new trial it will probably show up  
19 right away. You don't know, you don't have  
20 equipoise because you do trial work. You don't  
21 know if the new therapy really is better. It may  
22 have been given in an animal model if you're lucky

1 and you know something about it but it may not.  
2 There's kind of internet chatter of this is a  
3 great drug. The quickest way to licensure is to a  
4 double blind prospective controlled trial. That  
5 gets you the most data in the shortest time. If  
6 you randomize from the first participant in a  
7 trial, you'll get that data even sooner. It is a  
8 hard undertaking.

9 I know there was recently an approved  
10 therapy for spinal muscular atrophy. I know the  
11 community thought long and hard about doing a gold  
12 standard trial but that's what they decided to do.  
13 The families volunteered to be in a placebo arm.  
14 That trial was cut short. It was scheduled for  
15 140 people. It was analyzed with 85 people. We  
16 did our review in about three months. It just  
17 truncated the process dramatically because it had  
18 a good effect. So, if you can get to that, I  
19 think that's what you should aim for.

20 MS. LIPSCOMB: Okay we are getting close  
21 on time so let's go ahead and get these next  
22 questions. They are really centering on this

1 conversation that we had already. The next one  
2 is, what reasons would influence your decision for  
3 the study. This is exactly what you were talking  
4 about. Keeping in mind that to participate in some  
5 trials you might need to temporarily discontinue  
6 your current treatment or receive a placebo for a  
7 period. So, this is given everybody a chance to  
8 have that conversation. These are the reasons you  
9 would do this. My current treatment causes side  
10 effects, you think your condition is well  
11 controlled and discontinuation of my current  
12 treatment will not result in occurrence of new  
13 attacks so I'm willing to participate or I think  
14 my condition is well controlled but I'm willing to  
15 participate as long as I can receive proper  
16 treatment from an FDA approved product, should  
17 attacks occur. We'll give you a minute to answer  
18 this and then we have three questions we'll do at  
19 once and summarize. So, it seems like as long as  
20 you can get some treatment you'd be willing to do  
21 this. The next question is, so newer treatments  
22 are being developed all the time and many gene



1       therapies hold promise. It's extremely important  
2       to know how you're thinking about the benefits and  
3       the risk. So, even if there's the treatment might  
4       result in a cure but carry a small risk for a  
5       serious side effect such as cancer, would you be  
6       willing to participate.

7               MS. PERRY: We can fix HAE.

8               MS. LIPSCOMB: Point taken. So, what  
9       about the web?

10              MR. PIERCE: So, the most popular choice  
11       was maybe followed by no. 10 percent of  
12       respondents said yes.

13              MS. LIPSCOMB: Okay. Let's go to the  
14       next question. Would you be willing -- so for  
15       rare disorders including genetic, it's important  
16       to collect data to better understand the natural  
17       history. So, in these kinds of clinical trials,  
18       you won't be getting any particular treatment,  
19       they're just going to kind of follow the monitor  
20       you over time. Would you participate in this kind  
21       of study.

22              MS. FOX: You can continue?

1 MS. LIPSCOMB: Yes. They're really  
2 checking you on your treatment so yes or no. Let's  
3 go ahead and close that. So, most of you would do  
4 natural history.

5 MS. LONG: Can I just say, Donna, the US  
6 HAEA has a scientific registry which does this  
7 exact thing. So, it may account a little bit for  
8 the 100 percent but this is something that we  
9 value as well as very important to trace the  
10 history of these new medications as well within  
11 our patients and the effect on the quality of  
12 life.

13 MS. LIPSCOMB: Okay thank you. I think  
14 we've talked a lot about clinical trials. Does  
15 anybody want to make sure that their voice is  
16 heard in how you think about clinical trials,  
17 whether you participate?

18 MR. WILLIAMSON: I feel that as a  
19 community we've had access to medication for such  
20 a short time, most of us do remember what the dark  
21 ages were like. Therefore, a lot of us don't want  
22 to be complacent in our treatment and a lot of us

1 still want to strive for better treatment, not  
2 only for ourselves but for our children because we  
3 haven't had access to treatment that long.

4 MS. KLINGER: I just want to speak, this  
5 is Lydia, from my professional side of the coin.  
6 I've been working with clinical trials  
7 administration for about almost two years now.  
8 I've been in an academic medical center for 11  
9 years. I think a part from the patient side of  
10 the coin, the regulatory and administrative burden  
11 of getting clinical trials started, which I'm sure  
12 you guys hear about all the time, actually deters  
13 physicians from even becoming researchers. So, I  
14 think that we certainly need to do a good job as  
15 patients of advocating for ourselves and letting  
16 our providers know what risks we are willing to  
17 accept. I remember seeing the inclusion exclusion  
18 criteria for a study for Sjogren Syndrome recently  
19 where part of the criteria was that you couldn't  
20 have ever taken a biologic treatment which pretty  
21 much excludes everyone with that disease in a lot  
22 of cases. So, I think that from the FDA

1 perspective, just considering, and you guys  
2 probably already do, but some leniency for  
3 diseases like ours where while we don't want to  
4 get cancer, I'm okay with hearing that I may feel  
5 nauseated because it is probably not going to be  
6 as bad as the nausea I experience when I'm having  
7 an abdominal attack. I'm okay with understanding  
8 that every clinical trial has some risk of a  
9 serious adverse event if I have a physician or  
10 researcher who can really explain what that means.  
11 All those drug commercials now with the long, long  
12 list of things that happen to a fraction of a  
13 percentage of people in the study. I think those  
14 are important things to add when you're asking  
15 questions like, would you be willing to take on  
16 the risk of getting cancer. Well, what is small.  
17 If it's a 5 percent risk, well no. But is it's a  
18 half of a percent, maybe I would. Just kind of  
19 considering those things when you guys are  
20 reviewing new trials as well.

21 MS. BOMAR: Back in 2005, I had reached  
22 such a low end that I was willing to do anything.

1           That's when the  
2                           (inaudible) trial which was the  
3                           first in a long while which has  
4                           turned out to be Cinryze, opened  
5                           up. They told me the good news  
6                           after I went there for two weeks to  
7                           qualify that I was sick enough to  
8                           be in their study. I had never  
9                           been so happy in my whole life.  
10                          So, that lasted almost three and a  
11                          half years and it was a double  
12                          blind. I kissed the ground that  
13                          they walked on because Cinryze  
14                          changed my life absolutely. Over  
15                          the years, and I have been on it  
16                          since, over the years I have been  
17                          asked by various people would I be  
18                          willing to become part of another  
19                          trial. I would have had to have  
20                          given up Cinryze. I was not  
21                          willing to do that. I finally had  
22                          a quality of life and I wasn't

1                   going to give up a known for an  
2                   unknown. If it ain't broke, don't  
3                   fix it. Cinryze, who knows what  
4                   the production of it is and I'm  
5                   waiting for Haegarda. There may be  
6                   something that will be a  
7                   possibility and I will still have  
8                   to think about that very carefully.

9                   The other thing that I learned in  
10                  changing from Cinryze to Haegarda is an insurance  
11                  situation which really stunned me. Because as  
12                  expensive as all these medications are, I'm on  
13                  Medicare with a Part D. So, I was walking out  
14                  with thousands of dollars' worth of medicine every  
15                  month with no copay. Well, when I got a phone  
16                  call that said, oh by the way dear old person,  
17                  you're at the donut hole and now for the first  
18                  month you'll have to pay \$2000 and then the second  
19                  month you have to pay \$5000, I went whoa. Who can  
20                  cough that up. Well, obviously there is  
21                  assistance out there and I have pursued that and  
22                  so we're on the road to do that. Which then

1 brings me around to, we are in Washington, D.C.  
2 Congress is once again going to be messing with  
3 our preexisting conditions along with other  
4 things. I wonder, I do question, has anyone in  
5 Congress ever had a chronic illness? Has anybody  
6 there been sick? Does anybody know anybody who  
7 has been sick because once you have, you wouldn't  
8 feel the way a lot of people do. My cry is for  
9 people to do something about that and to press  
10 people that we exist and we have preexisting and  
11 some people are born with preexisting, there is  
12 nothing we can do about that. You can't be taking  
13 our insurance away from us or our help away from  
14 us.

15 The other thing is, I did want to ask,  
16 this is the first time Cinryze has been in a  
17 shortage or manufacturing issue. Does anyone have  
18 any kind of control or pressure over these kinds  
19 of pharma companies to make sure that there is  
20 regular supply or are we just at the mercy of this  
21 situation because it is really a frightening  
22 prospect for all of us sitting in this room.

1 MS. LIPSCOMB: Last comment and then  
2 we'll see if we can address an issue.

3 MR. EDWARDS: I'm Miles. One of the  
4 things I wanted to say about being able to get a  
5 hold of the drugs and get it properly, we've had  
6 drugs shipped to us that were supposed to be  
7 refrigerated that were not refrigerated. We've  
8 had wrong doses, we've had the doses  
9 mistranslated. A lot of the pharmaceutical  
10 companies do not know how to supply correctly.  
11 Personally, for my wife, I had to go up against  
12 the general counsel of a major drug provider and  
13 the general counsel of a major insurance company  
14 just to be able to get the proper medication for  
15 my wife. That is our only recourse that I've seen  
16 at this point that we have and if you don't have  
17 what it takes to stand up against general  
18 counsels than you're doomed. I don't know how  
19 many people have that strength.

20 MS. LIPSCOMB: Thank you very much. I  
21 think this is one more chance to ask the panel if  
22 you have any questions. Right now, we're a little



1 behind. We're going to do the public comment  
2 period and we have four speakers. They'll be  
3 doing about five minutes each and then we'll kind  
4 of close up.

5 MS. WARREN-HENDERSON: Good afternoon,  
6 everyone. For the transcriptionist, I'm Lonnie  
7 Warren-Henderson. First speaker, Paula Busse, Mt.  
8 Zion Hospital.

9 Dr. BUSSE: Hi, my name is Paula. As I  
10 mentioned before, I take care of a large group of  
11 patients with hereditary angioedema which I feel  
12 very fortunate too. One thing that we've been  
13 talking about is the designs of the clinical  
14 trials. It does bring a really good point up  
15 about the use of placebo and some of the designs.  
16 I don't feel right asking my patients to  
17 participate in trials if they -- I don't want them  
18 to feel obligated to me to come off of a  
19 medication. I understand some patients will do  
20 that because they want to get better therapies but  
21 it puts me in a bind and that's not good for the  
22 community of patients with HAE. If there is some

1 way that we can design better trials or formats  
2 using somewhat of historical data on patients or  
3 have a guarantee that we have crossover studies  
4 where all patients get medications. I know you  
5 have to show that the drugs work and I understand  
6 that, the reason for placebo but it really makes  
7 it difficult. Part of the goal for HAE therapy is  
8 to have patients have medications that can be  
9 given easily and conveniently without the use of  
10 injections and really to have patients maintain a  
11 good quality of life. I would just like to put a  
12 plug in for easier designs for patients to  
13 participate in trials.

14 MS. WARREN-HENDERSON: Thank you.

15 Second speaker, Mark Riedl, University of  
16 California San Diego.

17 DR. RIEDL: Good afternoon. Thanks for  
18 the opportunity to say a few words. I'm Mark  
19 Riedl, I'm a physician at the University of  
20 California in San Diego where I work at the  
21 angioedema center there with my colleagues Dr.  
22 Christiansen and Dr. Zuraw. A couple of quick

1       thank yous. First, I want to thank all of the  
2       participants here, the patients and their  
3       families. I hear these stories, I've heard  
4       hundreds of these stories and the good news is you  
5       never get accustomed to hearing these things. We  
6       should never become accustomed to hearing what you  
7       all go through. It is just a very poignant  
8       reminder of why we in healthcare do what we do  
9       regardless of the condition. We need to continue  
10      to work as hard as we can to prevent suffering and  
11      prevent these conditions from derailing people's  
12      lives. So, thank you for sharing your stories.  
13      Also, thanks to the FDA for this opportunity. It  
14      is actually very encouraging to know that you all  
15      are engaged and listening to patients. You have a  
16      tough job and I think it's very important that  
17      you're here from the people that are affected as  
18      to how this affects their lives.

19                I'll be brief but three quick points and  
20      you've heard all of these already today but I just  
21      wanted to punctuate what I see from my chair in  
22      taking care of a very large group of people with

1       HAE. The first is that while we've made a lot of  
2       progress in the last several years, we now have  
3       medications that have been shown to be effective  
4       and safe. We have not reached the finish line and  
5       I actually think we have a lot of work to do to  
6       make this, what I like it to be, which is a very  
7       quiet, predictable chronic condition. I think a  
8       lot of the stories I heard today show that. This  
9       is far from predictable so far. It is still very  
10      unpredictable and very troubling and disabling to  
11      a lot of people. So, pursuing medicines that will  
12      lend that predictability to this condition, that's  
13      sort of the holy grail in my regard. We haven't  
14      reached that point so we have work yet to do with  
15      developing medications.

16                The second point that you heard about is  
17      variability. It's absolutely true as you heard  
18      from some people that we do see individual  
19      variability to these medications. So, while big  
20      studies are great to show that these drugs work  
21      generally for a group of people, there is a lot of  
22      variance and one of our struggles has been trial

1 and error of figuring out which medicine works  
2 best for each person. I think Tony or somebody  
3 mentioned precision medicine and we've had an  
4 interest in precision medicine. It takes funding  
5 to do those sorts of studies but we're hopeful  
6 that pharmacogenomic studies will be better at  
7 determining what works best for each person.

8 Because of that, we need a toolbox of choices and  
9 while we have some now we could use more, in turn,  
10 because we still have patients that are non-  
11 responders or have bad side effects from some of  
12 the medications.

13 The third point is the pediatric issue.  
14 We really need more access to medications for  
15 children. We all recognize the challenges of  
16 doing pediatric studies and it is a vulnerable  
17 population that we don't want to cause any harm.  
18 But we really have very limited options for  
19 children right now. As you heard some of the  
20 stories, one of them was severely affected groups  
21 of people and they have severe symptoms. Just a  
22 plea to the FDA, I know you're working on it, I

1 know the companies are working on it but whatever  
2 we can do to accelerate treatments for children  
3 would be of great benefit. Thanks very much.

4 MS. WARREN-HENDERSON: Thank you. The  
5 third speaker is Sandra Christiansen, also UCSD.

6 DR. CHRITIANSEN: I may be a little less  
7 eloquent than my predecessor and colleague, Dr.  
8 Riedl. I would like to first mention that there is  
9 really nothing to add to the heartfelt stories  
10 that people have shared with us. As was  
11 mentioned, they still tug at your heart and we  
12 have work to do. The career that I've had has  
13 spanned over 30 years in HAE so I remember when we  
14 had nothing. We didn't even know why people  
15 swelled and it has been very gratifying to watch  
16 the arc and see what we have now and we're very  
17 grateful as our the patients. I think we owe a  
18 testament to the patients that have participated,  
19 the pharmaceutical industries that have helped  
20 develop these drugs and the science and the FDA  
21 and I thank all of you.

22 Mark made a point that I was wanting to

1 emphasize which we do have a current unmet need in  
2 addition to our wish for a brighter future, which  
3 is children. We have a single approved therapy for  
4 all ages and it is intravenous plasma derive C1  
5 inhibitor. It's not a special qualification but  
6 I'm also a mother. I can't imagine if one of my  
7 daughters was suffering and in pain and the only  
8 thing I had to do was start an IV. There is data  
9 which, I believe, has even been presented to the  
10 FDA, on trials in children down to the age of two,  
11 showing safety of a sub Q treatment for acute  
12 relief, icatibant. We've heard the troubles  
13 with clinical trials and ethical issues and I  
14 would not wish perfect to be the enemy of the  
15 good. I would hope that the FDA would consider,  
16 for this country, that it would be appropriate to  
17 approve for children what is going to be approved  
18 for children in Europe. We also have no  
19 prophylactic therapy that has been approved for  
20 children. We have safety data, we know things  
21 that work and as Dr. Busse was saying, it is a  
22 huge, huge burden to get drugs approved for

1 individuals. If there is no indication, it is  
2 almost a full time job battling with third party  
3 payors. So, again low hanging fruit, data we  
4 have, safety we have, need we have, I would hope  
5 that people would really urgently consider this  
6 while we again, hope for more developments and  
7 more improvements. Thank you.

8 MS. WARREN-HENDERSON: Thank you. From  
9 fourth and last speaker, Bruce Zuraw, also UCSD.

10 DR. ZURAW: Thank you for the  
11 opportunity to speak and thank you to all the  
12 patients who told their stories today. I've been  
13 working in HAE since 1983 taking care of a lot of  
14 patients over that time. I feel like as I listen  
15 to your stories, I was reliving history. The pain  
16 that we all went through early on, the lack of  
17 treatment and the remarkable progress that has  
18 been made. Obviously, the FDA has been very  
19 important. Pharma has been tremendously important  
20 and we've come a long way. But as the stories  
21 also pointed out today, we're not there. And as  
22 my colleagues mentioned, there is still a lot of



1 problems, we're not at all happy. I recognize the  
2 progress but we're not going to stop where we're  
3 at.

4 Another issue that has come up  
5 repeatedly that we heard today was the trouble  
6 finding a physician who would listen, who knew how  
7 to treat the disease, knew how to diagnose the  
8 disease and how do we deal with that. I would  
9 like to make a plea and I know that the FDA has  
10 been good about this. As a physician investigator,  
11 I threw in my hat many years ago with the HAEA  
12 deciding that if there was one group that could  
13 get the word out that could tell patients where  
14 they needed to go, what they should be doing to  
15 get the right care, it was the patient advocacy  
16 group. I encourage you to continue to work  
17 closely with the HAEA. I think they are the  
18 honest broker in the room. That's the way that  
19 patients get to them through the website and get  
20 diagnosed and then get treated.

21 So, I'll make a couple of last quick  
22 points. The FDA appropriately is concerned with

1 unmet medical needs in deciding as you go through  
2 new drug applications how you gauge an unmet need.  
3 I think it's important to recognize that it's not  
4 just abdominal and laryngeal attacks that  
5 represent an unmet need. As we've heard today,  
6 hand, foot swelling, really puts people out of  
7 work, out of school, goes on often to involve the  
8 abdomen and throat if they weren't treated with on  
9 demand drugs. I think any attack has to be  
10 treated as a serious problem and should be  
11 recognized as such. And that as you think about  
12 the need for new and effective drugs, we really  
13 need to get people to the point where we're not  
14 having attacks at all before we can say that we've  
15 reached where we want to go.

16 My final point and philosophically, I  
17 think it's an important one and it doesn't come up  
18 very much in medicine. If we can simply replace  
19 C1 inhibitor or inhibit kallikrein or perhaps  
20 factor 12 adequately, we have a disease now that  
21 is life threatening that is very highly morbid  
22 that we could essentially completely control.

1 People would be totally normal if we could simply  
2 interrupt that one pathway. It's a real  
3 opportunity to do something that we almost never  
4 get to do in medicine which is to make people  
5 completely whole. I know it keeps me going in  
6 this field wanting to push forward and I hope the  
7 FDA realizes the opportunity that we have as we  
8 move towards the future. Again, I want to thank  
9 you for having this meeting and for listening to  
10 all of these stories all day. Thank you.

11 MS. LIPSCOMB: Thank you. Well, I can't  
12 thank you enough. We're going to invite Dr.  
13 Larissa Lapteva up here to summarize the meeting  
14 and she's actually going to say goodbye. But I'm  
15 not leaving here until I tell you how moved I was,  
16 how appreciative I was that you were able to tell  
17 me your stories and your experiences. I will be  
18 forever touched by what I've heard. Thank you so  
19 much I can't tell you how appreciative I am.

20 DR. LAPTEVA: Good afternoon. So, we  
21 have come to the concluding part of our meeting.  
22 It has been a day full of honest sharing,

1       compassionate understanding, vivid descriptions,  
2       moving stories and above all, hope for future  
3       treatments, for new therapies that can change the  
4       course of HAE more so than the currently available  
5       treatments.

6                On behalf of my colleagues, I would like  
7       to extend our appreciation to the participating  
8       patients and families, to all those who came here  
9       in person and those who participated with us  
10      online. We have learned and will continue  
11     learning a great deal from you. Today we heard  
12     about what patients and families care about, what  
13     worries people and what makes them feel better and  
14     what kind effects they would like to see from  
15     their treatments. In the next few minutes, I will  
16     try to summarize some of the issues that have been  
17     discussed.

18               During the first session, we heard about  
19     frequent delays in the diagnosis of HAE. Over 50  
20     percent of people who participated in our poll  
21     here in the room said that the time that took from  
22     the initial symptoms to the diagnosis was about

1           10 years or longer. By having meetings  
2           like the one we had today and by continuing the  
3           efforts of multiple stakeholders including  
4 healthcare providers and  
5 patient advocacy organizations,  
6 we hope to improve  
7           the recognition of this rare disease.

8                       We also heard from patients who have a  
9           family history of HAE, from patients who are  
10          adults and also from parents and siblings of  
11          children and adult patients who live with the  
12          condition. We heard about the unpredictability of  
13                       the attacks and how it actually is  
14          to live with this feeling of unpredictability, not  
15          knowing when an attack will come and what part of  
16          the body it will involve. We heard about the  
17          painful abdominal episodes that often require  
18          medical care, even intensive care to be treated to  
19          resolution. Many people mentioned the  
20          discomforting, painful and disfiguring attacks of  
21          different body parts that interfere with all  
22          activities of daily life, prevent going to work,

1 to school, prevent from doing any kinds of social  
2 activities. Many people are unable to care for  
3 themselves, for their children, feeling left out.  
4 We have also heard about the exacerbating effects  
5 of HAE on some activities that many of us who  
6 don't have the condition, may take for granted  
7 which may range from exercising or doing some  
8 repetitive motions to getting dental work done,  
9 or gynecological exams, to giving birth to a child  
10 and sometimes simply being excited, or happy, or  
11 stressed about something.

12 A number of people commented about the  
13 influences of hormonal background, particularly in  
14 female patients that often are experienced during  
15 the adolescent years as well as peri menopausal  
16 years. Depression, anxiety, fatigue, drug seeking  
17 accusations, and unnecessary surgeries remain a  
18 reality for the HAE community. Many people  
19 mentioned their greatest fear and their biggest  
20 concern which is the possibility of developing a  
21 laryngeal attack and not being able to treat it  
22 rapidly and affectively. Endotracheal intubations

1 and tracheostomies do remain not to be an uncommon  
2 practice. We heard about the life changing  
3 experiences with the availability of treatments  
4 for HAE. And even more so, the vital importance  
5 of not only attack treatments but also  
6 prophylactic treatments.

7 Over 60 percent of folks who  
8 participated here in our poll in the room, do  
9 receive prophylactic treatments of different  
10 kinds. The importance and the place of prophylactic  
11 treatments cannot be overemphasized. They  
12 significantly improve the quality of life, they  
13 increase the time between attacks and, more  
14 importantly, provide peace of mind to  
15 patients and families.

16 In terms of product benefits, most of  
17 our poll participants indicated that in the new  
18 therapies, they look for both a reduction in  
19 attack frequency and attack severity. Although, I  
20 do recognize that that question really called for  
21 all answers to be yes. You would want to see a  
22 reduction in attack frequency and severity and the

1       rapidity in the response and the completeness of  
2       the response. Yet please also recognize that this  
3       information does help us to better guide product  
4       development. In addition to various sources of  
5               scientific information that we take into  
6               consideration, this helps us to better  
7       design future studies and select study endpoints.  
8       So, thank you for answering all of these different  
9       questions.

10               In terms of risk, people remain  
11       concerned about various side effects. Common side  
12       effects may not be as much of a concern. Only 7  
13       percent of people said that they would take them  
14       into consideration. Serious but uncommon side  
15       effects remain the concern. But again, the  
16       adverse effects as was mentioned by a number  
17       of participants, would need to be taken into  
18       consideration within the framework of the benefits  
19       that you would get from the treatments. So, we  
20       always take it as a benefit risk assessment.

21               From what we've heard, there is still a  
22       long way to the cure and to the complete control



1 and prevention of each and every attack that may  
2 occur in each individual. There is still a need  
3 for less invasive therapies, for therapies that  
4 take into consideration the hormonal background  
5 and hormonal changes that may occur in patients.

6 There are still issues with IV access, there are  
7 still issues with infections, so we do need better  
8 treatments, newer treatments, more helpful  
9 treatments.

10 There is still a need to observe long  
11 term effects of the current treatments and to  
12 develop newer treatments, not only for adults but  
13 also for children and to ensure smarter designs of  
14 future drug trials. These include  
15 methodologies that could help collect patient  
16 input and incorporate input of patients into the  
17 products' benefit risk assessment. Our polling  
18 questions results here in the room showed that  
19 about 65 percent of patients would like to  
20 participate in clinical trials. 100 percent of  
21 people would want to participate in observational  
22 studies.

1                   So, following this meeting, we will  
2           summarize the discussion and the lessons learned  
3           in the Voice of the Patient report which you've  
4 heard about, which we'll post online. While here at the  
5           FDA, we continue our efforts to facilitate the  
6           development of safe and effective new treatments,  
7           it is really the voice of patients that guides us  
8           in the right direction. Patient advocacy is very  
9           strong among the HAE community and today's meeting  
10          really would not have been the same without the  
11          tremendous support of the HAEA. On behalf of my  
12          colleagues, I would like to thank the association  
13          for always taking the proactive stance in  
14          supporting their community in many aspects: from  
15          distributing relevant information about the  
16          disease to patients and families, to promoting the  
17          development of new products, to providing  
18          substantive support to the community in times of  
19          product shortages and much more. Thank you for  
20          doing the great job that you do. The work of  
21          patient advocacy groups like yours remains of  
22          utmost importance to all of us.

1           I would like to thank everyone who  
2       helped to organize this meeting. It was really an  
3       effort coordinated across the FDA with  
4       participation from different centers and offices  
5           with the leading role of the Center for  
6       Biologics Evaluation and Research. And much  
7       appreciation should go to the office and the  
8       center leadership for their endorsing and  
9       very attentive support of not only this  
10      meeting but also many other collaborations related  
11      to patient advocacy and to incorporating patient  
12      input in developing new therapies.

13           Finally, I would like to thank all the  
14      participants of today's meeting. As healthcare  
15      professionals, researchers, industry partners, FDA  
16      staffers, regulators, we humbly learn from you,  
17      the patients, every day. And today's meeting is  
18      yet another testimony of how much you can tell us  
19      in order to help moving medical progress into the  
20      future. Thank you for that. Thank you and safe  
21      travels back home. We're adjourned.

22                           (Whereupon, at 2:50 p.m., the

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PROCEEDINGS were adjourned.)

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CERTIFICATE OF NOTARY PUBLIC

I, Carleton J. Anderson, III do hereby certify that the forgoing electronic file when originally transmitted was reduced to text at my direction; that said transcript is a true record of the proceedings therein referenced; that I am neither counsel for, related to, nor employed by any of the parties to the action in which these proceedings were taken; and, furthermore, that I am neither a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

/s/Carleton J. Anderson, III

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