UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PUBLIC MEETING ON PATIENT-FOCUSED DRUG DEVELOPMENT

FOR ALPHA-1 ANTITRYPSIN DEFICIENCY

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Silver Spring, Maryland

Tuesday, September 29, 2015

PARTICIPANTS:

Welcome

DONNA LIPSCOMB, Facilitator
Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research (CBER) FDA

Opening Remarks

GINETTE MICHAUD, M.D.
Deputy Director, Office of Blood Research and Review (OBRR)
CBER, FDA

Overview of FDA's Patient-Focused Drug Development Initiative

PUJITA VAIDYA, M.P.H.
Office of Strategic Programs
Center for Drug Evaluation and Research (CDER) FDA

Background on Alpha-1 Antitrypsin Deficiency

L. ROSS PIERCE, M.D.
Medical Officer, Division of Hematology Clinical Review
OBRR, CBER, FDA

Overview of Discussion Format

DONNA LIPSCOMB
Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research (CBER) FDA

Topic 1: The effects of Alpha-1 Antitrypsin Deficiency that matter most to you

PARTICIPANTS:

Presentation of Survey Data from the Alpha-1 Foundation

ELIZABETH JOHNSON
Alpha-1 Foundation

Large-Group Discussion: Topic 1

Afternoon Welcome

DONNA LIPSCOMB
Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research (CBER) FDA

Topic 2: Patients' perspectives on current approaches to treatments

Panel Discussion on Topic 2

Presentation of Survey Data from the Alpha-1 Foundation

GORDON CADWGAN
Alpha-1 Foundation

Large-Group Facilitated Discussion: Topic 2

Topic 3: Patient perspectives on participating in a clinical trial to study experimental treatments

Large-Group Facilitated Discussion: Topic 3

Presentation of Survey Data from the Alpha-1 Foundation

JOHN WALSH
Alpha-1 Foundation

PARTICIPANTS:

Open Public Comments

Closing Remarks

GINETTE MICHAUD, M.D.
Deputy Director, Office of Blood Research and Review (OBRR)
CBER, FDA

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themselves, but first I wanted to give you a few housekeeping rules. Our meeting is being recorded as well as transcribed and both the web -- both the web meeting and the transcription is going to be posted on our web so just keep that in mind when you're talking to us and only tell us things that you are okay with having public. We do have restrooms but they are a bit of a distance and they are located if you go out the back door, make a right, go down the hallway and then it's a little to the right. You'll find them there and there are water fountains there as well and there's a water fountain if you kind of go to the left here as well.

On your way down you might have noticed a kiosk. That's where if you did not bring your lunch we actually found out that you can preorder and I think a number of you have preordered your lunch so that will makes things much better because we have experienced some lines, so for those of you who have pre-ordered yeah. And it's simple like sandwiches and coffee but we are not

P R O C E E D I N G S

(9:00 a.m.)

MS. LIPSCOMB: Good morning everyone. Good morning, this is an overflow crowd and we are so excited to have everyone. If you are getting settled in we are going to get started and we ask that you do so. Hold on a minute. My name is Donna Lipscomb and we are happy to have you -- those of you who are in the room as well as everyone that's on the web. I'm with the office of communication outreach and the Center for Biologics Evaluation and Research and I'll be the facilitator for today's meeting. What that really means in real terms is if you are talking more than the allotted time I'm going to say, "Thank you so much for your information and we'll move on." Please not that that's really what my role is as timekeeper. But I thought facilitator had a nicer ring to it. Anyway your voice is extremely important to us and we are really looking forward to hearing what you have to say. I am going to give my colleagues a chance to introduce

going to have a break prior to lunch, so this is an informal meeting so if you need to get up and move around please do. We ask that you silence your cell phones. Um, but if there is something you need, please leave. We have two overflow rooms and we have a room that you can -- if you're tired and you need to kind of sit back and rest if you just go out and ask the people at the registration desk they'll direct you to those.

A reminder and I think you guys have probably -- this is probably just not necessary but the tables are reserved for the patients and their family and the caregivers. So if you are not one of those if you could please sit to the back or get to one of the overflow rooms so we have plenty of room. I think that's it for housekeeping. The Alpha One Foundation was nice enough to arrange to have an oxygen tank for refilling any of your tanks if you need to. It's right outside the door and I think that they can give you more information if you need it. So I think what we are going to do now is we are going

to look at the agenda for the day. I'm going to give you a high level overview because I used to be an eight grade social science teacher, so you know we don't go into a lot of detail. It's always part of the big picture.

My FDA colleagues are going to present a few presentations. And this is going to help set the context for our discussion today. We'll have opening remarks and then we'll hear about the initiative that brings us these patient focus meetings and then we'll actually have a presentation on the background of Alpha One and trypsin deficiency.

Following this I will provide you an overview of our discussion format. Now this public meeting is a little different than some of our others because the purpose is we want to have a conversation with you, but our part of the conversation really is going to be listening. We've got out listening ears on as one of my friends son used to say, "Click, click we've got them in listening mode" and that's really what

we're going to do, so we're -- very general questions we might be able to answer, but really this is to hear what you have to say and what your concerns are so we can use that to inform our decisions.

Now we will have an opportunity -- we're going to have three different topics that we are going to talk about. In the morning are the effects of Alpha One deficiency that matters most to you. We'll have some discussion questions around that then we'll have break for lunch and then this afternoon we'll talk about your perspectives on current approaches for treatment and then finally we'll talk about your perspectives on participating in a clinical trial. Throughout the sessions we are -- the Alpha One Foundation did have a survey which they are going to be presenting results to throughout the session so after the first set of remarks they'll be presenting and then after the second and so on.

Now as you can see we do have an open public comment period and this is the occasion for

those of you who want to speak or perhaps you had some off topic comments you wanted to make. We've outlined a lot of time for you. The sign up list is on the registration table, but there is only room for about 15 people to speak which will give everybody about two full minutes. I know that's a lot of time, but this is a first come, first serve opportunity so if you think you might be interested in seeing it or if you just want to make sure your voice is heard please go outside and sign up and we'll have our closing remarks.

So this is really exciting for us. I'm glad we're getting started and we're just going to kick it off now and I'm going to ask my colleagues to introduce themselves.

DR. MICHAUD: Good morning and welcome. My name is Ginette Michaud. I am the deputy director of the (inaudible) blood research and review and the center for biologics.

DR. PIERCE: Hello, I am Dr. Ross Pierce in the Division of Clinical -- in the Division of Hematology Review and the Office of Blood Research

and Review.

DR. MINTZ: Good morning, I'm Paul Mintz, I'm the Director of the Division of Hematology Clinical Review and the Office of Blood Research and Review at Sieber.

DR. GOLDSMITH: Good morning, my name is Jonathan Goldsmith. I am the Associate Director of the Rare Diseases Program and the Office of New Drugs and Seizure.

DR. SAHINER: Good morning, my name is Berkman Sahiner and I am a senior scientist with the office of Science and Engineering labs at the Center for Devices and Radiological Health.

DR. BONNA: Good morning, my name is Jim Bonna, from the office of orphan products development here at FDA.

DR. DURMOWICZ: Hi, I'm Tony Durmowicz and I'm from the division of pulmonary allergy and rheumatology products and now the Center for Drug Evaluation and Research.

MS. LIPSCOMB: Thank you guys. Thanks very much. Okay, first we are going to hear from

Dr. Ginette Michaud.

DR. MICHAUD: Good morning again and welcome to FDA. We're absolutely delighted to see the huge turnout this morning. The FDA's very pleased to host this patient focused drug development meeting on Alpha One and trypsin deficiency. Our goal today is to give patients and their caregivers the opportunity to share with us your experience with Alpha One anti-trypsin deficiency. We invite you to tell us about the symptoms that are a part of your daily life. The impacts of your disease on you and your family and your perspective on currently available treatments. This is an important meeting between the FDA and the patient community and so we are very happy to see the large turnout. We have approximately 250 participants here in the room as well as close to 600 individuals online who are joining by webcast.

I want to acknowledge you -- the patients, your families and caregivers and those who advocate on your behalf. We thank you for

your willingness to engage in today's conversation. I also want to recognize the participation of health care professionals and representatives from the pharmaceutical industry. You presence here today show your interest in directly hearing from patients. You may know that FDA is responsible for protecting public health by insuring the safety and effectiveness of human drugs and biological products. Also responsible for advancing public health -- we do this by helping to speed innovation and to make medicines and to approve medicines that are found to be safe and effective and while FDA does in itself develop new drugs and conduct clinical studies our role is to oversee and facilitate their development.

It's because of these responsibilities that we want to gather your perspectives on Alpha One and trypsin deficiency. We want to hear your thoughts on currently available therapies. We want to learn directly from you the patient, your family, your caregivers and your advocates. Your input will help us better understand the burden

that Alpha One places on you and your family. The ways that you best try to manage your disease. The side effects of your treatments and how your current treatments could be improved.

FDA has held several meetings like this one and I can say that at every meeting we learn from patient. We will consider your input when we advise manufacturers on the development of a new drug and on the design of their clinical studies. We will consider your perspectives when we assess the benefits of a new drug and its risks and your input will be helpful in identifying unmet needs or new ways to measure drugs effects in clinical studies. In the past few years FDA has hosted several patient focus drug development meetings on a variety of diseases and thanks to the participation of patients and caregivers such as yourselves we've learned a great deal about the burden of disease and gaps in the treatment of these diseases. Today it's your turn. I urge you to participate fully in today's conversation. This is your meeting. We are here to listen to

you, patients and caregivers because you have important information to convey and a very unique view on how your life has been changed by this disease? No one can better tell us about the benefits and shortcomings of treatments that exist today and so in closing I want to thank my colleagues at the FDA Center for Biologics Evaluation and Research any my colleagues at other centers at FDA -- the Center for Drugs, Evaluation and Research. The Center for Devices and Radiological Health and Colleagues from the Office of the Commissioner. All have helped in, um, offering their time and efforts to prepare for this meeting. I also want to recognize the Alpha-1 Foundation for helping us to reach out to you -- the patient community and for compiling the survey data that we will all hear about later today. And so in closing I wish you a very successful and productive meeting. Thank you.

(Applause)

MS. LIPSCOMB: Thank you, all right, now we're going to ask Pujita Vaidya, I had it

phonetically too. Sorry.

MS. VAIDYA: Hello everyone. I'd like to thank you all for coming today. I am Pujita Vaidya from the office of strategic programs in CBER. We are the office that leads the patient focused drug development initiative. This initiative helps to facilitate FDA dialogue with patients about what matters most to you. So people living with the disease have a direct stake in the outcomes of drug development. They also have a unique ability to contribute input that can inform drug development and evaluation. FDA recognizes a need for a more systematic way of gathering patient perspective on their condition and treatment options. This input helps inform the collective understanding of this therapeutic context of drug development which is important to our role as regulators and the role of developers and other throughout the drug development process.

So FDA's drug development initiative is part of FDA's commitments under the 5th authorization of the prescription drug user fee

act. As part of our commitment the Center for Drugs and the Center for Biologics are together convening a total of 24 meetings in a five year period. Each meeting focused on a specific disease area. These meetings are providing valuable information in their own right. They can also help advance a more systematic approach to gather this type of important patient input more broadly. So to determine the disease set for the five years FDA nominated candidates sought public input. With the public input and review division input FDA identified a set of 16 diseases for the first three years and then initiated another public process to identify an additional eight more diseases for the remaining fiscal years 2016 and 2017.

So here's a list of the meetings that are being conducted as part of the patient focused drug development initiative. Here are the meetings that have already been conducted and meetings still to be conducted. To determine the set -- of the meetings conducted to date we

estimate for each meeting that about 30 to 80 patients are patient representatives, have participated in person and about 100 to 300 people on the webcast, however from this meeting it might be higher now. So for the CBER meetings on the list they include Hemophilia A, B and other heritable bleeding disorders and there is one coming up in fiscal year '16 or '17 on hereditary angioedema.

And I do want to put a plug in as you see here that we do have a meeting scheduled for October 15 that CBER is leading on non-tuburculosis micro bacterial lung infections. So each meeting including the discussion questions is tailored depending on the specific condition aiming to elicit patient perspectives on patient's conditions and treatment approaches. In the process we consider unique characteristics of the disease context including the current state of drug development, the reviewed divisions specific interest and the needs of the patient population depending on FD's interest and current happenings

some meetings have focused on relevant current topics in drug development such as cure research in the case of RHIV meetings. And from these meetings we've definitely learned that patient involvement and participation is critical to the success of these meetings.

Each meeting results in the report that captures the patient input from the meeting in the participant's own words. This input by providing important patient context can support FDA staff as they conduct their benefit risk assessments for products under review, advise drug sponsors on their drug development program or identify opportunities for further discussion. We also believe these meetings can have value for development more broadly. For example, by helping to identify areas of unmet medical need such as aspects of patient's condition that is not currently being addressed with current therapies. This input may also help developers as they identify or create tools used to measure the benefit of potential therapies. This is a topic

and in a little while Dr. Pierce will be talking giving a background on the disease area. And so we have seen that potential in these meetings help raise awareness within the patient community. I'd like to thank you all again for coming here today and now I'll hand it over to Donna, thank you.

MS. LIPSCOMB: And now we're going to here from Dr. Ross Pierce.

MR. PIERCE: Good morning, welcome. Um, it's a tradition at these meetings to present an overview of the condition being discussed but I recognize that I'm here with a room full of experts so please bare with me when I present information much of which you are already no doubt intimately familiar with. So Alpha-1 Antitrypsin deficiency also called Alpha-1 Proteinase Inhibitor deficiency or A-1PI deficiency what is it? An autosomal codominant genetic disorder with over 100 different genetic mutations. So what does that mean? The autosomal means that this effects both sexes and the co- dominant means that you inherit this from both parents and if you

inherit from a severe jean deficiency from one parent you will show a mild decrease in your serum and lung levels of alpha-1 antitrypsin but you have only a modest or slight absolute increase in the risk of emphysema over your lifetime whereas if you inherit the severe deficiency from both parents you will have a profoundly reduced level in the serum, in the blood and the lungs of this protein alpha-1 antitrypsin an enzyme and you'll have a substantially increased but not a guarantee of developing emphysema during your lifetime and you are at increased risk of developing liver disease associated with alpha-1 PI deficiency.

This condition has a highly variable clinical presentation not only because of the large number of mutations but even among patients who have the identical homozygous inherited condition from both parents. This severe reduction in the serum and lung levels -- many of them will go on to develop emphysema but not all. And liver disease is much less common than lung disease but still very important. So the

prevalence of AATD is between 60,000 and 120,000 individuals here in the United States that have this severe deficiency and this corresponds to about one to 2,000 to 5,000 live births. The vast majority of individuals with AATD go undiagnosed. Doctors in the United States still do not routinely screen patients with emphysema or chronic obstructive pulmonary disease for AATD but we hope that screening will continue to be more widely adopted so a typical experience of many of you no doubt has been that you had to go to a series of several different doctors complaining about your lung symptoms before you were diagnosed and the same thing can go with patients with liver abnormalities because it's not the first thing that doctors look for because of its comparative rarity. So what does this enzyme -- what does this protein do in the body?

Well it's a key inhibitor of another enzyme neutrophil elastase that break down proteins in lung tissue and can also break down proteins elsewhere in the body. In normal lungs

neutrophil elastase is present in very low levels but in the lungs of people who have this severe deficiency of this protein the neutrophil elastase is present at higher levels and exerts a more important effect. In addition alpha-

Anti-trypsin has a variety of anti-inflammatory properties but the exact importance of those in the body at this point is still incompletely understood. So what is the mechanism of alpha-1 anti-trypsin deficiency lung disease?

Well this comparative lack of alpha-1 anti-trypsin to inhibit neutrophil elastase results in a faster breakdown of lung tissue with the development of emphysema. So what is emphysema? It's a condition in which the peripheral air sacs that exchange carbon dioxide for oxygen -- the alveoli become enlarged as their walls are destroyed resulting in overinflated lungs, partial airway collapse with airflow obstruction. So this measurement that we call the FEV-1 -- the forced expiatory volume in one second

how much air you can -- what volume of air can you blow out from full inspiration -- trying to blow it out as fast as you can that becomes aggressively reduced as the condition progresses and a decline in lung density, mass per unit volume but I could also mention that during exacerbation or pneumonia the lung density may temporarily increase because of increased cells and water in the lungs.

What are symptoms of alpha-1 anti-trypsin deficiency? And again here I'm speaking to the choir. Emphysema form of pulmonary obstructive lung disease includes shortness of breath, reduced exercise tolerance, exacerbations resulting in increased shortness of breath, increased sputum production, increased puss content of the sputum. As may be in some but not all patients and at later stages of the condition there can be wasting and malnutrition can develop. So as I mentioned there's a highly variable clinical presentation with this condition and many individuals with severe AATD do not

develop emphysema during their lifetimes, but especially if you were a smoker you were at much higher risk and you may develop symptoms in your 30's or 40's or earlier and in nonsmokers developing your first symptoms in your 50's or 60's is not uncommon.

We estimate that roughly 15 percent of patients develop liver disease that's clinical overt with this condition. So what is the mechanism? Well the various genetic mutations -- particular the (inaudible) results in an abnormally folded or protein so these mutant molecules have a different shape and they accumulate in liver cells because of their altered shape causing liver inflammation, cell death, scarring and sometimes cirrhosis. And this chronic inflammation may also predispose to liver cancer in the case of liver disease due to AATD. In childhood infants may present with poor feeding, poor weight gain, hepatitis and jaundice. (Inaudible) symptoms such as failure to thrive and elevated liver enzymes in about half of affected

children. In children the majority recover and remain healthy throughout childhood but some do progress to cirrhosis and there is thought to be an increased risk of liver cancer.

In adults there is scant published literature on adult AATD liver disease. But the liver disease in adults may occur without a preceding history of having had childhood liver disease. It probably increases with advancing age and the presence of cirrhosis from I think autopsy series has been as high as 40 percent. Some of that would be unrecognized. The management of the liver disease of AATD -- there is no specific therapy that is approved unfortunately and this is something that we're very hopeful will be addressed in the future with specific therapy but for the moment standard supportive care for liver disease that has compromised liver function would include efforts to prevent or treat bleeding episodes because clotting becomes abnormal in severe liver disease, blood clotting. Abdominal fluid accumulation, itching, malnutrition, fat

soluble vitamin deficiency, infection, recognizing and addressing slowed growth, falling off your growth curves as a child and screening for and treatment of if necessary liver cancer.

So one wants to avoid smoking and second hand smoke and alcohol avoidance is especially important with more advanced liver disease. In the presence of severe liver compromise it may require -- it may be necessary to lower the doses or avoid some medicines which are predominantly broken down by the liver, such as Tylenol, acetaminophen, paracetamol. Screening for liver cancer with ultrasound is recommended every six to 12 months if scarring, cirrhosis or liver enzymes are elevated. But less than a quarter of patients with liver disease will require a liver transplant at some point during their lives. Now we'll turn to the management of lung disease due to AATD.

The cornerstone of therapy has been intravenous augmentation therapy administered weekly according to the FDA dosing guidelines. Inhaled Alpha-1 PI has been under development for

many years, but it still remains experimental, so the only way that people can get access to that is through clinical trials. Smoking avoidance, inhaled bronchodilator use and judicious use of corticosteroids if necessary particularly for exacerbations, administration of influenza and pneumococcal vaccination so that pneumonia vaccine, use of supplemental oxygen as needed. Pulmonary rehabilitation, management of acuity exacerbations as I mentioned can include brief courses of steroids, early antibiotic therapy and sometimes respirator support is necessary in the ICU.

In severe cases that have progressed lung transplantation is a therapeutic modality that we use. So what is the rationale for Alpha-1 PI augmentation therapy and why is it called augmentation therapy? Well it's a replacement therapy but in the recommended doses it does not bring the levels in your blood and lungs all the way up to normal, is it augments those levels from the low levels that you have to begin with.

The theory predicts that if you achieve a balance between the level of Alpha-1 anti-trypsin and the level of neutrophil elastase and you achieve this balance in the lung, the site of destruction of the lung tissue that you would slow down or stop the destruction of lung tissue so slow the progression of emphysema. But in currently recommended doses off approved Alpha-1 Proteinase inhibitors these may not be sufficient to completely inhibit excess neutrophil elastase that we see in patients with a severe deficiency compared to normals. What are some things that we know about Alpha-1 PI augmentation therapy? We do know that it increases the blood and lung levels of AATD and that's really how the indication reads in the package insert.

It's generally well tolerated in terms of side effects. It has a very low risk of viral transmission that really has not been a problem. It is inconvenient as we will hear from you requiring regular intravenous administration with package insert recommending weekly dosing. What

are some of the things that we don't know about Alpha-1 PI augmentation therapy? We do not know the optimal dose or the optimal blood level or level in the lungs to achieve given the burden of neutrophil elastase in affected patients lungs and the variability in that from patient to patient. We do not know the affects or understand the effects of this therapy at different stages of the lung disease whether it would be better to start treatment earlier for example. We do not have good information on the long term effects on lung function. This has been evaluated up to four years in duration but the jury is still out as to those effects. The trials have been of somewhat limited size here today. The effects of augmentation therapy on exacerbation frequency and severity, we need more information on that. So far there has not been an indication from randomized placebo control trials that augmentation therapy reduces the frequency of exacerbations, but the results have been inconsistent across different trials with

different products. And the symptoms on -- the effect of the symptoms on symptoms and of quality of life remain uncertain at this point as does the effect on mortality. So in 20 minutes there's a lot that I cannot go into about this condition, so please forgive me for my omissions, but I conclude this talk by saying that saying that Alpha-1 antitrypsin deficiency can be a serious disease characterized by progressive lung and/or liver disease that may ultimately require lung or liver transplantation or maybe both.

There is no specific treatment of liver disease for AATD. Augmentation therapy with Alpha-1 Proteinase inhibitor is the only specific therapy for lung disease but at currently recommended does its effect on symptoms, exacerbations, quality of life, exercise tolerance and mortality remain uncertain. Ongoing studies provide opportunities to determine whether higher doses of Alpha-1 PI administered intravenously and/or by inhalation may improve symptoms and function, actually make people able to do more

things and to feel better. Additional therapies need to be developed to address the unmet medical needs of patients with AATD, lung and liver disease and I'm really looking to industry to provide some excellent innovation in the future with respect to the types of therapies that we can expect to see for this condition. Thank you very much.

MS. LIPSCOMB: Thank you so much. Thanks to all of our panelists. We really appreciate you sharing and now what we are going to do is I'm going to go over kind of the format of our discussion. What we are going to do is we are going to start with -- the first topic we are going to start with are the effects of Alpha-1 antitrypsin deficiency and we are going to ask our panelists to really speak on this. The symptoms they experience that have the most impact, specific activities that they are unable to do, how the condition and symptoms have changed over time and what worries them most about the condition and then we'll come out now and ask

questions to you, the audience, those of you on the web, people on the phone, we'll get a full discussion going. Then we will talk about -- this afternoon we'll talk about current approaches to treatment. We'll have another panel come up and they are going to talk about what they're currently using to treat their conditions or the symptoms -- how these things work for them, what the disadvantages or complications of these treatments, how it's changed over time, what has not been improved and what has the most and positive impact. And then we are going to ask you to -- if you can wave a wand what would be your ideal treatment and what it would do for you. Again the panelists will talk about these, discuss them and then we are going to open the floor to you. Finally, we are going to talk about perspectives and participating in clinical trials and really what are the factors you consider in deciding whether or not you would participate.

Now the format is we are going to hear some panelist, it's going to set the foundation

for the discussion and each of our panelists reflect a wide range of people experiencing Alpha-1 and then we are going to have -- after each panel we are going to have -- after each of the first two panels the Alpha-1 Foundation will present survey data and then for the clinical trials one we will have our discussion and then they will present their survey data on that.

The purpose -- we are going to broaden our conversation to include you because we are going to build on the experience that the panel says to hear for you I'm going to fight you to raise your hand to respond and if you have something to say 20 times and we come to you 20 times repeat your name. And from the experience last time people on the web sometimes have trouble hearing so make sure you have that microphone close to your mouth. And then we are going to have polling questions. Now this is a lot of fun, it's kind of like Jeopardy, but we only have 100 of the clickers so normally I would have had one to show you because there would have been an

extra, if you could just keep that up, so that's what it looks like and the buttons have both numbers and letters and one of the things when we were testing it we found is that our questions asked ABCD, pick ABCD however sometimes we're saying how many times have you had to go to the hospital and A might say zero, B might say one. If you look at the clicker A actually says one so make sure you're looking -- you're responding by letter not number.

Now those of you on the web we have not forgotten you, we are actually going to be throwing polling questions up and you'll have a chance to vote. The two numbers won't be merged but we are going to go to the web and find out what you've responded. For those on the web to -- if you have a question with a lot of choices you might have to scroll down on your screens to make sure that you see all of the answers, but you'll be answering the same questions the people in the room have. Now some additional comments and we mean this we really do. The docket will open

until November 30th, you can share your experiences, if there is something that you heard today that you want to expand on you can send it to us, comments will be incorporated into our summary report and anyone is welcome to comment. For people -- in your packets you'll see that this website gives you a click now button where you can talk. Now a little discussion about our ground rules, we encourage patients, caregivers and advocates to contribute to the dialogue. We're really here to listen. We're going to focus on symptoms and treatments so that's really what our questions are going to be. So if I find that your topic might be a little off topic as much as we'd like to hear it, we've got a room full of people, the web is packed, you guys have really represented and we want to make sure we hear everything. So if it's a little off topic I'm probably going to suggest that you either submit open public comments to the docket.

A reminder to that the views today expressed are personal and we respect everyone's

opinion and so respect for one another is paramount, we ask that if someone is talking don't talk over them, don't interrupt them and finally I think that's it. I'm going to ask the first set of panelists, if they could start making their way up to the podium, because we are going to actually start with some polling questions. So if the first set of panelists -- Roger, Jim, Richard, Henry and Charlotte could come up that would be great and -- so if those of you who have clickers go ahead and click. Do you live within the D.C. area? Are you outside the D.C. are, but within the U.S. or are you outside of the U.S.?

A little more explanation on the clicker, when it allows only one click. When you click it you'll see a response, the little LED light will light up and when that does you know that yours took and it just takes a little of time for it to come up.

If you are on the web you should have that opportunity as well. And although people are still polling we ask that if you haven't had a

chance yet to vote do it right now because we are going to close it now. So if you didn't get a chance, it's okay. This is not scientific. We are not using these results, they don't -- in any papers. All they are are a springboard for us to use. Well not surprisingly the majority of people here outside the D.C. area but within the U.S. but we do have 8 percent of you who came from outside the U.S. so thanks so much. We really appreciate you coming. What are the web results? Do we have the -- is there anything different?

Well we'll come back to the second demographic on them, okay.

MR. CHAZIN: No the web results are the same basically than the people in the room.

MS. LIPSCOMB: Okay, thank you, thank you Howard. Next question. This is one of the great parts, you can check all that apply so again which of the following best describes your condition? And if you are a caregiver answer as the caregiver please or A is I have Alpha-1, but no active disease. B is have emphysema, C liver

disease, D both liver disease and emphysema and E I'm a family member/caregiver of someone. And so if you have to vote multiple, again, you wait for the light to just see the light, when it disappears you can vote again.

Super and we're going to give everybody -- we are going to stop now and well goodness 50 percent have emphysema and 32 are family members. So that's very interesting, thank you. What about the web? Do we have those results tallied? Okay, when they come up we'll come back to you on that. Finally, what is you or your loved ones age in years. This is that tricky one. This is zero to 12. At least it's a range so it's easier, so A is zero to 12, B 13 to 16, C 17 to 49, D 50 to 64 and E 65 or older. All right, we're going to stop there. Well we have a representation all around but heavy and my personal favorite 50 to 64 age bracket, let's lift it up there. Not that I'm seeing anything, but do we have responses from the...

MR. CHAZIN: Yes, magically we were the

same on the web. The 64 group.

MS. LIPSCOMB: It's magic, thank you so much Howard. And finally male or female. What's our demographic here? Okay, go ahead and see what our results here are.

Percent emphysema and liver disease, very close. It looks like a split so if there's a dance later everyone will have a partner. I'm glad to here. What about on the web? Do you have similar results?

MS. WITTEN: It's a little bit more females.

MS. LIPSCOMB: Okay, great, thank you. Thank you so much. Well that gives us a good idea of where we came from, who we are that's in the room and on the web and now we are going to hear from you guys and we're real excited. We're going to -- this is our first panel. They are going to introduce themselves when it starts. These are the questions that they are going to be responding to and Roger?

MR. MINTZ: My name is Roger.

Responding to the first question shortness of breath is now and has been for several years the most significant symptom that I have encountered. I was diagnosed at the age of 26 with COPD and with Alpha1 anti-deficiency at the age of 42. Now at 67 the progress has been slow and subtle. I no longer play golf because it's harder to breathe and tires me out quickly. I use oxygen at night and also sometimes during exercise activities. Managing travel with oxygen can be difficult and complicates air travel to the point where I don't want to fly commercially if I can avoid it.

I must also say that exacerbations are of great concern too. It is my understanding that any of these events will reduce lung capacity and over time become life threatening. That is why augmentation therapy is of critical concern to all Alphas. Losing the infused enzymes which I call my little soldiers means coming face to face with extended hospital stays and loss of lung function. I am currently at less than 30 percent and can't stand to lose what I have left.

All Alphas must protect themselves from flu, colds, humidity, extreme cold or heat, smoke, chemicals and the list goes on ad nauseam. For question two I miss my golf. Alpha's face many obstacles on a daily basis, stairs come to mind immediately, walking from parking lots through the malls and stores, carrying bags or luggage and travel. Whenever it becomes necessary to spend time in hotels, airports and aircraft, obstacles present themselves at every stage. Handling luggage throughout the trip, navigating through airports with oxygen equipment and dealing with the logistics of rental cars or transportation at the destination creates so many issues that makes staying at home an attractive option.

Item 3 - the symptoms get progressively worse over time. That is why avoiding exacerbations is so important to Alphas. I've been actively involved with an exercise regimen for over 30 years now and have come to the conclusion that a regular and intense workout with cardiovascular and resistance training is

essential to my general health. I have participated in a pulmonary rehabilitation program, classes on health diets and proper nutrition. I believe I can increase my longevity by actively participating in my own long term treatment of this genetic condition and in concert with each current or future medical treatment enjoy an active lifestyle within the limitations of this disease.

Item 4 -- the disease progression and knowing that one serious exacerbation with pneumonia can lead to serious consequences and even death. I'm concerned about the availability of healthcare options going forward. It appears that some treatments could be curtailed in the future for political convenience and funding constraints. I will spare you my rant over paying for everyone else's care over the years and now facing those issues myself without a sympathetic ear. I applaud your efforts to fast track medication innovations and the research for the cure for Alpha.

My sister Carol who is also a ZZ died on January 15th of this year as a result of Alpha-1. She was 68 years old, just a year older than I and in my never to be humble opinion she left this earth whimpering in submission and unable to breathe. I have looked through the open door at my own fate and have resolved to go out kicking and screaming. Just like Alpha quitting is not in my DNA and giving into my ultimate fate will not be of my own choosing.

I realize that my Alpha has a past that has taken its toll on my parents and siblings and it is the future of this disease that concerns me. My children and grandchildren will spend their lives dealing with all of these issues. Doctors have told me that Alpha-1 is a rare condition but I disagree. It will multiply with each generation and could become as common as diabetes and arthritis.

It would be my honor and privilege to be a part of this effort to find better treatments and eventually a cure for Alpha-1. I can't think

of a better legacy than to leave this life having fought to this end. Thank you for the opportunity to share my experience with you today and to be part of the search for a cure for Alphas everywhere. Thank you. (Applause).

MS. LIPSCOMB: Thank you so much. Tim?

MR. QUILL: Good morning, my name is Jim Quill and I have Alpha-1 anti-trypsin deficiency and I'd like to thank the FDA for giving me and other the opportunity to be here this morning to share our stories, however I can't tell my story without first telling the story of the family members who have succumbed to this condition. First and foremost was my mother at the age of 46 who passed away from Alpha-1 related lung disease. Then my brothers Bill and Jeff both 47 dying of Alpha-1 related lung and liver disease. Following them was my sister Ann -- Ann Marie -- who was 46 and at that young age of 46 she passed away from Alpha-1 lung disease complicated by diabetes. And then probably our most devastating loss was my nephew Jeff -- Jeffrey -- at the age of two who

passed away from Alpha-1 liver disease.

And that terrible tragedy of Jeffrey was almost repeated again when his sister Amy at the age of three was diagnosed with Alpha-1 related liver disease, but she was able to fortunately get a liver transplant and she's now living well and happy in her 20's. Through the extensive family history of Alpha-1 I was diagnosed in 1980. My two sons who I adore greatly are both MZ carriers of Alpha-1 and four of our five children -- grandchildren are diagnosed MZ as well. After my diagnosis in 1980 I became symptom in 1988, began augmentation therapy in 1992 and was placed on a lung transplant list in the year 2001. I received my gift of lung transplant in 2006. Post-transplant I've retired from my career in education due to the environmental risks that accompany anyone that works in an elementary school setting and for someone with a post-transplant I'm now more actively involved in Alpha-net and the Alpha-1 foundation.

It was not until 1988 that I experience

the initial symptoms of lung disease which included shortness of breath, wheezing, productive coughing, frequent exacerbations, exhaustion and anxiety and I'm sure many in the room can relate to those symptoms. These symptoms continued to worsen over time. I would say that shortness of breath, exhaustion and anxiety caused by the inability to breathe were perhaps the ones that had the most impact on my life. Prior to transplant and as a young father of two active sons and as an elementary school teacher and educator and principal my ability to participate in activities that active children like to do was severely impaired.

I did not want to deny my family or children of opportunities because of my condition and I certainly did not want to give up a career that I truly loved in the field of education, so I was determined to look for way to adapt so that I could be involved as much as possible, engaging in sports, going on family trips and vacations that required any type of rocking, climbing stairs, et

cetera not only presented challenges and careful planning, but also resulted in severe anxiety. Therefore I would often go ahead of time before I would even involve my family in those events or even tell them that I was planning them, to be sure that I could handle them so I wouldn't hold them back.

Each day had to be carefully planned and orchestrated. Routine household chores such as mowing the lawn, taking out the trash, completing small fix up jobs, even the simple task of changing a light bulb became too difficult or challenging to do. My wonderful wife and caregiver lovingly accepted these responsibilities as many spouses of Alphas often do. My condition continued to gradually worsen and in spite of augmentation therapy, pulmonary rehabilitation and participation in the disease management program. Eventually I required supplemental oxygen which presented additional challenges for the work place as well as for daily living.

The personal challenge of wearing oxygen

in public as a young father and as an educator was very difficult for me. I finally overcame that struggle by actually involving the children in my elementary school in a school wide assembly program where everybody share how they are unique and special. The children showed how they were dealing with their asthma, there diabetes and all of the other things that kids sometimes have to be challenged to and I shared my challenge of oxygen in the assembly setting and that was a break through day for me and the kids at the school. It was a great event. My condition finally reached a point where I needed a lung transplant and after five years on the waiting list I was given my gift of new life in 2006.

Although I had been given that gift I continued to be someone with Alpha-1 anti-trypsin deficiency. I continue on weekly infusions to keep my new lungs protected, I have ongoing concerns about the possibility of liver disease, organ rejection and the future health of my family and grandchildren who are affected by this

condition. In fact I'm very concerned about everybody here in the room and every Alpha out there. Although there are augmentation therapies available designed to halt the progression of lung disease and there are a multitude of therapies to help with shortness of breath, there is still a lot more to be done. It is my hope that the development of new therapies are supported and expedited. Alpha-1 liver disease needs our attention now. Currently there is basically no hope other than transplant for those who suffer from Alpha-1 liver disease and I have seen the effects of this disorder first hand with my family. It often happens unexpectedly and progresses rapidly. Drug development and quick approval of therapies needs to happen as soon as possible so families such as mine do not need to experience the anguish and hard ache of seeing those in the beginning and prime of their lives succumb to such a devastating disorder. Thank again for this opportunity to speak here today.

(Applause)

MS. LIPSCOMB: Thank you, Jim. Richard.

MR. JOHNSON: Hello, my name is Richard Johnson. My wife Sarah and I are the parents of Grace, 9 and Lucas, 7. They are both Alpha-1. I would like to thank you for the opportunity to be here today on behalf of all people affected by Alpha-1. I've been asked is this a kid disease and I will submit to you all these gentleman and lady at the front and everyone sitting in this room were Alpha-1 kids at one time, but were not diagnosed. It's an important day for all of us. Our lives changed seven and a half years ago when my youngest son Lucas had a complicated birth which lead him to being admitted to an NICU. They were very concerned about his bilirubin counts and in fact they sent him home saying it looks like his bilirubin is normalizing.

If it wasn't for Sarah and I's diligence in pushing the pediatricians to continually check the bilirubin I don't know if we'd ever have the diagnosis of Alpha-1. We went through many, many tests with Lucas before we identified Alpha-1

antitrypsin deficiency. In my travels in speaking about Alpha-1 all across the country I've met with parents that have had their children's livers biopsied, had had surgeries and it's really a shame because in this day and time we have a finger print blood test that will identify Alpha-1. The pediatric community needs to get on board and look for Alpha-1 by doing a simple blood test. When we identified Lucas as being Alpha-1 the doctors came to us and said that we all needed to be tested, so Sarah, myself and Grace did the blood test, sent it in to see if we were Alphas.

I'll never forget that day that Sarah came in from the mailbox and she had three envelopes. Two were mine and Sarah's and they were normal envelopes. Grace's was a big envelope. We just looked at each other and we just knew we had another Alpha-1. Excuse me. After Lucas was diagnosed we went through a lot of turmoil in our family, but we started reaching out to other family members to ask that they be tested. This is a very difficult process. A lot

of family members will say that's not in my family. That can't be coming from our family. But through identification of different carriers and different genetic testing I truly believe I had an uncle that dies in his early 50's from COPD. He was jaundiced his whole life and was diagnosed with COPD in his early 40's.

It's been a long road that we've traveled and it's a very difficult process to be worried about your kids and their liver disease. Lucas is not doing as well as Grace. Grace you would not even know has Alpa-1. Lucas, his liver enzymes run four to five times normal. He's seven years old now. He would be running around all over the room right now. But he has a failure to thrive. At seven years old the last appointment we went to he weighs 39 pounds and if you know the growth chart he is not even on the growth chart. The GI physician suggested that we may need to look at an NG tube to supplement his nutrition.

So we very much worry about Lucas' health. It is important that we continue our

liver research. I noticed that when we did a polling question only three percent of patients answered that they were liver affected. But I will tell you that all the pediatric patients are liver affected. One hundred percent of them. Because that's how we find them. One of the things I would like to stress is that a lot of times the infants become normalized with their liver enzymes. And I would stress to parents don't forget that your child has Alpha-1. Just because the liver enzymes have normalized you still have a patient or a child that's going to be a 30 or 40 year old one day and it's important that we find a cure for this disease. We're sitting in this room today and we want to find a cure. We don't want to find another augmentation. We don't want to find something that will just help deliver. We want to find a cure and I would submit to you that I want to be here one day at the next FDA meeting when we are talking about the approval of a cure for Alpha-1.

I've had 25 years of my career has been

in healthcare. I currently sell a cancer drug that patients 10 years ago would die from their disease -- chronic myeloid leukemia. They would have died from their disease in a year or two. Now those patients are taking a pill once a day and they probably are going to die of a heart attack or a car accident more than likely their CML. I know we can do this with Alpha-1 and I would like to just thank you for this opportunity and on behalf of Grace, Lucas and other parents that I've met in this room that are representing their children thank you for letting us participate.

MS. LIPSCOMB: Thank you so much for that. Henry?

MR. MOEHRING: Good morning. My name is Henry Moehring and I appreciate the opportunity to share my thoughts with you this morning. I'm 56 years old and have Alpha-1 antitrypsin deficiency. I'm a primary liver affected ZZ Alpha, however over the past few years started to develop some lung related symptoms. I was initially diagnosed

in 1997, after about two years of testing. I'm generally healthy and able to work. I'd like to start with the last question first. What worries me? Because I think that's the most important message and the message I want to leave you with is simple.

We need to find a cure for Alpha-1 ant-trypsin deficiency and we as a rare disease community are strongly committed to that mission. Until we find a cure we need treatments for the liver aspect of this disease and faster testing and drug approval process so I don't have to -- so we don't have to lose any more friends to this disease. In the next few minutes I will try to share a bit about my Alpha-1 experience and what matters to me as an Alpha. I don't experience any outward physical symptoms due to my liver disease. I have chronically elevated liver enzymes and some cerotic changes based on my last biopsy. In the past few years I've developed some mild bronchiectasis and COPD. I experience some shortness of breath climbing stairs or hills. I'm

sensitive to airborne chemicals and have a chronic, sometimes productive cough particularly in the mornings.

While frustrating my lung symptoms are mild and controlled with inhalers. I cannot walk as fast as most of my friend and I currently require no augmentation therapy. There's no cure for Alpha-1 antitrypsin deficiency. There's no treatment for the aspects of this disease, for the liver aspects of this disease. My father died of liver failure and I'm challenged by the thought of what my family's future will be.

Other than some lifestyle changes that I have made and continue to work on there's nothing clinically that I can do about my disease. This thought worries me however I have my faith and a strong support system to help me manage. I benefit from the most current information on Alpha-1 through the Maryland Alpha-1 support group and the Alpha-1 foundation. This is a genetic disease. I've passed the Z gene on to my 23 year old son. As a father I want the best for my son,

however I was the one that got to tell him he has a genetic deficiency. He is in MZ, currently has no symptoms, but the potential is there.

He will someday marry and have children and the gene will continue to be passed through our family. This too is an emotional burden but we are blessed that he remains healthy today. The fact that I live with a disease with no cure or treatment is a challenge. I've chosen to get involved with the Alpha-1 community and the Alpha-1 foundation and its mission to find a cure is my way of overcoming this challenge. Research must continue and Alphas understand that without research there will be no cure. I enrolled in the research registry and been part of three research programs in the past. I'm currently enrolled in the five year lineal liver study. I'm willing to take informed risks to move us toward a cure. My son and his future family are a significant part of my willingness to participate.

We need to find a cure for this disease so that no other generation has to face the

challenges of Alpha-1 anti- trypsin deficiency. My one concern is that we as a country seem to have unintentional barriers to research and drug testing. The approval process is lengthy and costly. Science, public safety and benefit to the Alpha-1 community must be reasonably balanced. I ask you today to review this process so that its promising tests and treatments are developed. They can move forward in this country without undue delays and barriers. In closing let me restate the message that I started with. It's simple. We need to find a cure for Alpha-1 anti-trypsin's deficiency and we as a rare disease community are strongly committed to that mission.

Until we find a cure we need treatments and tests for the liver aspect of this disease and a faster drug approval process so that we don't have to lose any more friends to Alpha-1. Thank you for the opportunity to participate in this panel today. I look forward to continual working relationship with FDA as we journey together to a cure. (Applause)

MS. LIPSCOMB: Thank you, Henry. John?

MR. WALSH: Hi, my name is John Walsh. And like everyone on the panel I'm pleased to be able to participate in this panel discussion to really share our experience with the effects of Alpha-1 antitrypsin deficiency that matter most to us. I applaud the agency for conducting this series of patient focused drug development meetings and including Alpha-

In this important process. The rare disease community struggles to get new treatments or deliver methods so the focus of the FDA on rare disease drug development is absolutely essential. The Alpha-1 community looks forward to how the FDA will use today's session to inform the next phase of drug development. And we want to participate in the next phase of patient focused drug development with the FDA because the end goal is to engage the patient -- to involve the patient.

To have a cure we need scientists, we need companies that are willing to spend the money to be able to develop therapies and we need the

FDA to help make that all happen and we need individuals with Alpha-1 antitrypsin deficiency to participate in clinical research and our community has proven that we can do just that. It's not about us without us.

I was symptomatic at the age of 35 when I got back from overseas and was diagnosed with allergy induced asthma. A lot of us with Alpha-1 -- about 73 percent present and are initially diagnosed with asthma and it takes years to get a proper -- complete diagnosis. When we turned about 40 years old in 1989 my twin brother, Fred, the good twin called me up and said that he had received information about what was going on with us because we compared notes. He had the same symptoms, same diagnosis of asthma and that he had been diagnosed with this genetic form of COP called Alpha-1 antitrypsin deficiency.

Without his diagnosis I probably would have gone another 10 years before I got diagnosed but I went right over to NIH where there was a study which was a Phase Four requirement by the

FDA on the first drug approved for Alpha-1 augmentation therapy and was able to get connected right away and get my diagnosis confirmed.

Without that Phase Four requirement I would probably be another ten years along before I was diagnosed. Without the FDA's vision and acceptance of approving augmentation therapy based on biochemical efficacy I don't think I'd be here today. I've been on augmentation therapy since 1993 and I'm at 90 milligrams per kilogram as opposed to 60 milligrams which is a package insert and Ross Pierce said earlier we need to know what dosage we should be on to be effectively treated. If I'm on 60 milligrams or less I'm sick every time I get on an aircraft. It's critically important that we address that question once and for all. I have to say my most severe symptom or my most obvious symptom is the shortness of breath on any exertion, even limited exertion and it's -- when you can't breathe nothing else matters. It's had a significant impact on my daily existence. My inability to keep up with peers, play sports,

do aggressive exercise, carry heavy objects and even walk and talk at the same time are a constant reminder of my condition.

I used to be a frequent exacerbate and I was sick four times a year, sometimes hospitalized and often times not able to continue to work until I started my regimen of Zithrmyacin Monday, Wednesday, Friday. That stopped. I haven't had an infection in 43 months. So we need to explore how to use our therapies and definitely be as vigilant as possible to be adherent to therapies that our physicians prescribe. Prior to the onset of progression of symptoms I lived a very active life and had very few limitations. My first traumatic breathing problem was when I was scuba diving in the Red Sea and I thought I was going to die.

And unfortunately many of us with Alpha-1 have that moment whether it's skiing on the slopes or whether it's a real severe exacerbation that turns into pneumonia and hospitalization. That triggers our awareness

about Alpha-1 and often times but not always unfortunately it leads to a diagnosis. Losing the ability to function continues to be a gradual transition for me. Not being able to play sports, an inability to carry heavy objects were the first activities that limited my shortness of breath. Walking up inclines such as stairs as Jim has shared and in airports. I travel a lot, it's really tough and you're looking at floor surfaces. These carpets aren't really friendly to somebody that has to use oxygen. I use supplemental oxygen when I sleep, when I exercise and when I fly or at altitude. Being able to manage the logistics of having supplemental oxygen as has already been shared has been a real challenge. Do you have enough oxygen, are you on the right liter flow, do you have enough batteries, are you going to be able to get oxygen when you go to your final destination? Carrying luggage is a struggle.

Having to have a CPAP which is related to my lung condition as well as a portable oxygen concentrator, as well as for a long period of time

a percussion ventilator make travel real challenging. So I just look to the day when I'm not going to be able to travel at all unless we get the technology, the community, the device manufacturers to focus on delivering more effective drug delivery systems and being able to connect that pulse oximetry of a level directly to our oxygen delivery devices so we're getting the right liter flow at the right time when we need it.

Seeing my twin brother Fred deteriorate is devastating. And losing so many friends to Alpha-1. It's a constant reminder that that's my future and that's why I think about. I think it's critically important that we all focus on what our families are going through in the Alpha-1 community has certainly created a support network of Alphas serving Alphas to support each other.

But I don't know if I can be as resilient as Freddy when I get to his stage. I still have 34 percent. He's less than half of me and he's a hero. He's my hero. I don't know

whether I'll be able to continue doing what he does day in and day out when I reach that level. My diagnosis and subsequent active involvement in the Alpha-1 community has really changed my life completely so the most impact of Alpha-1 in my life is that it's given me an opportunity to work with our Alpha-1 community and build a research program and make certain that we take care of each other and we're so proud that we have such a great presence here today and also on the internet.

We're not satisfied with status quo. We want the next generation of augmentation therapy to be easier to deliver, aerosol makes good sense to us, it hasn't happened yet. We want novel therapies that will stop the progression of lung disease, we need therapies for liver disease, we have companies that are developing that are in trial right now in Europe and Australia for liver therapies. We ask that the FDA really focus and work with us and we know they will on design the clinical trials for liver disease related to Alpha-1. So we need to do more and we need to do

it quicker and we need to accelerate the therapeutic development and approval for Alpha-Therapies. And I know I went over my time. My apologies.

(Applause).

MS. LIPSCOMB: Thank you so much. Thank you so much, Charlotte.

MS. MATTISON: And I'm supposed to follow this? Good morning, I'm very please to be here to represent the Alpha community. My name is Charlotte and I'm one of the faces of Alpha-1. I'm a 71 year old widow and I have two children. I was diagnoses approximately 28 years ago, we kind of play in the same pool at NIH, (inaudible) but I have to tell you about how I got diagnosed. I had chronic bronchitis for a number of years, went to my GP, he sent me to a pulmonologist because we couldn't figure out what was wrong. The pulmonologists ran some tests, called me back into his office and I sat there and he said, "Hi, Ms. Madison." I hate to inform you, but you have this rare disease called Alpha-1 antitrypsin

deficiency.

He informed me I had two to four years left to live and he advised me to go home and get my affairs in order. When I left his office one of my first thoughts was I'll never see my children get married and I may never see my grandchildren born. Needless to say today both of my children are married and I have nine beautiful grandchildren. (Applause) And a granddaughter who just got married so maybe I'll make a great grandma before time is out. I spend my life working 35 years in the prehospital medical field as a paramedic and in the emergency room of a local hospital. And I now teach at one of the local colleges in the premed area. Teaching them how to assess patients and how to decide what's wrong with them and boy do I push Alpha-1.

Without my oxygen on and I'm on oxygen 24/7, 365 supposedly when I behave myself my condition shows very little outward signs as was said before of a disability. However, if I walk through a door where someone has been smoking

outside at the designated smoking area where cigarette smoke lingers, at the perfume counter, oh yeah, walk through the flower shop. All of these. Anywhere fragrance is can cause a very bad spasm of the alveoli in my lungs and brings on a great shortness of breath crisis. Shopping is no longer my favorite hobby. For me as an Alpha the ability to fight off infections and inflammation is also a problem. However, four years ago I was put on the same therapy John was of erythromycin three times a week and I have been infection free for four years. Love it. I own a home with two acres of land and I used to work at home in my flower garden. Love it. Now when I cut my grass on my riding lawn mower I have to wear a mask and put my oxygen tank between my feet on the power motor.

Weeding my flower garden ain't going to happen. Many of you take it for granted -- well not the Alphas in the room -- but the FDA personnel -- may take that for granted. It is a total impossibility for me because I do not have

the stamina to do that.

A couple of things that impact my life. Emptying my washing machine and putting clothes into the dryer takes 10 minutes maybe. Not me. I take 20. Then I have to rest and catch my breath for 10 more minutes. Walking up hills, carrying groceries, picking up my grandchildren, attending family functions, all of these are impacted by my lack of breath due to my Alpha-1 condition. I want to participate in all of the family functions and I want to participate in the foundation functions but sometimes the endurance that I need is not there. When one uses oxygen as I do my ability does become a major problem. The green tanks and I'm not going to repeat the travel stuff. Been there, done that.

The green tanks are very heavy. We can't anything and then they hand us a tank that weighs more than a bag of groceries. Liquid oxygen is lighter and lasts longer, but because it is more expensive it is not always available either due to insurance reimbursement issues or

financial issues within the family. For those of us with Alpha-1 stress -- daily stress is a factor that impacts our life on a daily basis. Environmental issues, financial concerns, the lack of family nearby to assist with daily needs. My children live way away from me. All this adds to a level of anxiety for many of us. Travel is difficult, we mentioned it earlier. It can be a nightmare to travel by air. I just back this year from California. I won't tell you about my trip. Traveling by car also is difficult sometimes because you have a concentrator, your oxygen, your medication, your CPAP machine, whatever, along with the luggage you would take and this becomes a real chore. Like the other I tend to want to stay home, but I don't. Walking is even more difficult and presents more concerns for us as Alphas. We can't walk distances. I used to hate using my handicap sticker. And now I use it all the time because I can't walk that parking lot.

If I'm walking and there are stairs involved I don't walk that way. If there are

entrances that are not handicap accessible I can't get into some buildings sometimes. I have been known to push my way through, but that's me. Hills, inclines and other things really give us a problem. What worries me the most is the loss of my independence and inability to care for myself and to be an active participant with my family. The loss of the control of my choices for treatment that are limited either due to they are not there, insurance issues, et cetera. We need those preferred treatment to find a way to get this condition under control.

Financial considerations and limitations also may be put on us as Alphas because you know we are Alphas. We don't fit the box. We don't fit in the box. To sum it up we need early diagnosis to give us a chance for lifestyle changes so that we can elongate our years that are good. We need physician education about the current knowledge we have of Alpha-1 and the current treatments that are available.

We need better research guidelines and

avenues of access to the new treatments that are coming out. This is going to help all of us to stay healthy and become a benefit to society and to our families. My real hope is that we can come together and fix this for my children, for my grandchildren, all of your children and grandchildren and the future generations to give them a better quality of life and the ability to be beautiful, good, invaluable citizens in our community. Thank you. (Applause)

MS. LIPSCOMB: Thank you so much for sharing. I think our panelists did a great job of sharing their experiences. Let's give them another round of applause. Thank you so much Liz Johnson. She's going to present the first part of the survey results.

MS. JOHNSON: Good morning, can you hear me? Thanks. So I want to introduce myself. I'm a lung infected Alpha and the Foundation asked me to present some of the results of the survey that many of you have participated in. If you haven't it's still going to be on the foundation web site

for another couple of years. Not years, weeks. The survey went out to the community on August 11th and there have been over 1,400 responses so far. And the foundation will still be accepting more surveys for the next couple of weeks. So back to the survey, what we have so far in terms of demographics.

Eighty six percent of the people are diagnosed as Alphas. Ninety percent are caregivers. And six percent are parents with children of Alpha-1. Eighty percent are lung affected, six are liver affected and 14 are both liver and lung affected. As we know Alpha-1 is a disease that can (inaudible) at any time. The survey reflects experiences of Alphas from six week to 87 years old. Nine percent of the respondents were from birth to 30 years old. Forty five percent from 31 to 50 years old. And another 45 percent are 50 and older. For the lung affected alphas they share what symptoms affected them most. Nearly 100 percent reported shortness of breath during daily activities. Thirty eight

percent reported shortness of breath at rest having a significant or extremely significant effect on their lives.

And here's some of the things that they said. Even moderate physical activity like vacuuming the house makes me take deep measured breaths as if I was doing aerobic activity. Simple things, like dressing and washing myself. Walking, bending down to tie my shoe, getting out of bed is a chore most of the time because of shortness of breath. Another person added that just unloading the groceries causes me shortness of breath. A grandparent said that shortness of breath impacted her plan with her granddaughter. Another said, "When you are an Alpha at some point your loss of lung function -- taking care of yourself becomes a full time job. In my case I could no longer do any of the things I once cherished, but rather than focusing on what I can't do, now I focus on what I'm still able to do."

Liver affected Alphas report that 71

percent have abdominal pain and 69 have abdominal swelling. Some of those people said my liver symptoms include enlarged spleen and resulting low platelet count. I currently have fluid retention and abdominal swelling and shortness of breath. I have been told I need further liver evaluation as I've had continuous right upper quadrant pain for years without relief or change. One person indicated that "with regard to liver symptoms tests revealed significant fibrosis. Some radiologists see early cirrhosis. I understand that I am at significant risk for liver cancer and that's my major concern. I wasn't aware of the seriousness of the liver disease of Alpha-1 until I was told I need a liver transplant. Also my lung function is only 40 percent."

A parent of a child with Alpha-1 who was diagnosed shortly after birth said as a parent I was devastated that I might lose my baby. It was a very scary time. Hospitalizations have a serious impact on all Alphas -- preaching to the choir. Seventy-three percent of all Alphas have

been hospitalized particularly before being diagnosed or during treatment and in addition to the stress and the health impacts on these individuals and their families, time off from work for patients and caregivers these costs also impact insurance and healthcare spending overall.

One patient reported, "Multiple heart and lung complications caused several misdiagnoses. It required constant short and long visits to the ED and hospitalization." As for social implications. They are serious. Seventy percent of the Alphas in the study reported experiencing bouts of depression and anxiety. One person said, "I no longer work at the level of my education and ability. My friendships have suffered because of the severity of my health. Another person said I have no life with this disease, since I was 36 and that's a shame. With reduced daily physical exercise and severe limitations on travel and vacation depression has entered my household. What is worse my watch our life together -- change our life dramatically?"

One caregiver expressed sorrow that she can't do many things with her husband anymore. The survey asked respondents about their concerns. The number one concern shown by nearly every respondent at 90 percent was a fear of other symptoms worsening and progressing. Many are waiting for the other shoe to drop. Parents are so worried about their children's futures. Here's some quotes from them. A 21 year old of one (inaudible) "I am so young, what if I need a lung transplant later on?" Another said, "Ultimately my biggest concern is the worsening of my condition to the point where it shortens my life. Will I die before reaching retirement age? What of my family?" Another said, "I feel like a ticking time bomb, not sure when the symptoms might show themselves or worsen. I try to stay as healthy and active as I can while I can."

Alphas have to be warriors everyday. So thank you very much. The discussion is coming up next and we can share our stories about living with Alpha-1. Thank you. (Applause)

MS. LIPSCOMB: Now I get to fulfill my fantasy of being a microphone holder. Usually at public meeting I start singing, but I've been forbidden to do this, so. I'm going to ask Chris to hold this. So at this point what we are going to do is -- can you go to the next line, we are going to start asking some questions, so go ahead and pick -- which of the following symptoms have a significant impact on you or your loved ones daily life? While everyone is voting, how many of you have heard at least some of your experience expressed in at least one of our panelists today. So that's nearly everyone. Give just a few more minutes to do. You can check all that apply. We'll give it just a little bit more time. If you are on the web you should have the same polling question. I know that not everyone has had a chance to vote but we'll go ahead and close it now. What are our results? They certainly may if someone wants to give them theirs. Shortness of breath is our number one, followed by chronic cough, and then if we look at our top three in

this group, anxiety or depression. What is the web?

MR. CHAZIN: On the web we have shortness of breath predominantly then we have chronic cough, production of phlegm and then we also have anxiety and depression and weight gain when taking steroids like prednisone. Those are the predominant ones.

MS. LIPSCOMB: Okay, I forget to add. We are going to ask the operator to open the phone lines and if we have time I'll take a call -- get results there. So if you have experienced multiple symptoms which symptoms has had the most impact on your life? Would someone like to share? Great, got two people here.

AUDIENCE VOICE: I would have to say shortness of breath has definitely been a huge impact on my life, starting at the age of 35 I was no longer able to work, I was no longer able to do the activities that I enjoyed with my children, I was no longer able to be intimate with my partner. It's very sad to be old at a young age.

MS. LIPSCOMB: Thank you for that. You had something you wanted to say. Can I remind you to say your name?

MS. WICHER: Sure, I'm Dell Wicher and I'm from Alabama. I'm a pretty healthy Alpha. I'm very fortunate. I was diagnosed because of liver enzymes being raised, but I'm in pretty good shape, but I have bronchiectasis so for me even though I don't have to be on augmentation therapy I don't have the shortness of breath -- I have the chronic cough and have had it for most of my life. So much so that my siblings say if they are in a Walmart and hear me cough they can tell it's me from way across the store. I get sick really frequently and I always have a very productive chronic cough that's very deep so like many people up there I have to take azithromycin three times a week to try to prevent exacerbations like that. Because also like them every time you are sick it chips away at your lung function so for me, you know, while I don't have the problems that many people do that constant chronic cough is a big one

for me.

MS. LIPSCOMB: Thank you so much. Anyone else want to speak?

MS. VARGAS-VILA: Hello, Judith Vargas Vila, I live in Concord, Massachusetts now. I cough a lot. When I was in university, I went to Queens University in Kingston, Southern Ontario. It was an old building and I coughed so much in the building that I could not sit in class. Quite often I had to get up because it disturbed the lectures and I would sit outside on a chair and do my work. I could not actually work in the library because at that point I didn't have oxygen. I was young and foolish and I had to borrow books and made a special arrangement with the librarian to be able to take them into a room that had no furniture but a desk and use them and then deliver them back and I couldn't take a lot of the older books home because the dust in the older books would start me coughing and I simply lost track.

I couldn't read, so this is something, this coughing means that I can't knit now. And I

can't do the fabric arts that I loved as well because there are always dust mites and dust involved. And I can't shop freely in stores either, because some stories have inadequate ventilation and sometimes the outgassing of plastics and material prevent people from walking through the whole stores and making their own choices.

Of course the internet has helped with all that, but nonetheless those of us who want to be present in their lives do suffer from this. Thank you.

MS. LIPSCOMB: Thank you. Okay, take one more comment and then we'll go to another topic.

AUDIENCE VOICE: I wanted to mention one thing about impact. You noticed on the panel only two individuals I believe mentioned their work. And the reason that most of us don't mention our work is that we have become unable to work and often times forced into disability. That was my situation that I worked for a large chemical

company. Spent 12 plus years getting my education and I could not take the chance of not doing a good job and losing my job, because back when I retired in 1996 I would not have been able to get another job. So I think that's one thing that has a serious impact on all Alpha's.

MS. LIPSCOMB: Thank you so much for sharing that. What are specific activities that are important to you that you cannot do at all or as well as you would like because of your condition?

MS. CHAKRAVORTY: Bonnie Chakravorty from Nashville Tennessee. One activity that I've had to give up completely is dancing. For many years, actually seven years I did flamenco dancing and that's totally off of my radar now. Although I do exercise I can no longer work -- exercise at the level that I previously did and this not only affects my physical wellbeing but also my emotional wellbeing in so far as dance was one of the ways that I expressed myself. I'm also unable to sing. I did sing and now that's a memory and

strange enough I can't get into verbal arguments with people. So I can't shout I just have to stand there. Thank you very much.

MS. LIPSCOMB: Thank you.

MR. STOKER: Robert Stoker, I'm from Derry, New Hampshire, lung infected. I'm one of the fortunate ones in that I had a transplant last year and I was down to 7 percent FEB1, still worked was really upset with the fact that I carried oxygen into an office. I worked for a drug company. Hey guys. I was on the other side and the dark side if you will, but that was one of the things that I lost, that I couldn't do anymore.

Even with the Americans with Disabilities act it's a joke. They say you can do this and you can petition all you want, but when push comes to shove they will always find a way to get rid of you. And they did shove but that was okay. That just meant I had more time with family, but the thing I miss most during my early years of lung disease was not being able to play

with my daughter. We'd go to the beach, we'd go on vacation, I was always the dad that sat back and watched mom play with the kid. I was the one that sat back while the uncles played with my daughter because every time I'd try to go out and play with her, I'd get her half way out, I'd throw her into the pool and I'd be gasping for air. So that's how it affected me, I missed out on those days. Now I can do it, but at 27 she's not real into daddy. You know? Now it's like dad help me move, dad help me do this. So that's what I missed and that's what I miss and knowing that I wasn't able to do a lot of the thing that I know many of us had to go through and that's one of the reasons we're here is to get that point across to you guys that something has got to be done. We can't just let this sit anymore, so.

MS. LIPSCOMB: Thank you. (Applause)

AUDIENCE VOICE: What I have missed is my childhood. I was diagnosed Alpha at 10 weeks old. I received a transplant when I was eight percent -- eight percent of my lung function. I

was so sick and at the time in '95 when I had my transplants they didn't have a good success rate in Boston, so they released my case. I went out to California and this is right in my elementary, right in my middle school age, I missed all my friends parties, functions, school events, field trips, I went to California, I got my transplant, I received three liver transplants within 21 days, I was in a coma and I had to learn how to walk again. I didn't know if I was going to be able to ride a bike or drive a car when I was older. Also, it has also impacted me in another way. My father who took care of me and my mom going through my transplants now needs a transplant himself. So I find myself yet again not having a young adulthood because my father is fading fast and I am now his PCA and I take care of him 24/7. So thank you for this opportunity.

MS. LIPSCOMB: Thank you for sharing. I know a lot of people in the room had raised their hand, but I want to give the web an opportunity. Did we hear -- is there any comments from the web?

MR. CHAZIN: We have some activities that people are also echoing from the room: Problems with dancing, mowing the lawn, walking outside, trouble traveling. Others have also echoed the issue about being forced on disability. So we are getting some of the same kind of comments on the web.

MS. LIPSCOMB: Okay, thank you. Operator, is there anybody on the phone that can talk to this?

OPERATOR: If you'd like to ask a question over the phone line, please press *1 now. We have some coming in, one moment.

MS. LIPSCOMB: Thank you. Hello?

OPERATOR: One moment, please, for the first question. We have a comment from Annie Garcia. Your line is open.

MS. GARCIA: Good morning to everyone and thank you very much for being there for those of us that couldn't make it. My name is Annie Garcia from Miami, Florida.

I didn't hear anyone, and maybe you

won't see me blush, talk about sex, but that is definitely one of the things that has gone away with the inability to breathe. It's not very romantic to be with an oxygen tank and let's put it up and let's put it down, and, oh, my god. (Laughter) So, to tell you the truth, the basic things that have been spoken are definitely something that I think that every Alpha here and who is not here today feels, as well.

The gentleman that mentioned a comment about the ADA, I couldn't agree more. I had a very high executive position for a very big company and I was relieved from my employment because of my oxygen tank bothered the upper echelons of the business. And no board room likes to see problems of that nature. No board room likes to see that.

And so with that, thank you very much for the opportunity and thank you for being there for us. (Applause)

MS. LIPSCOMB: Thank you so much. And I don't think I'm telling tales, but there was a lot

of nodding of heads, so I think you were speaking for a lot of people.

AUDIENCE VOICE: I am no longer able to mow my yard, do my gardening, shovel snow, or do exterior maintenance on my house because short of breath and so forth. So I've got to go through the hassle and expense of trying to find people to do those things for me. (Applause)

MS. LIPSCOMB: Thank you. Anybody else? We have time for one more. Let me get back there. Thank you.

MS. LAMERS: Hi. I can't believe I'm doing this. My name's Vanessa Lamers. My mom lives in Salem, Oregon. She just was listed last week for a liver transplant. She's very sick. And I just got married this past month. My husband is amazing, he helps take care of her, but she was not able to help at all with the wedding. And so if any of you have kids who got married or grandkids who got married and it's such an amazing process. It's great to be able to help and she couldn't help.

We planned our wedding for a year and a half, and she wanted to do so many things for us and make centerpieces and be there on the day and be there in the morning and be there when I put my dress on, and she couldn't. She was in her room until right before the ceremony and she was just exhausted the whole time. And her life echoes almost everything that everyone has said today, so thank you.

(Applause)

MS. LIPSCOMB: Thank you so much. I know so many of you have stories that are similar. Is there any other -- okay. Thank you.

AUDIENCE VOICE: Mine's real short, as am I.

(Laughter) But because of my lack of being able to do much, I was forced to move to a condo. That's horrible, a horizontal condo. I always enjoyed having a house to do a little tinkering and taking care of the yard. That was out the

window, so now I live in a condo.

MS. LIPSCOMB: Thank you. Okay, we'll have time for one more and I saw her hand, I'm sorry.

MS. STOKER: Hi, my name's Margaret. I'm Bob's wife. And from a caregiver's standpoint, I mean, she was very well-spoken, but I've been through this with my husband over 20 years. The first pulmonologist -- a pulmonologist, mind you -- told him he had a terminal illness, go home, you won't see your daughter graduate high school. She's now 27.

Luckily, I'm in the healthcare business and I won't take -- you know, I won't take that. But it's not just that. We as a group are standing here. We're educating ourselves. We're trying not to be a pain in the butt, and yet we are a pain in the butt and we're going to continue to be so because we need this for our families.

I'm worried to death about my daughter because she's inherited part of the condition, and I don't see a lot being done about that either.

So, thank you. (Applause)

MS. LIPSCOMB: Thank you. We've spoken a lot about the effects the disease on your lungs. We really want to concentrate this next question on those who have been affected on their liver.

Chris, could you do the next polling questions? If you have liver disease, how many times in the past year did you or your loved one experience a bleeding episode that required medical attention?

We'll give this just a little more time for the results coming in on the web, as well. And let's go ahead and close it. I know not everyone had a chance, but we'll see.

Gosh, it looks pretty even. And we didn't have numbers, so it looks pretty even.

If someone who's experienced that could speak about the impact of these bleeding episodes, for the liver disease. Can anyone expand on the symptoms?

Okay, we'll come back. I think our poll did show that we are much more represented by

primarily lung disease, so.

MS. LAMERS: Hi, everybody. My name's Vanessa Lamers. My mom lives in Oregon. She has had several bleeds. She had to have banding done through her esophagus. She's also had the TIPS procedure, which is a shunt that they put in the liver disease. If anyone wants to talk about that, I know all about it.

And her most recent and worse bleed was a couple of years ago. She started vomiting in the middle of the night and then she realized that she wasn't just nauseous. She gets nauseous a lot. I'm sure a lot of you know exactly how that is. She has the upper quadrant abdominal pain and so she didn't really think much of it. She actually crawled back into bed and then woke again and was vomiting, like 45 minutes later, realized that it was blood, actually called her friend to take her to the hospital. And she got there and the physician admitted her and they banded her and it actually worked out really well.

But she was very lucky. The physician

who admitted her told her that it's an 80 percent mortality rate for that type of bleed, which is potentially why you're not getting a lot of people getting up and talking about this.

MS. LIPSCOMB: Well, we have one other person and then we'll see what we have on the phone.

MR. YOUNG: Yeah, my name is D.C. Young. I'm going to speak for my brother. He is a lung-affected Alpha. I'm a lung-affected Alpha. We're not twins like some people are, but he is a little more handicapped than I am relative to his lungs. But very recently, he has found out that he's definitely liver-affected and bleeding disorders are a major factor now in his life. He's been forced to completely change his diet. He's had to lose weight and he's having severe problems with that. So those of us with lung disease, I think as we age we're going to be looking at issues with livers if we don't get a solution to this whole problem.

Thank you very much. (Applause)

MS. LIPSCOMB: Thank you.

MS. HORSAK: I'm Cathey Horsak and I work for the Alpha-1 Foundation. I came to work for them after losing my 49-year-old husband unexpectedly to Alpha-1 liver disease. He was never diagnosed until his autopsy results came back.

He suffered from esophageal varices bleeds. He was first diagnosed with an unknown liver disease five years before his death. They kept saying it was a form of hepatitis that hadn't been named yet. And he ended up going in for just normal blood work and was 6-foot-2, about 275 pounds, and he had a hemoglobin of 4. So the nurse said I don't know how you're standing up.

They put him in the hospital, they ran all kinds of tests. Every quarter for the next five years they would do endoscopy procedures and they would band or sclerose those varices bleeds.

And I answer the patient hotline at the Foundation and Alpha-1 liver disease may be a very small part of Alpha-1 patients except it

progresses very, very quickly. Somebody can be diagnosed and they can be dead in six months with Alpha-1 liver disease. We need a treatment for Alpha-1 liver disease. (Applause)

MS. LIPSCOMB: Thank you. Thank you so much.

AUDIENCE VOICE: Donna? Donna, I have someone.

MS. LIPSCOMB: Okay, thank you.

MR. STRICKLAND: My name's Jesse Strickland. I live in Ohio. We have a support group there, half a one, and we just recently had a person who was liver-affected and in his 40s, MZ. You're not supposed to have liver disease as an MZ, but his doctor told him it was primarily due to Alpha-1. He had a liver transplant three months ago. He's doing great.

My father died at age 81 with cirrhosis of the liver and liver cancer on the FM. And supposedly, F doesn't cause liver disease, but I don't think there's been enough research to know if it does or not. FM's not supposed to cause

emphysema, but I have emphysema.

So Alpha-1 doesn't treat everybody the same, so doctors need to realize if there is an MZ and they have COPD, maybe they do need treated. If they're an FM or FZ or whatever they are, I think you have to look at conditions and what they're going through every day, their symptoms, and treat everybody, whether you're a carrier or a full-blown Alpha, on their symptoms. (Applause)

MS. LIPSCOMB: Thank you. Thank you. Operator, is there anyone on the line that might want to speak to this?

OPERATOR: If you'd like to speak to this, please press *1 and record your name to signal to me. Again, that is *1. One moment, please.

MS. LIPSCOMB: We know there's a little bit of a delay in this. And, Loni, can you go over to that gentleman?

While we're waiting to see if someone comes on the line, we have someone in the room that will speak.

MR. BUTCHER: Hi. My name's Eric Butcher. I can't really speak to the bleed because I don't have varices yet. I haven't experienced that. But I am in Stage 4 cirrhosis. I also have Stage 2 emphysema.

But the -- my liver is currently compensating. The worst symptom that I deal with due to my liver currently is the anxiety and depression because I wake up every morning, it's like a Sword of Damocles hanging over my head. Once that little piece of my liver stops fighting, I'll get really sick really fast. And I always wake up every day wondering if this is going to be the day, so there's a lot of anxiety and depression that is tied up with that.

MS. LIPSCOMB: Thank you. What do we have on the web?

MR. CHAZIN: Regarding liver, we have reports of high NR, pain. One person has had a gastric bypass, and just, again, a limiting of activities.

MS. LIPSCOMB: Thank you. Did anyone

come on the phone?

OPERATOR: Yes, we do have Marvin on the phone. Your line is open.

AUDIENCE VOICE: Hello?

MS. LIPSCOMB: Hi, Marvin.

AUDIENCE VOICE: Yeah, my name's Marvin. I'm from South Carolina. Sorry I'm unable to join you there today, but I can echo almost everything that's being said on mine except one thing: Sex is hard, but I'm not giving it up. (Laughter and applause)

Anyway, all the things you're talking about, simple things like walking up and down the four or five steps, taking the trash out, there are times when I have to ask my wife to do it, I'm unable to do it. And I've been an athlete, I've exercised all my life. I used to be ranked in the top 15 in South Carolina in open tennis and now it'd be a joke trying to pick up a tennis racket or do anything athletic.

But the disease does progress. It's been slow, but the augmentation therapy does help.

It slows the progression of the disease and without it I don't know where I'd be. I've been having -- I've been taking infusions every week for 22 years.

And I appreciate everything that all the folks associated with Alpha-1 have done to help me. And the support group that I work with here in South Carolina has been outstanding and has been a blessing for me. Now we just need to work towards finding a cure, inhaler or pill, whatever it takes. We need a cure.

Thank you so much. Thank you. Thank you for giving me time to come on today.

(Applause)

MS. LIPSCOMB: Thank you so much. I think that was foreshadowing of this afternoon, but while we're still in this morning, we're going to go to the next set of questions. We have three questions that are specific to the lung disease and I'm going to ask each of them first and get the results from the polls, and then we'll come out to the audience and give you an opportunity to

speak.

So the first one is how many -- thank you. How's your lung symptoms? (Laughter) And how many problems have you had in the past year? This is one of those tricky ones where A is 0 and B is 1, even though it has a 2 on it, so when you're voting, please make sure you're voting for the number you want by the Alpha number you want.

Okay. Let's see what we have here. All right. So, well, clearly 4 or more has been the more, although we have the number of 16 percent for 2 and 1. They don't -- I'm assuming 2 is 16 percent, as well. Can you have a response from the --

MR. CHAZIN: Yes, on the web 4 or more is 45 or 46 percent and 2 is about 21 percent. So we have people with -- we have very few, 5 percent was 0. So the scores on the web are signs they're more skewed more towards more tax.

MS. LIPSCOMB: Okay.

MR. CHAZIN: Which is why they're probably not here today.

MS. LIPSCOMB: It's actually what we expected. All right, question 8? Of your lung symptoms in the past year, how many have required hospitalization? A is 0; B is 1; C is 2; D is 3; E, 4 or more.

Give you a little more time. It's slowing down. Okay, let's see what that is. I know there's more of you than 41, but we're going to see what that bit of response is for this.

Wow, something is telling me lots of no hospitalizations at all and then 1. We're going to double- check because the numbers aren't coming up here for us to do it.

No, no, I just meant percentages aren't coming up.

AUDIENCE VOICE: We're working hard on it.

MS. LIPSCOMB: Well, excellent.

AUDIENCE VOICE: You get sicker in the hospital. Don't go to the hospital.

MS. LIPSCOMB: We'll have time for that.

MR. CHAZIN: Yes, it echoes on the web,

65 percent have not had any hospitalizations and the rest 1 or less than 2, so the great majority have had less than 2.

MS. LIPSCOMB: And I'm sorry, I just meant the percentages above that would tell you that it was 65 percent said 0, not that I was questioning 0, so I apologize. I wasn't clear on that.

Great. So let's try the next question 9 before we start our conversation. Okay, in the past year how many required an emergency room visit or doctor's visit without hospitalization? So that's the key difference.

Well, it's an "or," so emergency room visit or a doctor's visit without hospitalization. So for those of you who are taking her advice and not going anywhere. (Laughter)

Okay, Chris, what's our responses? Well, it looks 4 or more, 1, and 2 are kind of similar responses with the most being 0. What about on the web?

MR. CHAZIN: On the web, 0, 1, and 2 are

about the same with a little less than 3 and 4, so, again, skewed maybe to the left a bit more.

MS. LIPSCOMB: Okay, great. Thank you. Well, we've seen these results. Can anyone provide specific examples how these affect your day-to-day life? Thank you.

MR. LONGMIRE: I'm Paul Longmire from Washington State, husband of a double-Z. Yeah, I did 30 years of active duty in the military, been in more war zones than I know of, got two Purple Hearts, and I'll tell you what, there is nothing worse than sitting there watching her gasp for air and try to breathe. And I got a nebulizer in one hand, a PB thingy in the other hand, and my phone ready to dial 911. You know, it's tough to stand there and do nothing, can do nothing.

The other side of it is our oldest daughter, she's married to a soldier, just got back stateside. Got two granddaughters that we can finally see. And I have to constantly watch her while she's out playing with a 10-year- old and an 8-year-old to make sure she can breathe and

make sure when she starts flushing and she can't catch her breath, to make her sit down and take a break and, you know, so she doesn't go into a fit. I don't know what the heck you call them, but, you know, you can't breathe.

And I'll tell you what, it's a tough one. It's a tough one as a husband and caregiver, whatever you want to call it. (Applause)

MS. LIPSCOMB: Thank you for sharing that. Do we have a couple over here?

AUDIENCE VOICE: Hi. My name is Liam. I'm from Massachusetts now, originally from Ireland, where a lot of people have Alpha-1. In my last hospitalization, it was for pneumonia and it took a long time for the doctors -- there must have been about 20 doctors in and out -- to identify what it was I had. And they informed me, after they had discovered it was pseudomonas, they informed me that there was mold growing in my lung -- our lungs. Yeah. That was very frightening to me. I had no idea that that could happen.

So I don't know if anyone else had that

experience, but that was mine. And I was in -- I don't know if I said I was in for 21 days, but it's a long time.

MS. LIPSCOMB: Thank you.

MS. LADIG: I'm Carla Ladig from Indiana. And I think one of the important things that you need to know is that most of us don't go to the emergency room because emergency room doctors don't know what Alpha-1 is. (Applause)

MS. LIPSCOMB: Thank you.

MS. SNEDDON: I'm Alyce and I'm from Massachusetts. And to the hospitalization, I think part of the reason we do not go to emergency rooms is because we're so proactive and we're aware of what our conditions are. We take a lot of our own treatment and we go ask the questions. We contact the physicians. We say we're not feeling well, this is what's happening to me.

I was a nurse. I know a little bit more maybe, but it just takes our own fight individually in order to get and stay and maintain our lives, which is not easy when you're short of

breath and you're trying to fight a cold or a sore throat or anything. And even to have to be sick and go to the doctor or go to an emergency room, you have to worry again about your oxygen and what's going to happen when you get there and how long are you going to have sit.

So those are the things we fight and we individually take care of our own health a lot of times.

MS. LIPSCOMB: Well, thanks for that, but I think that's a great jumping point to ask you more on what do you do if you're not going to emergency rooms or to the doctor's? How are you handling these symptoms?

MS. CADWGAN: My name is Ruth Cadwgan. And I think Alphas are very educated about their condition and proactive and they have -- their doctors have prescribed stuff because they have to start on antibiotics the minute they feel a tickle. And most people -- Alphas self-medicate because they know what they need to do. They've had to depend on it themselves.

My husband was diagnosed 23 years ago, but I want to speak to the people who aren't here. We're the healthy ones. You have to look at this room and know that this is as healthy as it gets. It's the people that were on the conference calls who are so afraid to get on a bus or a van and possibly not have their oxygen that couldn't be here today. But when you look around this is as healthy as it gets.

Thank you. (Applause)

MS. LIPSCOMB: Ruth, thank you so much for sharing.

AUDIENCE VOICE: Donna? Donna, I have one back here first.

MS. LIPSCOMB: Okay.

MR. LANTZ: Hi. I'm Mark Lantz from D.C. And I'm relatively healthy. I'm ZZ and I have emphysema, but I'm a competitive rower and kind of lucky in that way.

But following up on this question, the other group that aren't here are the people that don't know they have this disease. I have taken

to asking every physician I run into, and I run into a lot of them, and I've run across 30 to 40 in the last 6 months who have never heard of this disease. We do not have any regular testing in this country despite the fact that lifestyle changes and environmental changes will make a bigger difference in a long-term prognosis than any treatment currently available. And the fact that a one-year per person delay in infusion therapy will save a quarter million dollars. So blood tests look pretty cheap in that regard.

As I see it, there's 100,000 people out there with lessened life expectancy because we don't do basic education and basic testing for this disease that we already know how to do, that don't require inventing new drugs. And I think that's appalling. Thank you. (Applause)

MS. LIPSCOMB: Thank you. All right, we're going to go to just two more people. I know that there's a lot to be said, but we have a few more questions to get through and a lot of this is topics we'll be talking about more this afternoon,

so we definitely want to hear what you have to say, so please don't think I'm cutting you off, but I am.

(Laughter) Henry, real quick.

MR. MOEHRING: I guess I made the cut.

MS. LIPSCOMB: You and one other person.

MR. MOEHRING: My name's Henry Moehring and I wanted to follow on one of the comments and actually it flows that, you know, we're a rare disease community. And part of the reason you don't see us frequenting common health areas, doc in the boxes, emergency rooms is because they don't know what we have. And even in my primary care office, every time I go in to see my doctor -- which, thank god, is not that often because I am healthy -- I have to reorient her to who I am, what I have, and I usually bring a stack of literature. I don't think she has time to read it, given the work that she does, but it's a challenge when as a patient I feel like I know more about what's going on with me than she does.

And, you know, there's an anxiety level

there. I have a great provider. I have a great pulmonologist. I have great liver doc that I can pick up the phone and talk with long before it gets to be a problem. And I think that's why you see the number there.

I also have an Alpha net coordinator that checks on me and goes are you doing what you're supposed to be doing, which is something that I can only speak for this particular Alpha, but some of us need. So thank you.

MS. LIPSCOMB: Thank you. We're going to ask one more person, then go and see if we have any comments on the web.

MS. CORRON: Hi. My name is Allison Corron. I'm an MM married to a ZZ. I'm also a patient advocate and I work with patients who are newly diagnosed with Alpha-1 antitrypsin deficiency.

The question came up what do you do rather than go to the hospital? And I'd like to speak on behalf of three of my patients who, in the last two months, didn't know enough about

their condition to know what to do and who went to the hospital and didn't come out alive because they had to wait too long to be properly diagnosed and because they were in areas where their physicians and their medical facilities didn't have enough information about their condition to keep them alive.

Thank you. (Applause)

MS. LIPSCOMB: Thank you so much. We're going to go to the web. What are you hearing there?

MR. CHAZIN: On the web, I just want to share that many people say they avoid the hospital because of, you know, the bacterial infections, especially methicillin-resistant staph aureus. Some feel that ERs are very dismissive, as you all have said. Other people try to keep a supply of antibiotics and prednisone, working with their doctor to have it available.

MS. LIPSCOMB: Okay, great. And I was teasing, we do have one more person because I miscounted. (Laughter)

MS. BELL: Hi. I'm Robin Bell. I'm from Bakersfield, California. I'm 46 years old.

In regards to hospitalizations, last December, I had gone into Urgent Care. It was like 9:00 in the evening and my Urgent Care doctor immediately sent me to the hospital. And by the time I ended up seeing an emergency room physician, he looked at me and he said, well, you know, what's the symptomology that brought you in here in the first place? And I said, first of all, I'm an LVN. I had gone to Urgent Care and he's under the impression that I had a pulmonary embolism.

And he looked at me and he goes, why on Earth would you think that you had a pulmonary embolism? Well, I've got Alpha-1.

No, you don't. It's super rare. (Laughter) No, you don't.

And I looked at him and I said, oh. He said, well, you know, let's go ahead and do an X-ray on you and, you know, just check.

So two hours later, you know, I ended up

having a CT done. Sure enough, it came back that I had a pulmonary embolism. But in the emergency room and having seen a physician that was that dismissive in regards to a situation such as just blowing me off because of a disease that's not as rare as everybody think it is, you know, it's just something that needs to be very much looked at within the medical community. (Applause)

MS. LIPSCOMB: Thank you so much. Thank you. I want to take a minute to ask about the effects of Alpha-1 as you age. What are some of the surprising ways that symptoms of your disorder has changed as you've aged?

MR. NOONAN: Well, again, I'm Bob Noonan from Virginia here. One of the things, again, is the shortness of the breath. I go back to that because it's virtually everybody's biggest problem here.

And as you do age, you have more shortness of breath and there's more and more things that you can't do anymore. Golf, I miss that a lot. I say I can still hit the ball out of

a golf trap -- out of a sand trap, but I can't get myself out of the sand trap. (Laughter)

I would like to mention that we need more assistance in the development of better oxygen. When you age and you're short of breath and, all of a sudden -- well, not all of a sudden, but you can't breathe, oxygen is the answer. I mean, we all get the medicines and so forth, but if you have a good source of oxygen, you can do a lot of things that you couldn't do without it. And I just don't see it happening in the oxygen supply area, the ambulatory oxygen.

There's got to be better devices. There's got to be something that will give you what your blood oxygen is and would raise or lower the amount of oxygen that you're receiving as a result of what the blood oxygen is doing as try to get yourself out of a sand trap or do something else. So I'd like to see faster and more advancement in supplemental oxygen for not only the Alphas, but everybody else out there that's on oxygen. (Applause)

MS. LIPSCOMB: Thank you. Okay, Loni, you have someone over there.

MS. BROOKS: My name is Charlotte Brooks. I'm from San Diego. And I would like to speak on my husband's behalf, whether he wants me to or not. (Laughter)

We've been married for 57 years. I have watched him deal with chronic bronchitis, pneumonia, asthma for all of those years, slowly getting worse and worse and worse. And through four pulmonary doctors, through countless GPs, nobody every tested him until three years ago. Three years ago, when he was 75 years old, he was finally diagnosed.

He was put on augmentation therapy and got better, but not really that much better. His main component is bronchiectasis. He would cough. He missed years of our kids' and grandkids' lives because he couldn't go to plays or movies or soccer games or anything because he would cough and it would be so disruptive to them. In fact, he coughed so much he wound up with bilateral

hernias.

Finally, now I'll make this short, he's on augmentation therapy and antibiotic therapy and it's like a major miracle. (Applause)

MS. LIPSCOMB: Thank you.

AUDIENCE VOICE: One thing that I've noticed with the passage of time is a decrease in muscle mass. And although I work out quite a bit and do strength training, I still don't get as much bang for my buck as I did when I was younger. And I think that improving muscle mass would also increase my functionality, so I think that's another important effect of aging.

MS. LIPSCOMB: Okay, thank you, Jennifer.

MR. WALSH: Hi. My name is Fred Walsh from Massachusetts. One thing that is nice to have -- what it does to your ears is crazy, too, by the way. Looking like Yoda.

(Laughter) But one thing in particular is being close to a Bathroom if you're real short of breath.

As you age things loosen up a little bit. (Laughter) And really, the first thing I usually ask, where are the restrooms? And they're not too strategically located here. But that's basically it. When you have a choice to breathe or go, sometimes you just go and it can be pretty embarrassing, especially if you're on an airplane or not on an airplane. (Applause)

MS. LIPSCOMB: Thank you.

MS. GOULD: Hi. My name is Patricia Gould. One of the things I've noticed as I've aged is I've -- my mother is a ZZ. I don't know what my genotype is because I have had my serum tested three times during three different health incidents and never received the results from the doctor's office.

I was diagnosed as a young person with Gilbert's syndrome, which is elevated bilirubin. And we were told then that it was just a chronic situation that was essentially not going to affect my health or life span, anything major, I guess.

Then I was just in the hospital a couple

of months ago with what they diagnosed -- they couldn't figure out what my problem was, essentially. Gastric issues, I have pain, no bleeding, but just nausea. I've had ongoing pain with no real issues as far as enzymes are concerned for 15, 20 years. It's ongoing meaning that sometimes it's more noticeable than others, but discomfort I guess is a better word.

But my point is that as I get older my concern that whatever -- if this is something to do with Alpha-1, first of all, I don't even know what my genotype is, although I have been assertive and tried to find out what it was just as it happened due to, from my perspective, the doctors not taking it seriously enough to make sure that I get the results mailed to my home or that they even call me to let me know what they found the results to be. And then, also, that being the situation my concern is, is there something happening within my body that I'm not addressing, taking care of at this point? It feels like a crap shoot at this point just because

none of the doctors have kind of tied it together even knowing that my mother is a ZZ lung transplant survivor. (Applause)

MS. LIPSCOMB: Thank you for sharing. Thanks. We're going to have to wrap up, but I have one quick question that I want to follow up with. If anyone's a parent of small children, what are your biggest worries about their aging?

MR. JOHNSON: Hi, Dad. (Laughter) Bet you didn't think I'd grab this, did you? Ryan Johnson, Jacksonville, Florida.

I'm actually the brother of -- well, son of Richard Johnson, brother to Luke and Grace Johnson. Let me tell you, they're seven- and nine-years-old and they're every bit of that, wild and crazy. They're the most fun-loving kids in the world and I'll tell you one thing that really breaks my heart from somebody who's not even affected. I don't want to see them grow up and end up like the people in these rooms. Let's get ahead of, you know, something. Let's put something into these people's hands that can

assist them now and let's do research to help cure those who have the liver issues and the enzyme issues and the lung issues and let's get ahead of this. And let's, you know, fix something that is very common.

So thank you. (Applause)

MS. LIPSCOMB: Thank you. I'll take one more comment.

AUDIENCE VOICE: Having a little girl, I've got an eight-year-old, and she's an MZ, but at the elementary level. Like Jim had said earlier, you know, it's really hard when I'm a ZZ and she brings home, you know, her little contaminants for lack of a better term.

Anyway, you know, my biggest concern with having little ones and, you know, she's also asthmatic and I live in Bakersfield where it's the worst air quality in the nation, so it's a constant thing, you know. And then valley fever on top of it, you know, in the valley, so it's worrisome. You know, as every single parent in this room that has young children, you know, and

getting a handle on, you know, different medications other than just inhalers for asthma, something needs to be done.

MS. LIPSCOMB: Thank you. I know there's a lot of other comments, but we're running out of time for this morning. And so I don't want you guys to miss your lunch. We have a full afternoon where if we need a little extra time, we can use that.

Normally, I would say time permitting does anyone else have something to say, but that's not time permitting with you guys and you've been so forthcoming in your experiences, and I really want to thank you for that.

We are going to break and you'll have an hour for lunch and we'll be right back here afterwards. A reminder that anyone who's interested, is there still space on the public comments? We believe so. If you've not -- if you're interested in signing up for the public comments period this afternoon, please go and see if there's still space available because after

this afternoon we're going to pull up the sign- up sheet. And the time will be based on how many people are there.

Chris, I think there's another slide. Could you go to it? One more.

And before we break, we have one more Karen Erickson wants to talk -- say something.

MS. ERICKSON: Hey, guys. How are you? So a lot of incredible comments and we want to keep that rolling, so we called in a favor from a big friend to the Alpha-1 community and they happen to have brought an incredible video crew in to film your statements, how you feel about Alpha-1, where we need to go. So as you mill around at lunch, they are in the last room. As you come out here make a left and they're fantastic. We can send you and then hear what you have to say and it's going to be so powerful moving on, and it has been all day today. So don't let those comments go unheard.

And then finally, for any of you that wants to stay in the room, we're going to set up

some runners to go and grab your lunch if you want us to. So just go ahead and raise your hands and we'll handle that, as well.

All right. Thank you.

MS. LIPSCOMB: Thank you so much. We'll see everybody back in an hour at 12:30.

(Recess)

MS. LIPSCOMB: Thanks everybody for coming back so quickly. I understand that rumors of my singing in here was what got everybody back, to say to everyone who had heard the first part. So, thank you. I want to welcome everybody back this afternoon. It looks like everyone at least got lunch. I didn't see anybody looking forborne out there so I'm glad that everyone had that opportunity. I think we had a really good conversation this morning and we're really looking forward to this afternoon.

I want to remind everybody again that his proceeding is being recorded and transcribed. Both of which will later be posted on our webpage, which is a page that if someone Goggles they can

find this information. And we also have a few new panelists at the table and we're going to let them intro -- for the FDA side and we're going to let them introduce themselves. Start at that end.

MR. BAUER: Yes, hi, I'm Larry Bauer. I'm a regulatory scientist in the Office of New Drugs, Rare Diseases Program. This morning Jonathan Goldsmith was here and Jonathan and I work together. And I just wanted to say thank you to all -- it's so wonderful to see so many of you here. I saw an old friend, John Walsh, and I said it's just so great to see -- because I know that people are at different places on the spectrum on their ability to travel and it was really great to hear all the stories this morning and the experiences, so thank you.

MS. WITTEN: Hi. My name is Rachel Witten. I'm a senior clinical reviewer from the Office of Cell Tissue and Gene Therapy.

MS. MEHTA: Hi. I'm Ruby Mehta from CDER, Division of Gastroenterology, and Inborn Error of Metabolism.

MS. LIPSCOMB: Okay. I think that's our new staff. I want to welcome everyone who is going to talk about our afternoon talk. Can you hit the next button? We have Jean, Karen, Ken, Marcie, Fred and Jesse and I really want to thank them for their willingness to participate. The questions in this topic really are their perspectives on approaches to treatment. And they're going to answer what they're currently doing to treat the condition, how those conditions are working -- treatments are working. Talk about advantages and disadvantages.

Again, they each have about five minutes to speak and I'll be monitoring that. I really look forward to our conversation. And so I'm going to ask that Jean, if you don't mind.

MS. MCCATHERN: No, I don't mind. My name is Jean McCathern. I'm lung effected and might be liver effected depending on which doctor you trust. Currently I am on inhalers like most other lung effected Alpha's but unlike a lot of people I'm on an inhaled augmentation therapy as

part of a trial. Once that's done I'll go back to the regular IV augmentation. And one of the other things I consider a treatment is I did complete pulmonary rehab very early when I was first diagnosed and I think that's helped a lot.

The treatments, as far as the inhalers, I know they work because I tried stopping it and about a week later I couldn't breathe. So I know they work. I've been on augmentation therapy for 11 years and my FEV1 hasn't' declined at all and I didn't have some of the other tests with defusing capacity but since I've had those tests they go up and down but they're in the same area. So I'm very happy with the augmentation therapy.

However, augmentation therapy is -- does complicate your life. I have grandchildren and a daughter and they live in Arizona, and I normally live in Pennsylvania and in order to go Arizona and continue my treatments I have to have a doctor that's licensed in that state. It's not just any doctor. It has to be someone licensed in the state or the nurses won't infuse me and since they

have enough trouble getting my veins I don't think I could do it myself. So that does complicate things especially since my insurance says I really can only have emergency treatment outside of my home area.

The -- with the inhaled therapy I don't have that problem, however, with inhaled therapy it will be -- the trial ends in October and I don't think they're going to let me keep on with it, unfortunately. The inhalers don't complicate my life anymore but I will tell you when I was first diagnosed with Alpha-1 I was on steroids, inhaled steroids and I've been on inhaled steroids because back in 1980 I was diagnosed with asthma, and so as soon as they were available, which was about ten years in, right around 1990 because I was in a trial for Budesonide which is an inhaled steroid. They told me at the time you won't have any long term effects, and I found out myself before they even admitted it, that you can. So I got off those as quickly as possible by advocating for myself and asking the doctors to reduce the

amounts of steroids until I finally got off of them this past January.

I had osteopenia because steroids do cause bone loss. So, you know, that is a real disadvantage of some sort of like a miracle drug but it has all these little side effects. Overtime my treatments really changed. When I was first diagnosed with asthma I was on the same things, equivalent to the same things that I'm on today. However, back then you took pills, they didn't work, I'd have to sit up in bed to breathe at night. I was in the Air Force for 25 years and I didn't want them to know what was going on for a long time so I really, really had to work at hiding my symptoms. But then -- actually the first break through for me was that Budesonide trial, then I could breathe again and I didn't have the problems I had all throughout the others.

So I just -- I've seen so many advances for the symptoms that people with normal emphysema or asthma have. But since I've been diagnosed and I was diagnosed in 2004 there hasn't been really

any advances in augmentation therapy other than maybe some purification, more availability, which is important, but that's not what I call an advance. I'd call an advance another step. Something that would stop liver and lung disease would be great, especially if you could use it in children and especially if you could test children right when they're born to find out if they have that problem without having to worry about genetic discrimination because for life insurance and long term care insurance. I know you don't think about that as a baby -- when you have babies but if you're, you know, susceptible to this you want to be able to get life insurance and long term care insurance along the way.

The things that aren't improved is I still have emphysema. I still have some fibrosis or maybe no fibrosis depending on which liver biopsy you believe, and it was the some fibrosis that came before the no fibrosis which is kind of odd. So that didn't -- I don't have -- there's no treatment to improve that. So my treatment, if I

had one, it would be one time, as a baby and for all of us that have liver and lung disease, something that can cure that as well. And then I'd be happy. But unfortunately I don't have a magic wand but I think some people in this room have a lot of influence in those areas and I hope that this helps them decide to make some more headway. That's all.

(Applause.)

MS. LIPSCOMB: Thank you, so much, Jean, we appreciate it.

Karen?

MS. ERICKSON: Thank you very much for the invite to be here. It's an important day for our community and amazing that it's happening with such a full house. So I am Karen Erickson, and I am a daughter, and a sister, and an aunt, and a niece. I love to hike. I'm a career professional in biotechnology. I do dog rescue. I do not for profit fundraising and awareness and 15 years ago my identity changed to being an Alpha-1 patient. And over that 15 years I progressed to the point

that I needed a lung transplant and did finally receive that, but that progression and that path took away everything I ever identified myself with and I'm just now building that back.

The first thing that needs to happen in any good treatment plan is getting diagnosed. My diagnosis took a lot less time than many people in this room but it was riddled with misdiagnosis and they seemed to be very situational. I was a big tri-athlete and when I went and presented with breathlessness at an urgent care in my workout clothes, it was exercise induced asthma. When I went as a career professional to test for a device that I needed to use with a very dangerous substance, as I worked in Hemostasis and blood clotting arena, I was tested for a respirator. I failed miserably. I was told to come back two weeks later. I failed miserably again and rather than test me further they decided that the machine was malfunctioning and sent that out for testing. When I was in Vegas with some friends, and I may be a bit of a goof but I'm fairly straight laced,

I presented in the hospital with breathlessness and rather than run any vitals they proceeded to question me on drug use and what I had done that night that would cause that.

When I was diagnosed I was already at a lung function of 38 percent. My doctor was a wonderful man and put me on augmentation therapy straightaway, but he also put me on augmentation therapy when I was dosing at -- every month and so after a year of that when I did my next test I was already tested at 30 percent, and I had lost a lot of function and was then put on weekly augmentation therapy. Over the course of the last -- the decade that followed I stayed as fit as I could be. I was compliant, all my inhalers, augmentation therapy, but when you would catch something, I mean I worked in an organization with 10,000 people, you catch something you'd be hospitalized and you'd get just a tick lower, and just a tick lower, and just a tick lower, and when I hit 20 percent lung function a decade later I put myself on a transplant list. But I also put

myself on a higher dose of augmentation therapy and amazingly at 20 percent I stayed there until -- for three years. I did not budge, so that dosing was important for me.

I think my most vital therapy came in the form of community engagement and that participation and support that I received from all of you that are sitting here today and I don't think that the understatement -- or that engagement can be understated. I think it's vital. I think we saw it in the numbers of the hospitalization we have, that peer-to-peer contact is working. I participated in as much research as I could, but I was already very low when I came in to this community and that's when I was at 30 percent, and I was disqualified from many trials. I did what I could. I've had my biopsies, I've filled out the surveys but again it was pretty limited and so I decided that I could do the most good by putting myself at the table. I wanted to be part of the decision making. I wanted to be part of the review.

(inaudible) I wanted to talk to people about how they were designing their trials and what we needed as a patient community.

So that mandate that made my participation in research seem passive was very active to me. I had the experience that I had from the research that I did participate in. I had my background in biotechnology and most importantly I'd found what was this family that I couldn't possibly see progressing to 20 percent and being on full time oxygen and losing their job and their identity to this disease. So I did, on behalf of the patients that are here today, and on- line and aren't with us and aren't diagnosed, and the so many that we've missed because they've lost their battle with Alpha-1, I sat at that table lending my voice to trial design and what a patient would and would not do and should and should not do was important to me and that was my therapy.

We're not in a position to stop

effective therapy to be in a trial. And we're not poised to compromise the other organ impacted by this disease to be in a trial. You know, I was willing and able to do the biopsies when they made sense, but I'm not willing and able and I couldn't ask anyone that I care so deeply about to do bronchoscopies and liver biopsies in excess. There's got to be a way around that in designing trials.

For treatment opportunities I take the perspective that the Alpha-1 community is prime for both personalized and precision medicine. I saw it with me. The interval didn't work, I dropped my function. The dose didn't work, I dropped my function. We need to find people before their function falls, before their liver disease raises and we need to make sure that we're dosing them appropriately. And precision medicine, we're sitting on potential biomarkers that not only make some of these evasive measures very difficult, but how easy would it be to know where we're at in our augmentation therapy, what

we're using, where our liver disease is so that we can treat at the moment. It doesn't -- we don't sit with our levels the same at baseline when we have exacerbations or maybe it's activity, we don't know, but let's measure that. And most importantly as well, it's not just the non-invasive, but it's listening to the patient, it's that patient reported outcome. Clinical and diagnostic is important but your working with a person who knows their body better than anyone else who for the first time has had zero hospitalizations, some out of fear but most out of being very proactive and educated. That is therapy.

So while I'm extremely grateful for the therapies that I have, weekly infusions do limit me. Their complexity and difficult to manage the impact of Alpha-1's it was tough. Delivery of these medicines could be more friendly, they could take time in to account. I couldn't even shower and get out of bed, rushing around trying to get an infusion or take nurses who literally didn't

work for my energy level. I'd also be remiss if I did not strongly discount the perception that transplant -- the final option for both Alpha-1 and lung and liver disease is curative. It's not. I am forever grateful to my wonderful donor and their family. For the extra time that I've been provided and the opportunities like this that it's going to allow me. Time with my family, working with this community is a blessing but a transplant is not lasting, and it's not simple. It's life encompassing to maintain and it certainly won't prevent me traveling down that road of progressive disease with Alpha-1, or rejection and losing my identity again, and even more importantly there's no transplant or current treatments that is going to allow my family and my friends to be that. I will again turn them into caregivers and that saddens me and shouldn't happen and they will eventually watch me pass from Alpha-1 but it won't be before we put in a hell of a lot of effort to find this cure for this disease.

So again, thank you for giving me this

opportunity today and let it be an open door. Thank you, very much.

(Applause)

MS. LIPSCOMB: Thank you so much, Karen, we appreciate it.

Ken?

MR. RICHMOND: Hi, good afternoon. My name is Ken Richmond. I live in Arlington, Virginia. I'd like to thank Karen, and Jean, and all the other panel members who spoke earlier today. I'd like to thank the FDA for the opportunity to share my story here with you.

You know, I've been asked to speak on Topic Number 2, which is perspectives on current treatment, current approaches to treatment. My Alpha-1 journey, you know, started at age 35 when I was diagnosed by my primary care physician. After about three years of chronic bronchitis and trips to visit his office I finally threw the lawyer card down and said if you don't test me I'm going to have my lawyer call you. He called me three weeks later and said I've got good news and

bad news. The bad news is, yes, you are Alpha-1 deficient, the good news is I'm leaving the practice.

(Laughter) So I went to the next thing I could do is some Research and I found that the National Institutes of Health was offering some help in this matter and so I visited the NIH and got some verification, found my serum levels. And I heard the words that were probably the most important set of words I could take at that time. I was told that whenever possible to not give in to that take it easy mentality that common advice for diseased folks, folks with diseased lungs had received for so long. Don't take it easy, push, push, push.

You know, I can't say I've been successful in that, because I haven't. I'm imperfect, I'm flawed, but you know, I try and over the years what I've noticed is that I've heard from other speakers today and other folks talking about depression and the effects of the

disease, the Alpha-1 deficiency causes and, you know, it's hit me as well, and you know, I'm happy to say that right now I'm out of that phase. I'm here, I'm happy to be here, it's an honor.

My current treatment plan includes weekly intravenous augmentation therapy, daily use of long acting bronchodilators, inhaled and nasal corticosteroids, nebulizer solutions, over the counter products to relieve congestion in my sinuses and my lungs, several times each year, right around spring and fall, shocking, I have prolonged exacerbations leading to antibiotics and prednisone.

Another part of my treatment plan is exercise. It's been inconsistent but I've been doing pretty well this year. I walk briskly 25, 30 minutes a couple times a day, a couple times a week, as well as doing weight bearing exercises and through a combination of diet and exercise this year I've lost 30 pounds so far and (applause.) Thank you. And that helps my reactive airway disease as well as reduce possible

other co-morbidities.

You know, it's really hard for me to gauge myself on how my current treatments are working. So I reached out and asked some family members and some coworkers and some friends what their vision, what they see me, what their experience is and to a person they all said the same thing that in the last six months I've had fewer coughing episodes than previous. And you know, in years prior my reactive airways just seemed out of control. So I think whatever I'm doing seems to be working, I don't know.

Regarding some disadvantages or complications, you know, I've been infusing now 17 years and to say it's been disruptive to my work schedule is just about the biggest understatement possible. My infusion from beginning to end, where I get in my car to drive there and get back out of my car finished up is about three hours and that's reduced as a result of purification of product. That takes a pretty hefty time -- a slice out of my day. I've been fortunate -- by

the way, shout out to the nurses at Kaiser, I love you; they're on the webinar today. (Laughter) You know, we had nurses come to -- open the doors at 6:30 in the morning of their center so me and two other Alpha's could infuse before our workdays began and we did that for two years until the administration said that wasn't going to be possible. You know, but we do what we have to do to get the treatment we need.

You know, another complication for me, as I mentioned I've been taking corticosteroids for some time and I have to take some fairly drastic measures to rid myself of a nasty case of thrush and it's really kind of awkward. So I'm happy to share that (laughter.) So my ongoing care plan, you know, I'm lucky in that since 1995 I've had several changes in my providers of care and I've noticed that my initial pulmonologist who was an older gentleman, love him, great guy, I taught him a lot (laughter), he retired. And my current pulmonologist, young guy, on the ball, by the name of Dr. Win how you doing, good to see

you. He's on the webinar also.

He's on the ball. He's up to date with research. He's willing to hear what I have to say and provide me additional care as he sees. Things like, Ken, if you lost 30 pounds you probably would breathe better. You know, so I need that kind of work. You know, he rotates my products to help me not, you know, have them work most effectively. Sometimes there's some reimbursement issues, that's a problem but we always find a way around. And you know, just in the last year, I changed -- I have very reactive airways and so I did change my asthma medication to a higher level and I think that's made a big difference for me, just, I don't cough as much.

I do cough so much that I did buy stock in Ricola and if anybody would like some I bring them with me (laughter.) You know, medication is great and what we do on a daily basis keeps us at stasis sometimes. But you know, for me, I started at 98 percent I'm now down to 30 percent and I'm no longer the athletic person I once was. You

know, I was a multi sport athlete, you know, I did a lot of stuff and, you know, over the years I stopped playing competitive tennis at age 40, I stopped playing competitive baseball at 47. I stopped walking hills with a pack going hunting at 52. You know, these are things that are part of my identity, things that I won't get back. On the other hand, golf is looking pretty good for me. You know, other opportunities arise, you know, I do see this as the one door closing but two more opening up. And I'm optimistic that as long as I engage myself in the process there'll be more for me out there.

You know, as we heard from Ms. Garcia from Miami and Marvin from South Carolina, you know, one of the most difficult things for me to handle is during times of intimacy. You know, it's really hard to be in the moment when you're wheezing. (Laughter) I just can't do it, you know. Arrangements have to be made.

You know in this next section it asks about what treatment has had the most positive

impact on my life and it's really not even -- it's hands down for me. It's the participation knowledge, participation and the knowledge that I've gained as a result of my disease. You know, when I first went to the NIH and I found more about the disease I asked about solutions and I was told, hey, we've got a clinical trial coming up and so I said, I'm in. They handed me the consent forms and they were three or four pages long and I signed it without looking at it. Now, I reread one of those recently, interesting (laughter.) You know, super bugs kind of freaked me out. I think I've had seven bronchoscopies. I may exaggerate so it could only be five, but what I've found is that for me that participation early on in the clinical setting taught me about how to live my life today. Not 20 years ago, but today. I knew nothing then but I learned how to live as a person with 30 percent lung function.

You know, I was introduced to the Alpha family, you guys, you know, we're from different places but we share this common thing and I see it

as hope. I see it that we're all coming together to try and get this cure going on because, you know, the band aid doesn't work. The band aid just wears out and you know, I attended my first national education conference in Framingham, Massachusetts, and as many of those attendees who remember, the flue that followed was a lot of fun, but you know, over the hours we spent talking at the bar, I'm not sure about Alpha's in bars, but that's another thing.

You know, I really understand how the disease works differently in areas of my life and how I can manage them differently. Knowing that there are people from all over, the early internet web groups, you know, Paul Marks and Claude Burrell, you know, I mean that was hope. When you didn't have somebody you could reach out to and talk to. You know, you could tick a tick, how you doing, and those groups still exist in a different form but we have such mass media today we're available more than ever.

You know, my relationship with my

infusion nurses, you know, 17 years later, they're like my dear friends. You know, I'm not so happy when they stick me, but, you know, I know at the end of the day it's all for my good and they want nothing but my best interest.

You know, the question about the ideal treatment plan and, you know, I don't know, I'm not a visionary. But to me the possibility could be real simple. If we could get a state of gene therapy or gene modification, make that misfolding thing stop, just let it flush through, maybe then my lungs will get the needed (inaudible) ace inhibitor, you know, maybe, you know. Maybe just simple things like telehealth. Maybe I don't need to go to my doctor, drive a half hour, be in his sick waiting room. Maybe I can just Skype him and say, doc, (coughing) gotcha. (Laughter.) You know, I mean it doesn't have to be hard, there's a lot of science involved in some of it but it doesn't have to be hard.

Regarding clinical trials, my thoughts have changed over the years. You know, I really

feel the value of coming off of infusion therapy is really important for me today. In addition duration of the trials, number and type of procedures, you know, location, these are all important factors and I do firmly believe clinical trials are in my future again. I think the foundation has done a great job with promoting those and Alpha Net and our sponsors.

Again, I'd like to thank everybody for the opportunity to be here. Thank you.

(Applause)

MS. LIPSCOMB: Thank you, so much, Ken. Marcie?

MS. HEITZMAN: Hi, I'm Marcie, and I would like to personally thank you for inviting me to speak on my son's behalf. Just less than a week after what would have been his 13th birthday. I have a very different perspective than most, as my son is not a success story for Alpha-1. Hunter passed away six-and-a-half months after receiving a liver transplant.

I would like to start from the beginning

of his little life so you can understand more why a cure is so desperately needed. Hunter is our fifth child and when he was born he had no jaundice and was perfectly healthy. When he was several weeks old I would question the color of his eyes because the corners appeared yellow at times.

I took him to the doctor on call and he said that sometimes their livers take time to kick in but that didn't make sense because up to that point he was healthy. We saw his doctor the next week and she was very concerned with the jaundice and did blood work to check his liver functions. They came back elevated and she sent us on to a pediatric gastroenterologist. Hunter had a week of intense testing and when the diagnosis of Alpha-1 came back on December 12, 2002 we were in shock as he told us there is no cure and that transplant is the only option.

He went on to explain that only ten percent of infants would be diagnosed and of those only five percent will need a transplant. He also

said that they had no pamphlets for us on Alpha-1 but to research the internet. He felt that here would be a cure in Hunter's lifetime but due to his age he wanted him with a liver team. He gave him vitamins and stressed the importance of keeping him healthy so his liver doesn't work so hard.

We met with a liver team the end of January and were given hope. Dr. Carpin explained in more detail what Alpha-1 is and by then we had time to go do our own research. The Alpha-1 community reached out to us, embraced us, and they were able to explain, and support, and help us accept what Alpha-1 is.

We were extremely concerned with the transplant but Dr. Carpin did more tests and reassured us that he was doing good and to just continue medication, have weekly check-ups with our pediatrician. We were doing all they asked of us but by late February things began to change. Hunter's stomach was getting very large, but his arms and legs were becoming tiny. Our doctor sent

us back to Dr. Carpin immediately as she said that he was gaining weight due to fluid buildup in his abdomen due to the liver beginning to fail.

We saw Dr. Carpin on March 5th and he was very concerned, started him on a diuretic, gave him more vitamins, changed his formula once again in hopes that fluid would get better. He sent us home with a new plan but then called us each and every day to check on him. The next week he admitted Hunter to Texas Children's Hospital to start IV treatments in hopes to remove the fluid. Hunter was listed for transplant on March 19, 2003.

On April 3rd Hunter received the transplant. I'm sorry. We were so thankful for a new beginning for our son but it was short lived. The next day they took him in for another surgery because his labs were not looking good. It turned out there was a blood clot on the portal vein and this had caused the transplanted liver to fail. Hunter fought so hard the next few days and had to get another surgery, his third in five days. They

received notice there was another liver but Hunter didn't make it. On April 3rd -- or April 8, 2003 at 3:41 p.m. Hunter was in our arms as he slipped peacefully away, as he lost his fight with Alpha-1.

Hunter went through a lot in his short six-and-a- half months. The hardest aspect of the diagnosis was that there was literally nothing to offer him. Our thoughts over and over were how can we live in this day and not have some sort of treatment to give. How can a transplant be the only offer to fix this? How can it be that the best hope is him to not get sick and stay on vitamins?

How well did the treatments work? In Hunter's case the treatments didn't work. He continued to get sicker as his liver failed. By the time he got to transplant he was on 13 medications twice a day.

What are the most significant disadvantages or complications of current treatment, and how do they affect daily life.

Personally I think the biggest disadvantage is that there is no cure and very little treatment.

How did treatment change over time? They used every treatment available at the time and in a matter of weeks Hunter continued to get worse. Nothing they tried worked for him.

What treatment had the most positive impact on your life? The liver transplant had the most impact. His jaundice was gone almost immediately and for the first time in five months my son's eyes were white again.

What would the ideal treatment look like? Ultimately a cure or a treatment that will help strengthen the body to prepare for transplant. Participating in clinical trials. I know without a doubt if Hunter was here he would participate. I would hope that his life would be helpful to making someone want to research and bring a cure to this.

In closing I would like to say that I have four surviving children who are all MC's and I do get their liver functions checked early. I

feel that early intervention and education is what is needed most. We try to stay healthy and do all the right things as Hunter's short life taught us so much. We reached out to doctors immediately. We did all the things the doctors asked. We received the best medical care for our son, but in the end he lost his battle. We had no firsts with him, no crawling, no walking, no birthdays, because of Alpha-1. My hope is that if there is even the slightest chance that a cure can be found that you take every advantage and do so. I know Hunter was an extreme case and the doctors will never understand why it affected him so quickly and so hard, but their research and dedication, treatment, and a cure will give so many others a chance at life that my son never got.

Thank you for your time and I hope my son's story will help you understand the desperate need for a cure for Alpha-1 liver disease.

(Applause)

MS. LIPSCOMB: Marcie, thank you, so much.

(Applause) Fred?

MR. WALSH: My name is Fred Walsh. I was diagnosed years ago and at that point I had two children, two small children, trying to chase them around and having more and more difficulty doing so. And life changed almost immediately as this condition -- it is a gradual thing, a long term condition that you go through many changes along the way, which demands different and varying methods of treatment.

One thing that I hear a lot about, and I was just going to hit on, was the costs. The costs involved with the diagnosis of Alpha-1. The costs financially, the cost of expectations having to be modified, I never fully realized the cost of one's quality of life and changes that have to be made in order to adapt. And the cost of a shortened life, of a life never fully realized. So looking at each one of those, financially we know there's heavy costs with being diagnosed with Alpha-1.

The therapy is increased 300 percent in

20 years, inhalers, as you all know an inhaler can be a $30 co-pay, or it can be a $90 co-pay, or a $120 co-pay depending upon what tier you're on. If a drug is in a particular -- is on that plans formulary, if its brand name, and the on thing that irks me the most about all these, one drug in particular, the rescue inhaler, you have a rescue inhaler that's just brand name. I can't believe there's not a -- that they wouldn't force, that there isn't a generic available because it's the one medicine we all benefit from. Every one of us, they call it a rescue inhaler, and yet we're paying $30 for a co-pay for it. I find it's -- it really makes -- I'm embarrassed that we don't have a generic rescue inhaler out there. So the cost of all the medications that are involved in being Alpha-1.

Other ones, pulmonary rehab. I mean, everybody knows pulmonary rehab is absolutely a necessity to keep ones health in check. It's as important as anything, exercise, and you get a pulmonary rehab program for five, six, eight weeks

and it's gone and unless you can afford the maintenance program, which some many people pay up to $100 a month for a maintenance program at a hospital, or choose to go to Planet Fitness at $10 a month. But you know you're walking into a lot of other people. So a lot of people shy away from that.

Another cost that is associated with therapy and treatment would be nutrition and, you know, you get those gain weight drinks and they're extremely expensive and there's nothing that's prescribed that you'd maybe just have a co-pay for. So those are some of the financial costs.

But there's other costs along with that and that would be one thing I think is just the expectations, you know, you're a young family, you've got a kid, six year old, and all the sudden, bang, everything that was -- but all the sudden you find your world is turned upside down. And everything from savings, what you're doing in your future, everything has to be revamped because you have a sick child with liver disease or you're

40 years old, and you find yourself diagnosed with Alpha-1 and know that you can't go back to the work that you were doing and having choices to make, change of vocation, what do you do? It's very difficult and the spouse or the mate, or the -- what's the word?

MS. ERICKSON: Partner.

MR. WALSH: Partner, thank you. Partner, all the sudden has to take the slack out and it can be a very difficult strain on the relationship and the marriage and the kids are all along and they're saying it too. I mean it's the family dynamics are affected by that.

So what do we need? We need a cure, and we need a cure that gives -- gives us a future to look forward to and the cure is going to be in the liver, you know, some type of liver something or other is going to give us a better chance. Maybe not for us, but for our children. So we've got to stay motivated. We've got a good leader, pit bull John Walsh and we got one coming up who is snarling a little bit in Henry Moehring so

(laughter) so we got to just keep our faces up and alive with the guys to our right.

So thank you. (Applause)

MS. LIPSCOMB: Thank you, Fred. Jesse?

MR. YOUNG: Hi, everybody, my name is Jesse Young; I'm from San Diego, California. I was diagnosed with Alpha-1 when I was eight weeks old. I'm a ZZ. I was born jaundiced, my bilirubin numbers were abnormal. So they did some more tests and came back with Alpha-1. I had a liver transplant at USC Medical Center in Los Angeles in 2011. That's what I've done to treat my Alpha-1. I was 25 years old at the time. Currently I get lab work every three months to check my liver function. I also meet with my hepatologist and transplant team twice a year to monitor my health and discuss any issues. On a rare occasion I'll have to get an ultrasound to make sure everything is working all right and I've had to do a few pulmonary function tests, which have been good so far.

So far the treatment with the transplant

has been very well; it's working for me very well. I'm currently four years post transplant and I've had no major complications. I had to go in for an infection one time and that was it. Pre and post transplant for me were like night and day. The difference it really is just -- my color, I was so yellow before the transplant. I wasn't the same person. And then after transplant it was like a switch went off. I could do all the things I wanted to do. I could mountain bike and play softball and hike and it really is just amazing.

Some of the treatment disadvantages that affect my daily life are that now I'm immunocompromised because of the transplant so I have to take the anti-rejection pills. Remembering those can be a pain some times, every 12 hours, but a small price to pay. It's also difficult when I have a little toddler running around and he touches every germy thing in the world so I have to catch whatever he's running around with.

Before the transplant I was a veterinary

technician and I can no longer do that because of the high risk to infection. So when I go back to work I'll have to find something new. Luckily I've been able to be a stay at home dad for the last three years so that's worked out for me.

Some of the ways my treatment has changed over the years, since I was diagnosed so young when I was an infant I was on a special formula called Portagen that would often make me projectile vomit and so that was not fun for anybody around me. As a child I was on ursodiol for a short time but they determined that they couldn't tell whether that was helping or not doing anything at all. So we decided to discontinue that and then when I was 16 through 24 years old I required no medication. I leveled out since I was an infant from my childhood to my teen years and I was doing great.

And then when I turned 24 everything just went downhill. My liver decided it was not working with me anymore. I then needed various medications to management the complications of

liver failure. I was on diuretics the ascites; at one point I believe they tapped ten liters of fluid out of my left lung. So not breathing is not fun, I know this room knows that. I had insomnia very bad, cramping, I was on a low sodium diet, and it just completely changed my personality until I received the transplant when I was 25 years old. Excuse me, some of the negative aspects of my treatment, the anti-rejection medication they can be really hard on your kidneys so I could be looking at a kidney transplant eventually and they can also -- they put me at a higher risk for diabetes and skin cancer.

The treatment that has most affected -- the most positive impact on my life was, without a doubt, having the liver transplant. I had a live donor transplant when I was 25. My girlfriend at the time was my donor. So without her I would not be here today, shout out to my wife now. The day after I got out of the hospital I took her out for our belated anniversary and I proposed. I decided I really couldn't live without her (laughter.)

Since then we've gotten married and we have a -- he's almost three now, a little boy and we have a daughter on the way, next month, soon. And so I have that going for me, which is amazing.

If I could create my own treatment, I honestly don't know what it would be but I know that transplant can't be the only thing. It's just cutting it too close; you're at the end of the rope when you get to that point, so I'm not sure. Alpha-1 has just affected my life from day one. It sent me on a different path at different times. I couldn't join the military when I turned 18. I couldn't follow in my father's footsteps. Knowing that it could eventually affect my children's children is really hard. I don't -- so I also just want to thank my parents. I can't imagine how they deal with stuff being the parent of an Alpha. To all the parents.

Thank you. (Applause)

MS. LIPSCOMB: Thank you so much for sharing. I think all of our panelists did a great job. Let's thank them again. (Applause) Now not

surprisingly we're running a little bit behind but before we get to asking questions we are going to have a presentation from -- of the Alpha-1 Foundation survey data that matches this and we're going to invite Gordon Cadwgan to come forward. Was it close?

MR. CADWGAN: That's very close.

MS. LIPSCOMB: (Laughter) Well, thank you.

MR. CADWGAN: Everyone in the Alpha community knows to pronounce it Cadwgan.

MS. LIPSCOMB: Cadwgan.

MR. CADWGAN: All right.

MS. LIPSCOMB: Well, here he is. (Applause)

MR. CADWGAN: Well, thank you. Thank you for the invitation to come to the FDA and thank you to our afternoon panel. I think it was an outstanding panel and it certainly is a wonderful presentation as this morning.

So I'm going to talk a little bit more about the Alpha-1 survey or I should say, yes,

what is my position. I'm Gordon Cadwgan, diagnosed with Alpha-1 in 1992 and have been working diligently for the last eight or nine years to forward our mission at the foundation. I'm now chairman of the board of the Alpha-1 Foundation.

So the results I'm going to talk about we were asked to look at our current treatments, lung affected and rate them from extremely dissatisfied to extremely satisfied with categories in between. Five categories top to bottom. So I isolated the data for percentage of a respondents who are either satisfied or extremely satisfied with each of the areas I'm going to mention.

IV therapy, now remember we had 1300, plus, individuals, responding to this. IV therapy, 75 percent of the individuals on IV therapy said that they were satisfied or extremely satisfied with their IV therapy. I might point out that that IV therapy began approximately in 1990 and we owe the FDA a great debt for, in my

opinion, going out on a limb and approving a new therapy which had not been used or tried ever before and the only condition was that they follow Alpha's, as many of you know, a thousand Alpha's for five years, and report on those results. So kudos to the FDA for doing that. (Applause)

Oxygen use, only about half of us, 54 percent are happy, are satisfied or extremely satisfied with our oxygen therapy. Inhaled therapies, approximately the same, 60 percent say they are satisfied or extremely satisfied. Oral steroids, as you can expect, as we all know that's an double edged sword, 40 percent are satisfied or extremely satisfied. Prophylactic antibiotics, I was surprised at the number of respondents saying they are -- 20 percent said they are satisfied or extremely satisfied using prophylactic antibiotics.

Positive comments from our responders about IV therapy. I have less infections. My lung function is either stabilized or only declining slowly. My home infusions work very

well and many credited IV augmentation therapy with saving their lives and allowing them to be as healthy as they possibly thought they could be.

Now obviously there are also some things that aren't good about IV therapy. It's inconvenient. I have to do it too frequently. Where it is administered, if that's a clinic or a hospital. The cost and access to that therapy.

And finally, the efficacy. In other words, many of us still experience a decline in lung function in spite of being on the therapy. People say I hate needles. I hate that every week treatment, it's too long travel time to the clinic or the hospital. I worry about catching something at the clinic or the hospital. I used to be able to do my infusions at home, my insurance changed and now I have to go to the hospital.

So here are a couple of other quotes. Augmentation therapy saved my life. No hospitalization since I've been on augmentation. I can honestly say that the difference from having no augmentation therapy to having augmentation

therapy is monumental. Before therapy I knew I wasn't going to be long on this earth, granted, it took a bit of time, but my quality of life had improved tremendously. I have a life again. It gives us a fighting chance.

Oxygen use. Obviously it helps those of us who are oxygen therapy. It helps us with our day-to-day activities. Exercise, and just breathing and breathing normally.

The negatives. The heavy tanks or a concentrate are hard to pull around. It's embarrassing sometimes. People stare at me. It tends to dry my sinuses out and cause sinus problems. I have to plan my trips carefully to make sure I have enough medical and supplies to take care of my oxygen needs.

Inhaled therapies. The positive, of course, is that many individuals feel that they work very well for them. Short lived, the negatives might be that they're short lived; they don't seem to help the side effects of not being able to breathe. It's only temporary relief, no

perceived improvement in my breathing ability when I use them and, of course, you can't tell if long term inhalers, excuse me, are doing any good and of course the one person mentioned thrush and if you've ever had a thrush infection you know how debilitating and painful that can be.

For liver affected, current treatments, very few treatment options for liver affected Alphas. Few people reported even using any of the available treatments. But those that did use treatment said that they were satisfied with those treatments because it was all that was available. Liver transplant, 22 percent who have had liver transplant were very happy with that transplant.

Ursodiol, use of ursodiol, 13 percent were satisfied or extremely satisfied. Paracentesis, 13 percent said they were satisfied or extremely satisfied. One liver transplant said the last place any Alpha should be to get any treatment is in a facility where there are a lot of sick people.

(Applause) Non-clinical therapies.

Thank you. Non-clinical Therapies. I was amazed at some of the things that people identified. Non-clinical therapies, people said their Alpha-1 support group was the best therapy, 64 percent said that that was the best therapy they had after their medical therapies.

Next was peer guidance. So just talking amongst ourselves means a great deal to everyone. Lots of people reported having mental health treatment for obviously depression and other issues. I would hazard a guess that most of us have had this problem. It's no different than dealing when you're first diagnosed. It's no different than dealing with a death in the family. You have to go through the stages. You've got a lot to learn, you've got a lot to deal with, you've got a lot of reorganizing of your life to do, and that causes tremendous stress and anxiety. If you have a significant other, a great caregiver like many of us do you've got half the battle won.

Biggest challenges I had mentioned with

current treatments, the inconvenience, the cost. We want a more efficacious treatment.

What would be the idea treatment? Percentage of respondents who chose each of the areas below. Less expensive, 70 percent said that was top. Oral, nasal or sub cute administration, 70 percent chose that. Longer lasting, 55 percent. Gene therapy, 50 percent, and home infusion treatment 40 percent.

A quote, I'm worried sick about being able to afford my medications. Depending on my insurance we would have to come up with $3100 out of pocket per year. That is almost $300 per month extra. So we had to decide, what do we cut back on? Food, clothes? It worries me sick. I cannot share this with anyone.

So obviously it would be wonder to have -- I love seeing the pills up on the slide this morning, it would be wonderful to have a pill but that is highly unlikely that that's going to work for Alpha-1. Gene therapy is a great possibility that is coming forward.

Thank you, very much. (Applause)

MS. LIPSCOMB: Okay. Thank you so very much. I was remiss, we skipped one of our new FDA panelists, and I want to give him an opportunity to introduce himself before we start.

MR. CHAZIN: Hi, it's Howard Chazin. I'm deputy director, division of hematology, clinical review in the Office of Bloor Research and Review in CDER. Thank you.

MS. LIPSCOMB: Thank you so much. Just by a show of hands, how many have heard your own experience with treatments be it in costs or how it's affected you in one of the stories.

(Pause) That's a good number. I think it's about 100 percent.

(Laughter) We're going to go ahead and begin a few more polling questions and get back to the discussion.

Chris, can you go to the next one? In the past year what therapies have you or your loved one use to manage anything with your lung

symptoms? There's -- use of inhalers, oral antibiotics, antibiotics given by injection, oral steroids like prednisone, steroids -- other steroids or by injection. So you guys can read, I'll let you continue looking at that. If you are on the web and you haven't gotten -- you should have a polling question come up and when you hit it you might not notice right away that it's taken, but it has. If you're writing a comment, just a reminder to hit the enter button when you've done writing the comment so it will take for us.

All right. So we'll -- I won't close the web one right yet, but let's go ahead and close the on-line.

(Laughter) Well, there are -- everything but no treatments it appears. Use of inhalers and oral antibiotics and oral steroids seem to be prevalent. Can we close out the one on the web now and see what we have?

AUDIENCE VOICE: Use of inhalers was 84 percent, oral antibiotics 78 percent, oral steroids 68 percent, respiratory treatments given by a nebulizer at home 59 percent, those were the most frequent.

MS. LIPSCOMB: Okay. Great, thank you. So let's follow up on these. About seven percent have other therapies not listed, does anyone pick up that would like to talk about that?

MS. HELLER: Hi, my name is Laura Heller and I had a wonderful doctor in California a year-and-a-half ago give me sodium chloride seven percent for nebulization and I mix that with my albuterol and it helps being everything up without all the fighting.

MS. LIPSCOMB: Okay. Thank you. Any other?

AUDIENCE VOICE: I've just recently been having great success with a really old drug, theophylline, which is a pill form of like albuterol and it's really helped me out a lot in that I'm not sitting five different times during

the day with a nebulizer, it allows me to live life a little bit easier.

MS. LIPSCOMB: Thank you, so much. Well, the rest of you what's been the most effective treatment that you've had? Anyone want to talk about that? What they've seen is most effective?

MS. WARREN-HENDERSON: Donna, do you want to do her? She had her hand up for the last question as well.

MS. LIPSCOMB: All right.

AUDIENCE VOICE: One of the things that's been most helpful to me in recent years is regular massage. I have a therapist who comes every week, (inaudible) my back and feel if there's any congestion in my lungs and gets me working again. Now, it's an expensive hobby or treatment, or habit I guess really, it has done wonders for me. I will be 77 years old, my Alpha-

Therapy has worked beautify, my FEV1 is not much lower than it was 30 years ago. So I've been very blessed and I've done lots of holistic

things to maintain my health and the best one is regular massage.

MS. LIPSCOMB: Good, thank you. (Applause) We're going to try to give everybody a chance to speak but.

MR. CORRON: Thank you. My name is Tom Corron from Indiana. I would have to agree with whoever brought up the pulmonary rehab the first time. My quality of life improved so much between the before and after of that and I also want to highlight the support groups as well, and then also the coaching from the -- the health management coaching that's given by my Alpha Net coordinators over the years. So those three things.

MS. LIPSCOMB: Thank you. All right.

MR. STOKEL: It's me again. (Laughter) I would say when I -- prior to the transplant I would say it was inhalers but I have some serious issues with them. Number one, there are still inhalers that don't' have counters on them. I mean, how the hell am I supposed to tell -- if it

says I have 200 inhalations, am I going to sit there and tick each one off in my diary every single day? No.

AUDIENCE VOICE: (Inaudible)

MR. STOKEL: Or you can try magic marker on the side and I know all that kind of stuff but you want something that's accurate, clear, you can take a look at it. Most of us have failing eyesight due to the steroids; we develop all kinds of cataracts. You know, it's not an easy life, quite frankly. Now, with inhalers if you can put a counter on every single inhaler that would make life so much easier.

Secondarily, if you could also push the manufacturers on the covers to the inhalers, the covers to the mouthpieces, if they could make those out of the plastics that are antimicrobial because one of the worst things about having an inhaler, you're going through the airport check-in or here, and they say put your inhaler in this little box. You look in that little box, it's got stuff growing in it and you want me to use that as

a rescue inhaler and I've already got Aspergillus, MAC and God knows what else growing in my lungs. Just a little thought.

MS. LIPSCOMB: Thank you. He clearly was reading my paper which said what are the disadvantages of some of the treatments. So thank you for having, you know, (laughter) a little ESP.

MR. YOUNG: I'm D.C. Young from Utah. I'd like to follow up a little bit on Tom Corron's comment. I can't help but follow Tom Corron. Pulmonary rehab, I have a lung function that's surprisingly above 50 percent and has remained there for 13 years now thanks to augmentation. And my doctor says someday you're going to get pulmonary rehab and I say, well, what does pulmonary rehab do and they say, well, it helps you preserve lung function. Well, I want to preserve lung function now, why do I have to get sicker before I can have pulmonary rehab (laughter?) I've never understood that but my insurance won't pay for it. The doctors say, no, I can't prescribe it because your insurance won't

cover it.

MS. LIPSCOMB: Thank you.

MS. CHAKRAVORTY: Bonnie Chakravorty from Nashville, again. I'm just going to talk about pharmacological treatments for exacerbation. I find that prednisone has been very helpful. The problem is the side effects are not very pleasant. I bounce off the walls anyway. So it contributes to that, but when I do have to take them over a long period, I have developed osteoporosis over time and osteoporosis can disqualify one for a transplant. And it's a choice of would I want to continue with high dose prednisone. I have had my prednisone decreased but it is very helpful. But I have found it helpful in exacerbations.

MS. LIPSCOMB: Thank you.

MR. LIBBY: Good afternoon, my name is Bill Libby from San Diego and my son has recently become a chiropractor and it was while I was -- he was in school while I was diagnosed and so he was focusing on the lungs during his time in school and I find that he had found adjustments that

relieve the pressure on my lungs and I am able to breath after adjustment. So chiropractic.

MS. LIPSCOMB: Thank you. Is there -- what's the web? Is there anything from the web that --

MR. PIERCE: We have quite a few comments. Actually one was -- one individual said that they were unable to take one brand of augmentation therapy because of an allergy to a preservative, there was also concern raised, as was mentioned here, about osteoporosis from steroid use and a request for needing better drugs. There were comments regarding not being able to afford augmentation therapy. One person indicated that their annual -- or their expenses for this condition in their family went to over a million dollars and they had just lost coverage for their pulmonary rehabilitation. There were several people who are interested in the promise of gene therapy and also people wondering about using stem cell therapy and correcting the defect in stem cells. There was interest to know whether

gene therapy clinical trials had begun. So those were some of the web comments.

MS. LIPSCOMB: Great. Thank you. Well, I want to focus now, one of the things we heard was on transplantation. So we want to focus a little on that and we're going to ask you two questions before we come back and kick it back out. But I also want to ask the operator to open the phone line; we'll take a question from the phone on this.

So Chris, could you go to question 11? Thank you. Have you or your loved one undergone lung transplantation for emphysema because of Alpha-1.

Ah. Now let's try this again. Now, go. Sorry, if you click forward too fast which is a mistake -- thank you -- All right, let's see what we have there, Chris. So 18 percent have. What about on the Web.

MR. DURMOWICZ: For lung transplant the Web is about percent.

MS. LIPSCOMB: Ten percent okay; 18 and

10. Let's go to question 12. We have undergone liver transplant. All right, Chris go ahead, and let's see these. Oh, 6 percent. How about on the Web? They stopped the voting?

MR. DURMOWICZ: The liver has about 6 percent.

MS. LIPSCOMB: About 6 percent, too?

MR. DURMOWICZ: Yes, the same.

MS. LIPSCOMB: So we have about the same on both. For anyone who has had impact, has had a transplant, what's been the impact of that transplant?

MS. GOULD: Actually on lung transplant. My name is Cathy Gould. I had a lung transplant four years ago, and my life has totally changed. I am doing everything I can, ever I dreamed of. I'm 72 years old, and I'm doing things I couldn't do at 50. I enjoy life, my PFTs are 140 percent, but I want to tell you that it's so important, is exercise. I had, like, 8 percent lung function before I got my lung transplant, and I was on a treadmill, and I can't say I was actually walking,

but I was moving on it.

I was lifting weights, I still exercise as much as I could with hardly any ability to breathe at all, and even now I go 5 days a week for two hours a day. Thank you very much.

(Applause)

MS. LIPSCOMB: I'm a little ashamed here.

MR. PRICE: My name is Chuck Price, I had a lung transplant 2013, April 28, 2013, and like the lady said, it's just night and day, going from oxygen. I was at 9 percent lung function, and again, she's right, exercise is -- you know, pre and post is the only way to go. I wasn't diagnosed -- I'm 46, I wasn't diagnosed till I was 41, and by then my lungs were destroyed so they just kind of led me through till they could get me on a list.

I went to UVA. I actually got the call on my grandfather's 100th birthday, for my transplant, but yes, night and day. I didn't have any augmentation therapy prior to the transplant,

and actually on none now, and doing pretty well. The same thing, lung function well above 100 percent, and this -- I grew up with a training background, prior to becoming sick with Alpha-1, and I was a power lifter, worked in the iron industry and was a lot heavier than I am now. But, yeah, like I said, I cannot think of another way, I don't know what the augmentation was like, so I don't have anything to compare it to other than the steroids and corticosteroid and stuff.

MS. LIPSCOMB: Thank you. Jennifer?

MR. QUILL: Hi. Donovan Quill from St. Louis, Missouri. The impact of getting a transplant, I think you ought to look back through the journey to get to that point, and obviously transplant comes when it's kind of the end, you have no other choice. But the impact that we had as kids growing up and watching our hero, our superman go to basically nothing, lying on a couch with oxygen on 24 hours a day was very tough.

And getting to that point and watching, you know, dad go through that was one of the

hardest things to get through. Now, he's superman again, and he has that with his grandkids and, you know, running around with them last week, so I'm glad that we have transplantation, but the impact of getting to that point is tough on kids and tough on the family. So, you know, my mom was a rock through the whole thing. So, thanks.

MS. LIPSCOMB: Thank you. Do we have anybody on the --

AUDIENCE VOICE: I have one more in the back.

MS. LIPSCOMB: Well, I'm going to find out if we have anybody on the phone. Do we have anyone on the phone?

AUDIENCE VOICE: Yes. We do have a comment from Nora.

AUDIENCE VOICE: Yes. My name is Nora, and I'm calling from Iowa City. Can you hear me?

MS. LIPSCOMB: We can. Thank you.

AUDIENCE VOICE: Okay. I opt to attend but I am tired up from a previous travel, so I couldn't come. I was diagnosed at age 64, and the

day I found out I have Alpha-1, I had never heard of it, ever. And I work in an academic medical center for 20 years, and yet I had never heard of it.

So, I'm a ZZ Alpha, I'm doing pretty well. I've had augmentation therapy, I'm liver -- excuse me -- lung affected, and both my parents died fairly early from application during the fact that it's a liver heterozygous. They both had one alveol, they were MZ Alphas; they smoked, my dad drank, and it helped them.

I would like the FDA, or another Federal Agency, to make a public awareness and public education campaign to all kinds of media, because the Alpha Foundation cannot do it all, we individuals Alphas cannot do it all. We need to really go public on this. It's not a hidden disease, it shouldn't be a hidden disease. It's not even rare. If you consider the heterozygous folks, about 1 in 25 Americans has either homozygous or heterozygous Alpha-1. That's what I have to say.

MS. LIPSCOMB: Well, thank you for that.

MS. MONZO: Hello. My name is Natalie Monzo, I'm here on behalf of my daughter's father, who passed away from a lung transplant a month ago today. So transplant doesn't always go as easy as it's supposed to, he had the double transplant in February, he was diagnosed in 1999 with Alpha-1, and it's been very, very difficult. So what transplant has done for my daughters is it's taken from their father from them.

MS. LIPSCOMB: Thank you. I know there's a lot more to say, however we have more to get through and time is ticking away. So, please, this is one of those prime areas where I encourage you to go to the docket and additional comments. So please don't think I'm meaning to cut this conversation short, I wish we had all evening to do this. Can we go to the next question? We are going to now focus on augmentation therapy. "Are you or your loved one currently receiving augmentation therapy?" Okay, let Chris -- Wow. That's overwhelming. What's the result from the

Web?

MR. DURMOWICZ: Went to about 85 percent, 86 percent.

MS. LIPSCOMB: Okay. So, very similar. The next question? "If you or your loved one are being treated with augmentation therapy what is the current frequency of your treatment regime? So, only treated at the time of -- needed; regular treatment every week, regular treatment every two weeks, every four weeks or less often." Okay, Chris, let's see. Oh! Overwhelming majority: regular treatment every week. What about on the Web?

MR. DURMOWICZ: It's very close, about 88 percent.

MS. LIPSCOMB: Okay, great. Thank you. And question 15, "If you know your dose, do you receive a dose higher than 60?" If you guys know what that means; "Yes, no, I don't know my dose." And we'll give you just one more second. Yes, Chris. Okay, so 31 percent does have a higher dose, and 60 percent do not, and 9 percent aren't

sure of their dose. What about on the Web?

MR. DURMOWICZ: Again, it's very similar. It's just about 38 percent that have a higher dose, and about 12 percent don't know their dose.

MS. LIPSCOMB: What's the next question, Chris? "Which of the following best describes how you or your loved ones feel about your current treatment regime? You are satisfied with your current treatment and do not want to change it? You are satisfied but are willing to consider new options? Or C, you are not satisfied?" Okay, Chris, can we see what the results are?

Okay. So, I think the majority in this poll are satisfied but are willing to consider new treatment options. What about online?

MR. DURMOWICZ: Again, it's very similar.

MS. LIPSCOMB: Thank you. So, I guess it --

MR. MATTISON: My question is a bit deceiving, can you split that out for being long,

for the results of (inaudible) --

MS. LIPSCOMB: Okay, let's talk about that. So for those of you who are doing treatment for long, is that what you think the most of it's the 76 percent?

AUDIENCE VOICE: Yes, it is.

MS. LIPSCOMB: Okay. So then let's talk --

AUDIENCE VOICE: And that's the liver patients since they (crosstalk).

MS. LIPSCOMB: And we are going to ask that question. For liver patients, what would you say? Okay, so for those of you who are satisfied, what's your biggest reason why you are satisfied? And we'll kind of parse this out, and you can stand up and say what your issue is.

MR. MATTISON: If I can (inaudible).

MS. LIPSCOMB: Sorry?

MR. MATTISON: We would like -- consider new options.

MS. LIPSCOMB: That you are willing to consider new options. But what would -- Okay

then, I guess the question -- Let me clarify what I'm asking then. What would you look for in a new option? Ah! There we go. Okay, we hear a cure.

AUDIENCE VOICE: Easy access.

MS. LIPSCOMB: Easy access, they are also (inaudible).

MS. FORTIER: I'm Courtney, and I actually did one of the trials with doubling my Zemaira dosage, and it's a world of difference, and that's why I'm not -- I'm satisfied with what I have, but I'm not satisfied, because we definitely need increased dosage on it.

MS. LIPSCOMB: Okay.

AUDIENCE VOICE: I have someone, Donna, back here?

MS. LIPSCOMB: Okay.

MR. FROST: Tim Frost, from Virginia. Also on this question of dosage of augmentation, one of the questions I have is at what point, for those of us who are lung-affected, do we start our augmentation therapy? Do we need to be at severe COPD Emphysema before we get augmentation therapy?

We've heard from many people who say that with augmentation they feel much better, but many of us had to stop work because we were at severe emphysema we were feeling with augmentation. But can we start at an earlier age, so that our lung function stays higher longer and makes us much more productive in society rather than having to be retired from our work? Thank you.

MS. LIPSCOMB: Okay. Thank you.

MS. STOKES: Maybe base the augmentation, start on your level, instead of waiting to -- for a dysfunction. That's seems -- Why are you going to make someone dysfunctional, or handicapped in a society when -- if you can start something earlier, you can avoid that?

MS. LIPSCOMB: Okay.

MS. WARREN: One more, Donna.

MS. LIPSCOMB: All right.

AUDIENCE VOICE: Hi. I'm Wendy from Virginia, and I have a 5-year-old son who was ZZ liver affected. I would like more options for my

son.

MS. LIPSCOMB: Thank you. That was quick, so another?

MS. FARIS: My name is Katie Faris, I'm from New Jersey, and I'm the mother of three ZZ children, and I'd go with what this last woman just said.

MS. LIPSCOMB: Thank you. We have someone over here on this side?

MR. MATTISON: My name is Charlotte Mattison, and one of the things I fight for is early diagnosis. Early diagnosis so we can put people on augmentation therapy, or therapy for liver problems, so that we prevent. The key thing we hear now from health care is prevention, and we are not really working that hard toward it. Early diagnosis, get them on the proper drugs, the proper treatment, and we prevent the decrease and decline of a person's quality of life.

MS. LIPSCOMB: Okay. Great. Thank you. While we are asking this, I guess my question is; do any of you have any concerns over long-term use

of the therapies you are on?

AUDIENCE VOICE: Hi. I'm Brad from Kansas City, Missouri. I'm a parent of a ZZ Alpha, and I just wanted to echo these comments again, there are no options for our children other than the doctors told us, watch them, see if he gets sicker, he might need a transplant, he may not survive, or he might get better. And that was it. And so we need something for our children. Thank you.

MS. LIPSCOMB: Thanks. Jennifer?

MR. LYNCH: You know, the previous speaker said about this thing of being fairly well and getting augmentation, the same thing applies to the transplantation; the person has to be practically at death's door before they get it, and therefore they are less likely to survive it. In my own case I was diagnosed very early and it's helped me for 25 years almost at a certain level, so in as much as it can be supported and covered by insurance, I don't know how the insurance company look at it, but we all know it's extremely

expensive. So, if you are getting it for 25 years, or 10 years it's a very big difference. Thank you.

MS. LIPSCOMB: Well, that was a wonderful segue into our next question. Thank you. And he was not a plant. Chris, the next question? "So, what's your level of concern regarding the cost of augmentation therapy? Are you not concerned, mildly concerned, moderately concerned, or very concerned?" Okay, Chris, can we get the responses? Ah! I could have guessed this one, I might even have given it that number too. So, what about on the Web?

MR. DURMOWICZ: There's 88 percent that are very concerned, so it's very close.

MS. LIPSCOMB: Okay. Thank you. Does anyone have any thoughts about cost concerns that's not already been expressed? Okay.

MR. MOEHRING: I'm Henry Moehring. And I think one of the things that we need to look at in one shape or another, and I'm not sure who it falls to, but we talk about the cost of therapy,

we don't talk about the opportunity cost of therapy. If people are not on augmentation, if people are not using their medication, and have multiple exacerbation, multiple ICU stays, those costs are never stacked up against augmentation, and I think that the supposition is if you did that, you would see that providing the therapy is the more cost-effective way to go, and I think that's something that we need to push forward faster to have better answers for questions on some of these.

MS. LIPSCOMB: Thank you.

MS. CORRON: Again, my name is Allison Corron. And I'd like to speak as a patient advocate. The patients in this room are all very lucky, they are of a financial persuasion that they can afford insurance or therapy or both. I think we need to speak for those patients who are lower, middle class, who have this condition who are what we would maybe call the working poor.

They are working at minimum-wage jobs, they can't afford to quit, because that's how they

get their insurance. They can't afford insurance without a job. They certainly can't afford this therapy without insurance. I have many, many clients who are still working and trying desperately to pay for their medication, just their co-pays, and while there are some financial assistance programs available, those financial assistance programs are running out of money at an extremely high rate, and very, very early in the year.

So if you are diagnosed in January, you might be able to get financial assistance. If, however, you are diagnosed in July or August, you may not be able to get any financial assistance for you medication.

MS. LIPSCOMB: Thank you. We are going to take one more on this one.

MS. CADWGAN: My name is Ruth Cadwgan, and I want to touch on, kind of what Henry said, in that, why are we going -- why aren't we backing up to eliminate some of the cost going through this horrible process of getting to the point

where you are able to comply with getting a transplant? You know, that's pay it forward instead of pay it back and wait till people suffer.

And the other thing, I wanted to touch on the numbers for the transplants. I think everybody in here that I heard regarding transplant, was less than 10 percent, usually 9 to 8 percent, which is barely living, and that's how sick you have to be to get there, and part of that is the allocation.

Now I'm going to step out and say something that I only know from life, but I believe it was changed a while ago, and it was implied that Alphas do better than some of the other conditions that require a lung transplant, Alphas live longer, even if they only 7 percent lung function. And so I think even the allocation system for who gets transplants also needs to be looked at.

MS. LIPSCOMB: Thank you. Again, I think this is one of those cases where there's a

lot of more discussion we could have but we have to move on because we are already about 40 minutes behind. So, can we go to our next question? "If you are not currently on augmentation therapy, would you start with an inhaled formulation if one were approved?" Okay. I think maybe hypothetically-speaking, is what we are going for here? I clearly did so.

(Off the record discussion)

MS. LIPSCOMB: Well, then we won't talk much about this when we see it if this is -- Can we go ahead and see the result? Okay. So, between those of you who on it already -- Let's go to the next question, "If you are currently receiving augmentation therapy what factors would influence the decision to possibly switch to an inhaled formulation if one were approved by the FDA?" Check all that apply.

Convenience, tolerability, efficacy is compared. Well, the ticker stopped going out, so let's go ahead and see, I know we don't have very many responding right at this point. Okay. So,

convenience is a big factor. What about on the Web?

MR. DURMOWICZ: I think you could have had an, all the above, answer.

MS. LIPSCOMB: Oh. Thank you. So, we don't have much time to really talk about this, so we can only take like two responses. So, I guess my question for you is; "What considerations helped you answer this question?" I think I see someone's hand that I haven't heard from Lonnie, over there.

MS. FOULL: My name is Jenny Foull from Pennsylvania. And the only thing that I can add to that, the convenience, tolerability, efficacy and cost, and the consideration is, I have a benefit that I receive from augmentation therapy that isn't -- what I understand is typical. I was diagnosed with fibromyalgia before I was diagnosed with Alpha-1 Antitrypsin deficiency. When I started augmentation therapy, within two months I no longer had the symptoms of fibromyalgia at all.

And I believe, I've been told that that

it's because of the high anti-inflammatory properties of the protein. So, for me to go on an inhaled version of the therapy I am concerned because I might lose that systemic benefit. And honestly in the nine years I've been on therapy my life is so much better than being off of therapy and having the symptoms of what was called fibromyalgia. So, that's another consideration that I have in another kind of therapy.

MS. LIPSCOMB: Okay. Thank you. Let's, because we are behind, let's spend a few minutes talking on what you think is an ideal therapy. The next slide, Chris? "So, tell me how existing therapy --" and I know we've mentioned that some of these questions are -- you've hit on in other questions, so what we are really going to ask you talk about are, what do you think, how current therapies could be improved, or what are you looking for in an ideal therapy? And any other comment, that has not already been discussed today. Bonnie?

MS. BUCHANAN: I think the big question

is the cost of the therapy, otherwise probably the room would all value the therapy forever.

MS. LIPSCOMB: All right, thank you. Thank you.

AUDIENCE VOICE: I would like to suggest that we find a therapy that we can give ourselves, we don't like to have to go to the hospital, or have people come in to give it to use, you can see we are all responsible we do what we can, so give us a form of therapy, augmentation if necessary, that we can actually do ourselves, and we'll do it.

MS. LIPSCOMB: Okay. Great. Thank you. All right, I have a couple --

MS. GOULD: Cathy Gould again. I ran a support group for about 12 years, and two of the people in my support group also got lung transplants, the only difference between them and myself is that I continued on the augmentation therapy, and I don't know exactly how this works even though I'm a nurse, but the other two didn't.

Their doctors didn't keep them on IV

augmentation therapy, and they were in the hospital, in and out, they are still -- right now one of them is in the hospital, and I can actually say I never went. Since I've had my therapy I've never been in the hospital, and I've continued for 16 years with my augmentation therapy. So the efficacy of it, I believe, is 100 percent. Thank you.

MS. LIPSCOMB: Thank you so much. Lonnie, do you have someone?

MR. GEIGER: Hi. My name is Glen Geiger. I'm a ZZ Alpha-1. I'm one of the lucky ones, in that I was the one diagnosed instead of a loved one, because I don't think I could have handled that. Also I'm one of the lucky ones in that I had a lung transplant, so I'm 13 years out with double lung transplant. But the topic that I just wanted to bring up was compliance with medication. Efficacy is tied to compliance, right, and the easier it gets to take a medication the easier it is to not take a medication.

It's like blood pressure medication. I

mean, how many people are actually complying with that, or even your own inhalers? How many people really use that Long-Acting Beta Agonists on a routine basis, as it's supposed to be given? A lot of people don't, and so that's just a concern that I'd like to bring up. I mean, if you have an appointment every week, or a nurse comes to your house, or you have an appointment where you go somewhere, you do it. And you might miss a week or two, but you just don't fall off the grid, because nobody is really tracking you anymore.

MS. LIPSCOMB: Okay. Thank you. Jennifer, do you have someone?

MR. FROST: Tim Frost again, from Virginia. We've been talking a lot today about Alpha-1 and Antitrypsin deficiency as a liver disease, as a lung disease, I'd like you to be thinking more strategically, more holistically. Let's think, and we've been talking a lot about strategies for dealing with symptoms; let's look for strategies dealing with causes. So there's an awful lot of very promising research being done

right now that is intended to arrest or possibly even reverse the Alpha-1 Antitrypsin liver disease.

Let's think about some of those where our livers are no longer creating the malformed Alpha-1 Antitrypsin, that we may have therapies using stem cells, or using genetic therapies that allow us to create the proper Alpha-1 Antitrypsin. And then let's think about lung disease, are there therapies that can help us reverse the causes of our lung disease, and reverse the damage to our lung tissue?

We hear the miracles from a number of our colleagues who have gotten a liver -- excuse me, a lung transplant and a liver transplant, and how transformative that is. Can we do that with the tissue that we have on our own? Let's think innovatively, let's think aggressively on how we can cure Alpha-1 Antitrypsin.

MR. QUILL: My name is Jim Quill and I'd just like to touch on a few things that have been said as far as treatments are concerned, and one

of the -- probably the most effective treatment that I had when I think about the fact that I've had a transplant. I've lived many years with Alpha-

Prior to the transplant. But probably my most effective treatment was AlphaNet. And the reason I say that is because my AlphaNet coordinator was extremely instrumental, first of all, it was someone who also had Alpha-1, and it was someone who was constantly reinforcing all the things I needed to do to keep healthy.

You know, making sure that I had my vaccines, making sure that I was keeping my doctor appointments, making sure that I was doing my augmentation therapy on a weekly basis and staying on schedule, making sure that if I was taking trip, I knew what I needed to do as far as oxygen adherence was concerned. And all of those things medically that we need to do to stay healthy, and I know it was mentioned a lot and in pieces here today, but I know through AlphaNet, and I hope everybody here that is an Alpha is connected to

AlphaNet, because it's is through that program, that truly has brought me to where I am.

And it's also, I think that it's the hope of all the AlphaNet coordinators, and there are many here in the room, that are here as Alphas themselves to participate, but they are also here as advocates for all of you, and I'm certain that if you connected with your AlphaNet coordinator, and listen to the sometimes annoying, you know, the nudging they do every month, but all of it is in the avenue of keeping you well, and helping you to adhere to all the things that we talked about today. So thank you for the opportunity.

MS. LIPSCOMB: Thank you. All right. I have an inkling from enthusiasm of these conversations that you guys have a lot more that you might want to mention. Again, go to the docket. And we are going to go to our next section, and I'm going to go ahead and thank our panelists up here, and they can go ahead, let's clap, and we are going to talk about clinical trials. You can go back to your seats. (Applause)

And for this, operator, we'll open the phone line and take a bit of questions about clinical trials. So, this is going to be your perspective on participating in a clinical trial, and I think, based on based on some of the conversations I've heard we've got people who believe strongly that they would they would, and strongly that they would not. So, it's really what we are going to be exploring a bit more.

So, Chris, can you go to the next question? "So, if you have the opportunity to considered participating in a clinical trial studying experimental treatments, what things would you consider when deciding whether or not to participate?" I guess this is not a question; this is just kind of asking you, what would you consider?

AUDIENCE VOICE: I've seen some trials that a part of the group is on a placebo, and my lung function isn't good enough that I can risk being on a placebo for six months or two years, or whatever the duration.

MS. LIPSCOMB: Okay. Lonnie, did you have someone?

MS. WARREN-HENDERSON: I thought I had someone, but I don't.

MS. LIPSCOMB: Okay. Then I have someone who I don't believe have spoken yet.

MS. VARGAS-VILLA: Excuse me, I have spoken, yes, so I'll defer.

MS. WARREN-HENDERSON: No. No. You can go ahead.

MS. VARGAS-VILLA: Okay. Thank you. Judith Vargas- Villa, Concord, Massachusetts, again. If you saw the results of how we feel about our progress and our augmentation, it seems to me that it's not really appropriate, that you should ask us to stop doing something that we love so much, that's giving us back our lives. We are willing to give you every piece of information you could possibly want about how this has changed our lives because any of us are very introspective and we pay attention to details.

So, I would offer all my history to you;

and you can publish it wherever you like, but I don't want you to take away my augmentation. I will take it in any form that you want me to try to take it in, but please don't take it away. Thank you.

MS. JOHNSON: Hi. Liz again. I would not want to give up augmentation either, actually I would not give it up, but if there clinical trials for liver, I am right there.

AUDIENCE VOICE: Over here, Donna, next.

MR. ZELK: Hi. Brad Zelk, from Kansas City, again. One thing I'd like to see is more opportunities for children to participate so that we can get some treatments for them. I know it's very difficult, there are ethical issues all around it, but with no option for kids, how else can we get one if we don't provide someone the opportunity to provide a trial. I would sign my children up. I mean, if it's going to go via an IRV, and it's going to have full disclosure, give me the chance to say yes or no. Don't just say it's too hard to do something for kids. Give us

the chance.

MS. LIPSCOMB: Thank you. Lonnie do you have someone else?

MS. WARREN-HENDERSON: Yes.

MR. YOUNG: I'm D.C. Young, again. I have some experience on clinical trials. I started augmentation in 2004, in 2006, there was an opportunity for a clinical trial that I joined, and I had to stop my augmentation for three months. Now I look back at that and that was a mistake, because in that three months I got sick again, whereas I had gotten much better during the first two years of my augmentation. And since that time, I've had opportunity to join several trials, and have joined some, and I'll join any trial, because I can travel, that does require me to get my augmentation. Thank you.

MS. WARREN-HENDERSON: The one in the middle?

MS. LIPSCOMB: Okay. We are going to take one more response.

MS. WARREN-HENDERSON: It's sort of like

two though.

MS. LIPSCOMB: We are going to have a couple more questions about this, so I think you'll have an opportunity. I see everyone pointing to her.

AUDIENCE VOICE: Hi. My name is Debbie, I'm from Virginia. And I'd just like to see more trials for those that are not necessarily ZZ, there is a lot of other variations up in Eslie, there are very few trials, but I think we are important to know how this affects us just as much.

MS. LIPSCOMB: Okay. Thank you. I see your hands, but I promise you these next questions will be effective for you too. Let's go to the next question. "Have you participated in any type of clinical trials studying investigational treatments?"

I think we've heard yes, but let's go ahead and get a number here. And Chris let's go ahead and close it, I know we are doing that a little faster. And what do we have? So, 48

percent have, 26 percent not sure if they've been part of one. What about on the Web?

DR. PIERCE: I believe it's about one-third have participated in a trial.

MS. LIPSCOMB: I'm sorry. How many?

DR. PIERCE: About a third.

MS. LIPSCOMB: About a third? Okay. So, what I'd like to know now is, what are your considerations for participating, and what factors influenced your decision? And she doesn't even have her hand up, but I'm thinking it's similar to the last question, and since so many people -- Oh. Well, we'll do this question then. "If you or your loved one had the opportunity to participate in a clinical or investigational treatment, which best describes your thoughts? You are willing to consider? I'm not willing to consider, and my participation would depend on various factors?"

Okay, Chris, let's see the response. So, generally willing, or maybe. Okay. What about the Web.

DR. PIERCE: On the Web it's 28 percent

willing, only 3 percent not willing, and 68 percent, maybe, depending.

MS. LIPSCOMB: Okay. I'm just going to go to you and let you just -- Cathie, whatever you want to talk, for about 30 seconds.

MS. HORSAK: This is Cathie Horsak, and I think you are echoing, everybody is echoing they are concerned about bronchoscopes, they are concerned about liver biopsies, because their health depends on it, and then one of other people mentioned, MZs would love to be in a study, SZs would love to be in a study, almost every study that we have is limited to ZZs, I think you've got a willing -- our community is very willing to participate, give us things to participate in. Thank you.

MS. LIPSCOMB: Lonnie?

MS. HELLER: Hi. Laura Heller again. About eight years ago in Philadelphia there was a study of doubling the amount that you took of the Prolastin, and I hired a baby sitter, got subs at work, took the training, went through a whole

series of tests, and the woman looked at me like I was a dog that had been run over by a truck. And she said, your breathing level is only at 30 percent we can't use. So I think a lot of the people in this room who were afraid of losing on the therapy, they are not even -- they wouldn't be considered to do something that's dangerous.

MS. LIPSCOMB: Okay. Thank you. Lonnie, you have someone behind.

MS. LADIG: Carla Ladig from Indian. I think that maybe, part of the factors of that is travel, a lot of people are already compromised with their health and they can't travel to the various locations that have the different opportunities for study.

MS. LIPSCOMB: Okay. Thank you. This is a hot- button topic; we are going to take one more, and then I'm going to ask another question.

AUDIENCE VOICE: I'm a ZZ, my three daughters are all ZZs and my husband is an MZ, we've probably been in 15 studies combined, and the one daughter has never been on any of the

infused Antitrypsin, and so she went down to Florida for six months. Three months turned out to be a placebo, and this was an awful waste of money and time and effort, because if you haven't been on anything, that's like being on a placebo all your life up until that point. So I would rather they started out with maybe one dose a day, and then double it for the next three months.

But I've been to the St. Louis Hospital, and had a biopsy, a liver biopsy last month, with Karen Fraser, and my other daughter had a biopsy in Florida, and it's very, very simple, to me easier than getting a filling in a tooth. So, please consider it. I had to go to St. Louis, by the way, because I'm too old for Florida.

MS. LIPSCOMB: Thank you. We have one more question that's along the clinical trials. Let's see what that is. Would you be willing to participate in a placebo controlled clinical trial conducted in patients -- I don't even know why I'm asking this question, but would you? I get you. And we'll go ahead and see what we have with only

70 -- Wow! I'm shocked. I would not have guessed this. What about online?

DR. PIERCE: The yeses are 11 percent -- 12 percent, the nos are 73 percent, and the not-sures are the lower 13 percent.

MS. LIPSCOMB: So, a little more not=sure there. Let's see.

MR. STOKER: (Inaudible no mic) for active placebo, you do it all the time in epilepsy, why don't you do it Alpha-

And Antitrypsin? It's very simple. Lower the dose to half normal, give that as your -- in your placebo, and then go either full dose or double dose. And as well as any retrospective meta-analysis you want to do, but simply, active placebo, that way everybody is still on drug, it will still cover them, it may not be as effective, but you are not taking them completely off.

MS. LIPSCOMB: Okay. Thank you. We have a couple more comments.

MR. TOLAND: Don Toland from Oklahoma City. It's real simple, to me, I was on the

double-dose study, and you either got 60 or your got 120, what we need to do is readdress our focus, what I want is the enzyme, and I want the enzyme given so that during the entire week I'm up in normal levels, because after the study they upped my dose to 90, and now during the entire week of augmentation therapy I stay normal on Antitrypsin.

That's the secret, not what you ought to measure on how much the dose ought to be, it's to get the normal dose of Antitrypsin. Now, give it to me anyway you want, I'll take it any flavor or any combination as long as my enzyme keeps me at the normal level during the week.

MS. LIPSCOMB: Okay. Thank you. Well, I know there were a lot of hands going up, and a lot things that could be said, but it's been a little bit of heartbreaking that we are kind of coming to the end of this open part of the discussion, but I know that the Alpha-1 Foundation, in their survey, asked some questions about clinical trials and willingness to it, and

we are going to have John Walsh, we are going to invite him to speak for five minutes from the podium.

MR. WALSH: We have to tell Vana I can't spell five minutes -- I mean Donna, not Vana. Donna has done a great job, big hand for Donna, she's incredible. Well, I think there's no question that we've established beyond any doubt to the FDA that we did what they asked us to do, to bring a representative group of individuals with Alpha-1 to this meeting.

I almost feel I shouldn't waste time going over the survey results regarding the questions on clinical trials because what you just went through, the exercise I just went through hits it, you know, to the tee. So we had 1,425 individuals take the survey, 1,000 opted to answer the questions on clinical trials. Probably the only reason for that it's an open-ended question. So the question was and anybody who hasn't taken the survey will be scolded here. And those online that aren't taking the survey, it's still on the

Alpha-1 Foundation website, take it, we want more numbers than 1,425.

"If you or your family member had the opportunity to consider participating in a clinical trial studying experimental treatments, what things would you consider when deciding whether or whether or not to participate?" Duh, I mean I think the big one out there it's not an elephant, it's bigger than an elephant. The majority of our respondents, 39.6 percent indicated that access to the trial was the most important issue. That includes issues like location, travel time, cost and convenience.

And you know as we do trials in our community we can recruit for a Phase 3 pivotal study that doesn't involve a placebo, in somewhere between 6 and 13 weeks, and we have 80 percent of our community enrolled in our research registry. So we can reach out and touch right away, and have you participate. We don't have any trouble recruiting for trials, but it's got to be the right design.

Outside of that, 30.6 percent were concerned about safety, and whether the trial would harm their health, or worsen their health. So, many and this is probably the reason. Many would not enroll in a trial if they had to stop their augmentation therapy, some respondents even noted that they previously participated in the trials, but their health worsened by stopping augmentation therapy during that time.

We've heard that over and over again, the last few minutes, so augmentation therapy -- Ross, I now you were questioning whether there is enough data out there, I know it's not a perfect study, we can't let perfect get in the way of good, but there's no question in the minds of individuals on augmentation therapy in the United States that are fortunate enough to have access to augmentation therapy, that it works.

So I think that the rapid trial that was 13 countries, most people outside of the U.S., because it was a placebo -- over $100 million invested, which was published in the Lancet, and

EMA just accepted it, and that's going to open the door, hopefully, for access to augmentation therapy to our cousins in Europe. Another concern surrounding clinical trials design that we found through the survey, that Alphas are willing to do just about anything to participate in the clinical trial.

We have a waiting list, and they've shut down the trial now, for lymph perfusion, delivery of gene therapy, University of Massachusetts, and that is incredibly invasive and we had a standing line for that. We are currently we have 160 people in the two studies that take a liver biopsy for adult liver study for the natural history of liver disease.

Whoever thought that would happen. We've got a waiting list at those sites for people who go in to have liver biopsies. That's pretty invasive. A couple things that I might just highlight here, comments that people made: "I would happily donate myself alive," whew, "To a lab to do test treatments on if it meant a cure

for Alphas." That is the mentality, that's the mindset of our community, sacrifice for others, but obviously a concern about our own health on the other side.

"I think discomfort and safety," another quote, "I think discomfort and safety are continuously redefined as this disease progresses. Nothing was too much to ask at the end, and I would do anything, assume any risks to avoid that, and save my friends." A final comment in this section, "I would try anything that may help, because this is not living, this is just being here."

So, overall, it was an incredibly favorable, positive response to the willingness of individuals with Alpha-1 to participate in clinical research. The benefits of clinical research need to be weighed against the risks, and that's not the normal risk benefit formula you consider. Not just meaning safety of the treatment, they include the risk of stopping therapy that they know works, and participating in

a trial that they mean -- that they may mean to receive a placebo.

And one respondent summed it up, "I have taken part in two clinical trials early in my diagnosis before I was able to start augmentation therapy, I have considered taking part in a few recent trials, but the distance to get to the clinical site is a detriment. But most importantly, I'm not willing to be involved in a double-blind study, where I might receive a placebo."

The bioethics community of America agrees with this, IRVs all across the land are refusing to let their investigators participate in clinical studies with placebos. There has to be a better way. I would want to be able to continue with my infusions, since I know that they are working and take the trial treatment to see if there's more improvement. I would not consider stopping what is already working for me. It is terrifying not to be able to breathe."

One more quite here, placebos, "I just

got back to feeling almost normal, I don't want to take the step back, just to participate in a trial, so, I think one of the things that we would like the FDA to consider," this is from the foundation perspective it wasn't a question here is, "In some of these Phase 4 requirements, or even study design requirements, let's force industry to work together.

MS. JOHNSON: Amen.

MR. WALSH: I mean $100 million here, $100 million there, $100 million through a third company or a fourth company to do a trial that's a little bit different, looking at things a little bit differently. We've got two Phase 4 clinical trials right now going on that require the use of placebo. It's not going to be done in the U.S., it's going to be done overseas. The one double-blind placebo study that's been completed through rapid study, we will never see a study that large, that definitive ever, ever again in our community.

And I think the investigator community

would totally embrace that, our scientific leadership certainly does. So, let's work together to get the companies out there that are now working on Phase 4, drop the placebo make them work together, and let's find out what the dose is. And let's work with the Biomarkers Team at the FDA and identify a biomarker like Desmosine in the COPD biomarkers quantitative consortium has selected this as one of the biomarkers that we want to take forward, and let's be able to measure whether or not augmentation therapy works and alter it based on the Desmosine level.

So, I guess we -- the Alpha-1 community is ready, willing and able to do whatever we can to help advance and accelerate therapeutic development. We are partnering with you, the FDA, in this effort, with industry, and with the scientific community, and we need solutions, we cannot let perfect, at gold standard double-blind placebo get in the way of good. So thank you for the opportunity to present this data.

MS. LIPSCOMB: Thank you so much. Well,

we've come to our open, public comment period. The docket is full; we have 15 people who are going to get two minutes to speak. And what we are going to do is, we are going to call out their name, and we are going to walk to them. So, Jennifer?

MS. SCHARPF: I'm behind you Donna. Hi. I'm Jennifer Scharpf, I'm with the Office of Blood in CBER, and I spoke with many of you as we planned this meeting, and I just want to extend my thanks to everyone here for your participants today. So our first speaker will be Jennifer Murray.

MS. MURRAY: No. Thank you.

MS. SCHARPF: No. Okay. I think a lot of folks who have signed up may already expressed their opinions. That's okay. So, if you decline just let us know. Eric Butcher?

MR. BUTCHER: My name is Eric Butcher, from Knoxville, Tennessee. I'm both a lung and adult onset liver- affected Alpha with stage 2 COPD, but stage 4 cirrhosis. Currently a part of

my liver is compensating but no one knows for how long. I am only 42 years old, a father of three, and quite frankly, I'm not ready to die yet. There are currently three American pharmaceutical companies who have developed very promising treatments for the liver, but have so far, had to perform their trials overseas.

A good clinical trial must be developed that will get us, liver-affected Alphas a treatment that is both safe as well as effective. We cannot let the pursuit of perfection get in the way of providing us a good treatment. When we have 1,500 people or more dying each year, while waiting for a liver, in this case something is better than nothing, we have something promising now, we need to get it available to patients as soon as possible.

I also represent nearly 350-liver-affected Alphas from around the world. One of them mentioned that he would like me to relay thanks to the FDA for their role in fast-tracking augmentation therapy so many years ago,

without that a lot of us would not be here now. So, thank you.

I would ask that you help us get these liver treatments through trial and ultimately to market the same way. Additionally, we desperately need a widespread and frequent standard testing protocol, because that is the key to identifying the complete breadth of our problem; the number of Alphas actually out there. Thank you.

MS. SCHARPF: Thank you, Eric. Robin Bell?

MS. BELL: I'm a 46 -- let me put my glasses on, I can't see. I'm a 46-year-old lung-affected Alpha with stage 3 COPD. Having shortness of breath due to emphysema and asthma is quite a burden to live with, with being a loving and involved mother to an 8-year-old daughter.

Exacerbations are particularly bothersome for me, as I have to be extra careful, having an elementary-age-old child. As we all know germs are passed around literally through schools systems. When these are brought home I

run the risk of becoming infected, having exacerbations and thus damaging my lungs further.

Both my little girl and I currently dance on a regular basis, however, with dancing I'm finding it increasingly difficult because of my emphysema and my shortness of breath, dancing is my passion, but currently without completely following my inhaler regimen, as well as daily use of why Rescue inhaler is both troublesome and worrisome.

In 2012 I donated my left kidney to my twin sister, two weeks prior to this my oldest sister died -- I'm going to start crying -- of liver cancer probably due to Alpha-1, but was never diagnose. After experiencing many complications resulting from donating my kidney to twin sister, and compromising my own health, I was finally diagnosed with Alpha-1 a year later. Had my sisters and I been tested and diagnosed much earlier, our lives and their lives may have run a different course. We, as a community need a standard testing protocol developed and

implemented to enable earlier diagnosis.

MS. SCHARPF: Thank you, Robin. Sandy Sandhaus?

MR. SANDHAUS: I'm probably the first one here who is not a patient unfortunately, or fortunately, but I am representing the over 5,100 patients that AlphaNet follows and I help direct the care of through AlphaNet. I also have run the Alpha-1 Program at National Jewish Health in Denver for the last 35 years, and I was asked to present the opinions that, and questions that patients presented to me, and sent to me over the last several weeks, that weren't mentioned here, and I'm happy to say I've been gradually checking off and eliminating the comments.

So I'll go through these very quickly. Our view is that we teach Alpha-1 patients to be the experts of their disease, because we usually don't find an expert in their own local community. The issues that were brought up; is the need for newborn screening for Alpha-1 and Antitrypsin deficiency; the need for a post lung transplant

augmentation therapy trial, the need for an augmentation therapy trial in the use of Alpha-1 augmentation therapy and nontuberculous mycobacteria infections. And I'll be back here in two weeks to talk about that.

We need a registry of Alpha-1 liver-affected individuals including children and including children on the waiting list for transplant, because this is one major impediment to drug development in children with liver disease. We would hope that a fast-track approval for drugs could be facilitated because that can impact the course of liver disease since many individuals have a very short time, from the identification of liver injury in Alpha-1 to liver failure, death, or liver transplantation.

We would ask, and this is a strong comment from a lot of patients, that all studies looking at novel therapeutics for COPD, in general, and liver disease in general, include Alpha-1 Antitrypsin deficient patients in those studies. (Applause) You are taking up my time.

Virtually every drug that Alpha-1 patients take other than augmentation therapy is a drug that's never been tested in Alpha-1 patients for their indicated usage.

And finally, I actually have a plea of my own, and that is every week, often several times a week, I get emails from patients asking about the Lung Institute, the Stem Cell Institute, the Stemgenics, all of these industries that have popped up throughout the country that purport to cure COPD and cure liver disease and cure lung disease, by giving people injections of their own stem cells.

I've been to the FDA website, it has a very beautiful explanation of the concerns about that, and also the reasons that the FDA feels they don't have a role in regulating these institutions that are essentially money- making scams. But the fact that the FDA doesn't do anything about those centers, those centers are using as essentially advertise that the FDA leaves them in business and I think that a lack of action, is a tacit

approval, at least in terms of the opinions that I hear from patients. And if it's the FTC that has to get involved, if there's a referral, that would be great.

MS. SCHARPF: Thank you so much. Thank you. Alyce Sneddon?

MS SNEDDON: Hi. My name is Alyce Snedden, I'm from Fitchburg, Massachusetts. I'm here today, not only for me, but for my father. He is failing fast, I'm here just to ask, do we really have to have our loved ones go sick in order to have a transplant? Is there something that can give them ease and comfort from their sick and dying bodies that can be done? The pressure and the anxiety just living in a shell of yourself, I see through my father every day, and it's just not fair. In 2015, I think there's something that could be done and I think that it should be done. Thank you.

MS. SCHARPF: Thank you, Alyce. Ruth Cadwgan?

MS. CADWGAN: I'm Ruth Cadwgan, and I

think you've heard here today, a minute ago, we have educated our doctors. In 1992 when my husband was diagnosed there wasn't an Internet, there wasn't anybody that I could reach out and touch. And we educated people. We went to the source, got the information, take care of ourselves, very little hospitalization because we take care of ourselves. We know how to do that. We are living longer, and living longer, unfortunately, because we take care of ourselves, we are going to have more liver problems, that is certain.

Once those occur we don't have time to do a lot about it. Take care of yourself, you can't fix it. We have two MZ daughters, and we lose an Alpha a day. At the National Conference we have the ceremony in the morning, Fred and Joe run that service and every year the list gets longer and longer of loved ones that we have lost. We've got it diagnosed and treat, life expectancy just last year, I think it was at the conference, went from 55, which was what it was when my

husband was diagnosed at 48, to 61 years old. Not most disease communities are making the life expectancy longer, by working as hard as we do to take care of ourselves and learn what that is. Thank you.

MS. SCHARPF: Thank you. Judith Vargas?

MS. VARGAS-VILA: Yes. Judith Vargas-Vila, Concord, Massachusetts; you've heard from me too much, probably, this time. But I've been -- I came off the list, and I'm going to go back over it. As fit as we are, we have survived. I would like to give that gift to the young people, the children who were born, we take a hair-prick of blood for PKU, for most newborns. My daughter is a midwife and she tells me that. Why can't we add the diagnosis of Alpha Antitrypsin to it?

We could save liver people and lung people. I was actually jaundiced for three weeks when I was born, way back in 1941, they just put me in the sunshine, in the hope that I would get better. I did, but from what I hear in this

meeting, maybe I'm just lucky on that one. Oxygen is free for all in this world, isn't it? Except to us, we are the kind of people to whom oxygen is a controlled substance, and you people have a great deal to do with how it's controlled.

I want liquid oxygen for myself, in Massachusetts, but the delivery people, the providers of oxygen are closing off access to liquid oxygen in Massachusetts. I don't know if you at the FDA have a lot to do with that, but I've had to beg twice now to get liquid oxygen. And if I have to wait until I have 9 percent lung capacity in order to get my transplant, ah, I'd really like to have liquid which makes my life so much easier, and in Massachusetts we have winters, so therefore if it's going to snow and blow, and freeze, and the electricity for a week, I really would like to have liquid oxygen in my house, instead of depending on the electricity that isn't there, or have to perhaps get and electricity generator to run my oxygen condenser so I can continue living.

That's something that's interesting to me, why can't we have liquid here, they have it in Europe. Now I'm also interested in getting oxygen outside, why can't we have oxygen provisions in drugstores. Why can't we have drive through oxygen units? You put your card in and you get out oxygen. We need it. You've heard us talk about carrying oxygen on our backs, running around with our machines living with our houses with our long tubes, we would like to go places. Why can't the airlines loosen up a little and let us have some of the oxygen they've got stored in the places?

We have to go through weeks of organizations, and getting prescriptions and filling in forms, in order to go anywhere. You can see, I'm not dead yet, sometimes I want to go see my boy in California, and I can't unless I prepare for a couple of weeks ahead of time. And I want an oxygen machine that knows who I am, that responds to my needs.

Last week I went to MIT to attend a

hackathon, and while I was there, I had my glasses that had oxygen delivery through the frames, I showed it to them, and I said, these don't work because they've got gaskets that don't work, so those boys wrote -- excuse me, there was a girl and two boys, wrote up a program.

They took it to a friend who had a laser printer, that night they laser-printed me a pair of oxygen delivery glasses. Now these have little hooks for my nose, they deliver the oxygen and it goes all the way through, and I put them on and I had oxygen. I wore them around for about 10 minutes, and my oxygen level stayed up. I was showing this to some of the children we have here in the hotel this morning, and they all wanted them. They said, "I want some of your 3D glasses and I can have the oxygen I need, so --

MS. SCHARPF: Thank you, Judith. If you could summarize; thank you.

MS. VARGAS-VILA: I can summarize, I'm saying there's a whole generation of people who want to invent solutions, and we want you to

authorize them and give back to us with your stamp of approval. Thank you.

MS. SCHARPF: Thank you. Peg Iverson?

MS. IVERSEN: I am Peg Iverson from Des Moines, Iowa. I'm a ZZ Alpha. I was diagnosed in 1974, that was 41 years ago. I was diagnosed because my mom was diagnosed unbelievably correctly at the Mayo Clinic in Rochester, Minnesota. There, of course, back then there was no treatment available for Alpha-1. My mom never met another Alpha, nor had I until years later. My mom did not live, she lived about nine years after she was diagnosed, and nothing to be done.

We weren't fast enough for my mom, I am extremely fortunate, probably every Alpha in the room, all my Alpha cousins, would give anything to have been diagnosed at age 21, when my lung function was over 100 percent. After my mom died I participated in the National Institute of Health Study in Bethesda, Maryland, which rolled out into clinical resource centers which, for me, was in Iowa City, at the University of Iowa.

I've been followed from that young age to watch my lung function. When it dropped enough for insurance to cover augmentation therapy for me, of course after they could prove that I had emphysema. I was started on augmentation therapy. My AlphaNet coordinator at that time was my lifesaver, and guiding me through that, helping me understand that I know I could live a good life, educating me, thanks to AlphaNet's Medical team, Dr. Sandhaus, but we are still not fast enough, we've lost so many Alpha-1 heroes, so many Alpha-1 family members, so many people that are suffering. We need to speed it up.

Our community is so involved, so passionate, we are here, we are ready to go, please help us get there faster. One of -- my current AlphaNet Coordinator is in a hospital right now with ICU with pneumonia, where we need to speed it up, and get us there, please. And I thank you, FDA, for this amazing opportunity for hearing us today, and our concerns, and we are counting on you. Please help us.

MS. SCHARPF: Thank you, Peg. Bonnie? And I'm sorry I can't read your last name. Is there a Bonnie who signed up to speak?

MS. CHAKRAVORTY: Thank you very much. I want to reiterate what so many others have said, it's important to include the usual care control group in order to increase participation. I have participated in clinical trials in the past, and at this point, at this stage of my disease, I don't want to give my augmentation, it seems to be working very well. So, I'd like to emphasize the usual care condition would be very useful.

I'm 63 years old and I was diagnosed in 1996, and as my conditions progressed, I would say I've become dependent on supplemental oxygen. I would like to see more options for restoring function. I'm looking towards the transplant, but I am very much aware that it is a cure, and there comes with it many risks and many other negative possibilities. I'm hoping for the best but I am planning for the worst.

I'm using supplemental oxygen, and while

it's helpful, and we've discussed some of the direct problems into our Doribax using oxygen, indirectly it also makes things very vulnerable, and in this way it can restrict our participation in public events and being a part of the social world. So, to summarize again, I would like to see a usual care control in clinical trials, and I would like to see some greater focus on alternatives to transplant and as restorative treatments. Thank you very much, and thank you for listening to all that we've had to say. Thank you.

MS. SCHARPF: Doreen Flook? Doreen?

MS. FLOOK: Hi. I'm Doreen Flook. I'm from Michigan, and I'm here to talk, not only for myself, but for the people that I speak to in the State of Michigan. There is folks out there that desperately want to participate, and there's not a lot of clinical trials near us that they can go to. Travel is an issue, finance is an issue, the medicine is an issue, oxygen is an issue, they want to give more, and they are out there and they

are hungry.

Being in Michigan and having the winters, and needing to go seek that care, it's very tough. If you don't have an automatic start, let your car warm up, scrape your windows. That's all you can do, you have to go back and sit down for 20 minutes, it's a tough way to go, and they are up there and they want that help. Whatever you can do, whatever decisions are out there, any new advances it would be appreciated from all. Thank you.

MS. SCHARPF: Andrew Jefferies?

MR. JEFFERIES: Hi, everyone. My name is Andrew. I'm the nephew of Gordon and Marissa Duggan. I just wanted to speak on two things here. I know the FDA, just looking up here, it says, talking about protecting and promoting public health, and so I just wanted -- trying to get a little bit of feedback too, about what you guys can actually do from my understanding.

And I think the first thing is quality of life, in helping patients who are suffering to

make their -- to give them the quality of life, if your -- like with me, with being -- I'm deaf myself, and I was provided with two interpreters to help me understand clearly when I wasn't -- if I missed something they would clarify it for me.

And I think it's the same thing with Alpha it's just, I think, across the board, maybe through policy but including ideas to help bring awareness to workers, I mean, I think one gentleman talked about here, about coming in, he had used his -- put his inhaler into a box that had stuff growing, and all the germs from that, just raising more awareness in that sense to help quality of life, and with promoting public health, I think that fits hand-in-hand with you guys.

And the other -- and I just wanted to end on this note too, with this being a rare disease, I find that I'm (inaudible) -- with me being deaf, it's obviously you don't -- not every day you meet a deaf person, and it's not every day you meet a person with Alpha unless you are at this event, obviously. But my pastor once told me

that every member has a name, every name has a story, and I believe that is so with Alpha, and I, even to build on top of that every story is affecting more than one person. So, you might have one person with the disease but it affects the whole family, and with my uncle having it is affecting my own life too. Thank you.

MS. SCHARPF: Thank you. Chuck Price? No Chuck? Okay. Richard Lovrich?

MR. LOVRICH: Hello, everybody. My family. My name is Richard Lovrich, I'm 60 years old. Number one, I'd like to know why it took until just two-and-a-half years ago for me to be diagnosed with Alpha-1. I've been hospitalized for breathing, I have after an operation for peritonitis, for my burst appendix, peritonitis. I couldn't breathe for a few weeks at all very well, and I wasn't even tested then.

So, how can it be that a person goes to a physician and is not receiving any significant help from the medications they are taking and they not automatically test for that? I think if you

came in not breathing at all they would automatically recommend burial, so I think we deserve a break, so it doesn't seem like a big education leap. I'm on the same medications that you are all on. I'm on Zemaira and steroids and Rescue inhalers, and antibiotics, and I have to say for that cocktail it seems to be working rather well. I echo everything that everyone says about their treatments.

Note, why are there warnings for addiction risks to the label for OxyCotton, when there are no warnings on prednisone for users to avoid their spouses, work, Fox News, or just anything annoying, how is that possible? I wonder about that. (Applause) You know, health is so much more than just treatment; health is so much more than medication.

My doctor finally acquiesced, and I'm on oxygen for sleeping, and that's helped a great deal after being tested, but why did I have to find out for myself that oxygen has transformed my life when it comes to exercise, it's transformed

my life when it comes to yard work, to exertion, to sex, thank you, who brought up sex before, that was so brave. I'm sorry. Are there any children left? Cunnilingus, just try that, it's really good. Sorry.

So, I'm going to go out on a limb, why are Alphas so strong. Look at this room of strong people, and all of these strong people tuned in today? I have a theory. In 2014 our nation was horrified at the story of poor Eric Garner, "I can't breathe." Why did those words strike a note in America, across the world? T-shirts, buttons, "I can't breathe." Everyone in this room has overcome that fear, and has to overcome that fear on a daily basis, and I think that's why you are strong, and I applaud you all. And can you give yourself an applause? Thanks.

For all the Alphas here, at home today, and for all the Alphas that are undiagnosed, and therefore suffering doubly, I say, while we are all struggling to breathe we will all continue fighting for every breath. I thank the

Foundation, its brave leaders, and the FDA for this amazing experience today. Thank you.

MS. SCHARPF: Thank you, Richard. Katie Faris?

MS. FARIS: Good afternoon, my name is Katie Faris, I'm glad to e here. My son was diagnosed with Alpha-1 when he was two-and-a-half, as a result of having a swollen liver. We believe it was with a virus, we are not sure what the virus was, they were guessing possibly Epstein Barr, but through a series of blood work when his liver enzymes never decreased to a normal level, his doctor, thankfully, kept pressing and tested him for Alpha-1 Antitrypsin deficiency.

He has the ZZ gene, when we discovered that we tested our whole family, and found out that of our other children, we have four children, three of them total are also ZZ. I'm very thankful for an early diagnosis, so I echo all of the advocates for early testing. That has made a significant difference, I believe for our family already. We have not experienced many of the side

effects and we haven't needed some of the medication that have been discussed today, but my understanding in coming here, is that you want hear what life is like for families with Alpha, and as a caregiver for three children with alpha, some of what I experience might not five some of the questions that were asked today.

But for me, I am now given medication on a daily basis, I line up their medicine cups, like they have inhalers, they are all diagnosed with asthma. So just on a regular day -- morning I'm giving medication on a regular basis. When anyone gets sick, it's easy for all them to get sick, and our house turns a just medical zone. I have times when all of them are nebulizers, and I'm giving treatment throughout the day.

One of my sons had pneumonia twice this year, so he was on Prednisone, and so I go into prevention mode. What can I do to prevent my son's infect infection from getting worse. Doctor's appointments for our family, our children see a number specialists. We see five

specialists, I believe, on a regular basis, between our children, or maybe it's four, but we've seen other specialists for specific needs along the way.

Another issue that have encountered, besides the asthma, is that some of our children have coexisting conditions, so we have questions; are those related to Alpha- 1? We do not know because that research hasn't necessarily been done. Our daughter is diagnosed with three rare diseases. I don't know how they interplay with each other, the diseases would be Alpha-1 Antitrypsin deficiency, she's also is diagnosed with something called FPIES, which is a rare food allergy, where she has a GI response to particular foods. And then she's also diagnosed with ketotic hypoglycemia.

So we have to make sure that she's getting food on a regular basis. She's been hospitalized twice for that this year. And so, when I'm in the hospital with her, I have to make sure that the nurses are giving her, her other

medications appropriately. And a challenge for me has been having multiple specialists who are very good in their field but don't necessarily know how everything interacts with each other, and maybe aren't studied in Alpha-1 to know how that affects the big picture of their lives.

So, as a parent I'm thankful for the early diagnosis, I would desire that for other families as well. My focus is prevention for my children, particularly as we move forward, and I appreciate your desire to listen to our conversation. And, again, I'd be happy to answer any other questions that you have. But, thank you.

MS. SCHARPF: Thank you, Katie. And our last speaker will be Lisa Kosak. Hush!

MS. KOSAK: I've been picked on and I haven't even started. I was lucky enough to have the National Jewish Hospital in Denver, in my backyard. I grew up in Minneapolis, I moved to Vail, Colorado, just a little west of Vail in 1996. And at 40, I'm still pitching softball,

running the bases, kept getting slower and slower, that from one turn to a double, then to a single, because I didn't want to run around the bases.

At first I thought it was my heart, went in for the heart catheterization, and it was sleep apnea, and they sent me to National Jewish Hospital for a sleep test. Two days of testing, lo and behold. At that point I was on oxygen 24/7 and told me; you are going to have augmentation therapy for the rest of your life. I'm like, I don't do needles, I hadn't done a drug, a prescription since 1994, it was prenatal vitamins. You know, I just don't get sick, I didn't get sick.

With that after -- I owned two businesses, I had two kids, very active in the community. I was on the Board of Directors for the Chamber of Commerce, HOA Board, every charity in Eagle County. Well with being on oxygen 24/7, living at 8,000 feet is not conducive. Put my house on the market, hired a great general manager, and took early retirement at Vero Beach,

Florida.

How it affected by family even more? My older son who is 24 now, started his senior year; my youngest who is 21 started his freshman year in a school where they knew nobody. And they've been very supportive. At one point I didn't think I would see them through high school, they both graduated from college. One is in the University of Texas in Austin, working on his Master's.

There is hope, there's a lot of things. I was fortunate to have Jenny Faull as my AlphaNet coordinator, in Florida, and eventually I became an AlphaNet coordinator. I'm studying my third clinical trial. One of the great things about clinical trials, you get great workups from great doctors that know stuff about us. So they can look for things, they can -- that normal doctors can't. So I highly recommend that.

But the biggest thing for me would have been if my kids were tested as infants, because they would have been -- they would come up as MZs, and then it would have been suggested that people

get listed. Never would have had lung damage, I would have had -- probably I wouldn't have moved to Colorado, I would have stayed in Minneapolis, because there was no oxygen at 8,000 feet.

So, that's what brought me here. Thanks to Jenny I got involved, and I'll be involved. I want my kids and my grandkids -- I don't have them yet -- to have a better shot at this than I did. So, it's on you guys to help us out. Thank you.

MS. SCHARPF: Thank you, Lisa. Thanks to all of our speakers. I'll turn the program back to Donna now.

MS. LIPSCOMB: Well, I think you guys can give yourselves a big round of applause. (Applause) Chris? And with that for closing remarks I turn it back over to Dr. Michaud.

DR. MICHAUD: Thank you. I'd like to start with a personal reflection. I'm really struck by the solidarity among the members of this community and the support that you give one another. It's really -- it's truly admirable and something that I think is leaving a mark. We've

had a very good day today, and I think my FDA colleagues will agree that this has been an important meeting.

We thank you for your participation because that is what made this a success. The information that you've shared with us, will help us in our interactions with manufacturers and investigators to facilitate the development of new drugs, and for the design of new clinical trials. What we've learned today will ensure that the way measure benefits of new drugs in clinical trials are measures that matter most to patients. The information that we heard today, your input, will also be useful to manufacturers of new therapies.

I want to touch on a few points before I close the meeting. I can't recap all that we've heard today, this meeting was very rich with information, and we will be pouring over the transcript to make sure that we've captured everything.

What I heard was a resounding call for a cure for this life-altering disorder. There is a

need for research that will lead to new and innovative therapies. Improvements in the therapies that exist today, whether in terms of the delivery of the drugs, different dosing, and I also heard a call for earlier treatment, and that's something that may be reflected in clinical trials in the future.

We also heard about many of the challenges you face with current therapies. One example is oxygen therapy and all the challenges that that poses whenever you leave your home. Also in terms of availability, as we heard in some comments, we certainly heard that there is opacity of therapies for those affected with liver disease. Variable responses to the therapies that exist today, and a call for faster drug approval, accelerated development of therapies, I think that was heard by all of us.

You talked about the huge burden of lung and liver disease on patients and on their families, and how that translates into demands on your caregivers, I mean full impact of this

disease on your families. You talked about the profound challenges of shortness of breath, how life-limiting the lung symptoms or the pulmonary symptoms are, and we also heard about the rapidity with which liver disease can progress, and the life-threatening complications of liver disease.

One person put it best by saying that the impacts of Alpha-1 Antitrypsin deficiency can be summed up as life never fully realized, and that, I think, sums it up quite well.

On another theme we heard a lot about late diagnosis and missed diagnosis, and your many experiences with the health care systems, some of which were obviously quite distressing. We heard your concerns about a lack of education within the medical community about this disorder, and the fear of being hospitalized because you get sicker in the hospital, as one person put it.

It's very clear that this is a well-educated community, very proactive in supporting research and this is a community that seeks to have a voice in study design, and where

individuals are very motivated to becoming enrolled in clinical studies.

The Alpha-1 Foundation has spoken about the advocacy that it performs for patients, in terms of study designs, the use of biomarkers, the use of patient-reported outcomes, and also talking about what's acceptable to patients in terms of the use of placebo arms, for example, or other factors that may be involved in these clinical studies.

Just to close then, I want to thank you very much for being here, or for joining us online. Your participation was essentially to making this a success. We've learned a great deal from you today, and we are very grateful for that. If you have more information you'd like to share with us, please send us your comments on the docket, and we will be reviewing all of these comments.

Thank you also to my colleagues for organizing this meeting, and to the Alpha-1 Foundation for your support and your help in

making today a very productive meeting. And finally on behalf of the Center for Biologics Evaluation and Research, I thank you for your time. Have a good rest of the day. Thank you.

(Applause)

(Whereupon, at 3:37 p.m, the 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.

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