Ron: Good afternoon, everybody. Ron Bartek here, immediate past President of the Alliance for a Stronger FDA and President and Co-Founder of the Friedreich's Ataxia Research Alliance. Thank you all very much for joining us today.

First a quick word about the Alliance for a Stronger FDA. We are a multi-stakeholder coalition that advocates for increased appropriated resources for the Food and Drug Administration. We've been an important force in doubling of the annual available budget resources from $1.6 billion to $3.3 billion. We're the only advocacy organization focused on resources for both food safety and medical products, as well as other components of the FDA's mission.

Our members include consumer and patient groups, research advocates, health professional societies, trade groups, and industry. We have about 150 members, and we always welcome more to further strengthen our advocacy efforts and education efforts.

In regard to procedures for today's conversation, our speaker has kindly agreed to the format that's worked for well for us in earlier webinars. Namely, he will interview himself based on questions the Alliance has provided, followed by ample time to answer some of your questions, which you may submit by clicking the Q&A button at the bottom of your screen.

Before introducing today's speaker and moderators, the Alliance would like to thank Charlene Jenkins and Sarah Walinsky of Dr. Marks's staff for their help in coordinating this event. Our distinguished moderators for today's webinar will be Mary Dwight, President for the Alliance for Stronger FDA and Senior Vice President for Advocacy and Policy of the Cystic Fibrosis Foundation. Also, Dr. Zuckerman, founding President of the National Center for Health Research, and Kate Donigan, Senior Director of Science and Regulatory at the Biotechnology Innovation Organization.

I now have the distinct honor and privilege of introducing the speaker who has been kind enough to address our group today, Dr. Peter Marks. Dr. Marks is the Director of the FDA's Center for Biologics Evaluation and Research (CBER) which is responsible for ensuring the safety and effectiveness of biological products including vaccines, allergenic products, blood and blood products, as well as cell, tissue, and gene therapies. We know that these responsibilities constitute very heavy lifting in ordinary times, and

that in the past two extraordinary years, Dr. Marks and his team have played an absolutely pivotal role in advancing COVID-19 vaccines and therapeutics at Operation Warp Speed. During this same time, of course, CBER has received a multifold increase in submission for cell tissues and gene therapies, a field in which Dr. Marks continues to be a truly remarkable leader. For both reasons, these extraordinary times have obviously placed substantial additional strains on CBER's personnel and budgetary resources.

A bit now about Dr. Marks's other background. He received his PhD in cell and molecular biology and his medical degree at New York University. He then completed an internal medical residency and hematology medical oncology fellowship at Brigham and Women's Hospital in Boston where he subsequently joined the attending staff as a Clinician Scientist and eventually served as Clinical Director of Hematology. He then moved on to work for several years in the pharmaceutical industry on the clinical development of hematology and oncology products prior to returning to academic medicine at Yale University, where he led the adult leukemia service and served as Chief Clinical Officer of Yales' Smilow Cancer Hospital.

He joined the FDA in 2012 as Deputy Center Director of CBER and became Center Director in 2016. Dr. Marks is board certified in internal medicine, hematology, and medical oncology, and is a fellow of the American College of Physicians. Dr. Marks, thank you so much for all you've already accomplished for us and continue to accomplish for all of us, and for generously agreeing to spend some time with us today to share CBER's current status and the resources the Center needs moving forward in its vital work so important to the American people. Dr. Marks, the floor is yours.

Dr. Marks: Thanks so much for having me today. Thanks so much for sponsoring this meeting – or this event. So, I'll look forward to interviewing myself, which comes pretty naturally since I'm talking to myself constantly. It actually makes it more natural here.

So, the questions here, I think, were really great ones that were posed. Let me just start and dive right in. One of the questions was: What are CBER's long term priorities based on the President's Budget Request and CBER and marketplace needs. Really, right now, I would say that our team at CBER is one of response and recovery because we are still very much steeped in responding to the COVID-19 outbreak.

I'm not going to spend a lot of time on COVID-19 response efforts today, but I do need to say that we still have a very important role in COVID-19 vaccine authorization and approvals. That includes dealing with additional vaccine submissions for emergency use authorizations for expanding populations into, for instance, the youngest pediatrics, and for dealing with booster vaccinations. And then transitioning these Emergency Use Authorizations over into traditional approvals, which will likely also have to occur during the next year. So, lots on that plate.

And it's a challenging plate because there's a lot of interest in this. Just a simple statement about pediatric vaccines can be very challenging to deal with when we make it. So, we have a lot to deal with that.

But I want to move on to other issues, including the fact that one of the issues about response and recovery is trying to deal with. Our second priority in this list of what will be eight priorities that I'll give you is essentially eliminating our backlog of applications by years end. Now, we've done a pretty good job of not missing major PDUFA goal dates, but we are lagging behind in getting people feedback on their applications in some cases. And we are running behind where we would normally like to be in getting through our applicant load. So, we want to try to do our best to catch up on that backlog of applications by year's end.

And then we move on from what are related to COVID-19 to things that are related to looking forward and leaning in. One of them, which is near and dear to my heart, is enhancing our gene therapy interactions and expediting our feedback and reviews for gene therapies. There's been a lot said about whether the Center is taking a more cautious attitude or a more liberal attitude towards gene therapy, but I think at the end of the day, we view this as an incredibly exciting field which obviously will require a lot of nurturing as any nascent field does when it's growing. So, we will continue to work diligently with sponsors and with stakeholders to try to move this forward.

Some of this, in particular, for me has to do with a priority that we have of trying to get back to giving the type of feedback that we would like to in a timely manner. So, that's another very major priority, which will relate to a later priority of staffing up. We'll also look to make sure the we are most appropriately all of the different cellular therapies. That's an exploration that I think is important to

do in as much as we are trying to lean into those things that we regulate to find the best methods to bring them forward to the benefit of patients. Whether we'll find a different solution there, I can't say, but I think it's worth exploring.

As another priority, we will advance our blood donation policies. This is the fifth item on our list. Whether we'll get to that- we'll get to that in the course of the coming few years. This year is a critical one for completing a blood donation study, looking at our blood donor deferral criteria and how we can potentially move past our current set of deferral criteria, for instance, for HIV, to what would be perceived as a gender-neutral deferral criteria. So, we're going to continue to work in that direction.

As a sixth priority, we would like to take our regulatory science to our next level of focus and impact. That includes doing additional work in the focused applied science of manufacturing and product characterization. Sometimes people don't realize this, but we do have about 80 principal investigators that work at CBER and the various offices. These are researcher reviewers, and they make a big difference because they need to keep up with the leading edge of the science, which helps them better review the products that come before them.

And then the final two things are more across the Center: business process and human resource issues. One is, obviously, we need to modernize our business processes and our information technology systems to better serve public health. And I'll try to describe that a little bit more. And then, finally, and possibly what makes all of the rest of what I described possible, is that we have to recruit, retain, and train a diverse professional workforce that's capable of keeping up with the wealth of novel products that comes before us.

So, eight general priorities. Some of them, I'm sure we will make more headway on than others this year. But they're all important in their own ways.

The next question was what I would do if we had more money in the next fiscal year than what's in the President's Budget. Probably I can think of three things right off the bat. First of all, we'd hire more vaccine and gene therapy reviewers because, I think, we are clearly in a position that we are not giving the kind of feedback that I'm comfortable with in real time, or in more real time to both vaccine developers and particularly for those in the gene and cell therapy

field. So, that would potentially help us in that area. Now, we are hiring up now, but we would even go further.

We would also, the second, I think, accelerate the information technology modernization process. That is with an eye towards adding value to what we do by improving our ability to make good regulatory decisions.

Finally, we would advance our safety surveillance systems, which could also be used, in some cases, for even looking at effectiveness. But in particular, in the safety surveillance system end of things, we'd very much like to start implementing more work with artificial intelligence, including using natural language processing to be able to start to let the computers do better than we can with the thousands upon thousands, and now bordering on almost millions, of adverse event reports that come in in a given year, in order to sort through and detect signals more readily.

So, those are kind of three things. Obviously, you could do a lot of things with more money. But those are three things that I think would have the most impact on what we actually are doing.

Which leads into the third question which is: What are your major IT needs, how critical are they, and is there enough money in the proposed budget to significantly address some of those needs? Well, there's not enough money in the budget to address the needs, I'll say that to start out. We really do want to modernize our business processes, which will require new IT systems. But we'd really like to move to a next level of safety surveillance systems, and that really will require a fair amount of investment in IT partnerships and contracts to make that happen.

And there have obviously been challenges during this pandemic, including the fact that when people are not seen by their primary providers and insurance is not billed for something, like what happened with the COVID-19 vaccines, it becomes very challenging to do safety surveillance because the data on immunization are kept by immunization information systems and there are 60 of those scattered around the United States and its territories. We have had to essentially claw our way through agreements with each of those 60 in order to get our data partners access to the data necessary to do the type of safety surveillance work that we would like to be able to do for vaccines.

So, this is something that we would love to fix moving forward. That will require both funding, as well as some probably even legislative help.

The next question comes to: What are our hiring priorities? First of all, we have to get to an adequate level of staffing throughout the Center with highly qualified individuals. We're going to have to focus on the key areas for the additional staffing first. That is in vaccines and, particularly, in cell and gene therapy because those went into the pandemic way understaffed in the gene therapy end of things. The pandemic did not help us. So, we need to really staff up there in order to make the kind of difference that we'd like in terms of the ability to interact with sponsors, have the kinds of meetings we'd like to, and make a difference for patients in a more timely manner.

I think one of the things, in terms of our hiring priorities, that's been made a little bit easier by COVID-19 is that we have kind of shattered the previous connection where people had to be in the DC-Maryland-Virginia general area so they could come to campus. And now we have realized that we can have at least a reasonable fraction of our workforce, if not a significant fraction of our workforce, at remote locations. Hopefully, that will allow us to draw on a larger talent pool to get the diverse workforce with the experience that we're hoping to have.

All through that, being able to educate that staff to the latest in technologies to be able to have them have excellent development opportunities will be critical because we don't just need to attract staff, we need to retain them and grow them into future leaders of the organization.

So, how has CBER changed to respond to COVID-19 and are any of those changes likely to be permanent? Well, I just noted that this use of virtual work will probably be continuing on into the future. Now how much of our workforce will be virtual versus how much will be in person in the office, I can't say for sure. But I do know, like I think many do know, that we're not going back to February of 2020 again. It's not going to be the same as then. We'll probably have some new version of a workforce where there are some people that are in the office all the time, that may be the minority, some who are in the office some of the time, maybe the majority, and some who are never in the office because they're remote. That will be a change.

And I suspect that going forward, when we reconstitute, we will see a larger mix of in-person and virtual meetings because sponsors can save a fair amount of cash from not having to travel large teams to FDA if they're coming from a distance. They also save a lot of time. It is true that some sponsors really like in person meetings. I think we can be flexible, ultimately, to accommodate both types of meetings.

I think the other things, though, to me – I'll start from less important to more important. Some of the changes that occurred during COVID-19 were our ability to do things more rapidly because we realized we could when we put our minds to it. I think, for instance, guidance development is something that took a quantum leap forward because I think we realized that if you figure out what you want to say in guidance before you start having meetings about that guidance, you actually can get to where you're going more quickly. And so, that is something that I think will come out of the pandemic: being able to get out guidance somewhat more facile, which I think is really a great thing because, especially in the cell and gene therapy areas where things are moving so rapidly, we need to be able to get out guidance in a timely manner because the shelf life of a guidance is only a few years before the fields are advancing away and the guidance needs to be updated.

But finally, and this is possibly one of the most challenging things because it goes to the need for significant staffing, is if there's anything that I sit back at and look at as a success from the Operation Warp Speed process for vaccines, one of the things, obviously, is that we did things in parallel. Manufacturing during pre-clinical work, during clinical trials.

But one of the most important pieces that's underappreciated that facilitated rapid vaccine development was the level of interaction between the sponsors who were developing the vaccines and the Agency. There was a constant line of communication. We did not have the normal bounds if you get in a meeting request and then you get online. Questions came in in the morning and they were oftentimes answered by the evening.

So, this was, I think, something that was really fundamentally different. I can't promise that this will change because of COVID. But I think that it's certainly led me to very much want to potentially pilot what it might look like to continue this for some priority

products because, I think, if a pilot showed that one could increase the speed of development towards getting a potentially lifesaving product to patients, I don't know, 50 percent faster, one could probably make the case for staffing up to be able to do so.

This is, to me, something that we will have to think through and potentially pilot because it could make a real difference, both to companies and to patients. This is one of those things where potentially a win-win all around if we could staff it.

Another question: how have we prioritized non-COVID workload? We've unfortunately had to deprioritize a certain applications and meetings. That's why at the beginning I talked about this need to recover. The real thing to me that has been the saddest casualty has been our elective meetings, which sometimes are our most productive ones, our INTERACT meetings. These kind of pre-IND meetings and our CBER Advance Technology meetings have been fewer in number. I think being able to get back to more of those meetings will be really important.

And also, being able to reduce the number of written response only that the agency and CBER in particular are producing would be a good thing. I think sponsors do like the ability to interact in real time, and that interaction really is important.

So, the next, last kind of questions here go more into where we're going with computing and novel technologies. So, how is CBER going to evaluate products based on new technologies such as artificial intelligence, blockchain, and continuous manufacturing? Do we have the needed experience to do so?

I think the good news is we have a lot of excellent experience on hand that's familiar with everything from AI to continuous manufacturing. We will need to continue to build on that experience. But additionally, we will have to have the time for people to take and the resources to allow them to take the continual professional development steps that they need to do to keep up with these rapidly changing fields. We're dealing now with CRISPR-Cas9 genome editing, which 10 years ago didn't exist. It didn't exist scientifically. It wasn't discovered. And now we have INDs that are not just using even first generation CRISPR-Cas9's but are starting to use iteration of the technology.

So, we really need to be able to continue our professional

development. I think we have a very good basic researcher/reviewer model and that has helped us in handling these highly innovative products. But we'll also probably continue, in addition to our growth and development internally, to use grants and contracts to help foster innovative manufacturing technologies. That also helps us learn. These pilots that we have helped run have helped us to learn about these technologies as well.

And then, finally: can you tell us what CBER's doing to improve post-market safety oversight? The post-market safety surveillance is something we've had to lean into because of vaccines and some of our other products. It's become something where, unlike medicines which might be a steady state, vaccines are often rolled out. For instance when you think of influenza vaccine, you want to understand what's happening with their safety relatively rapidly. So, you need near real-time safety surveillance.

That's why some of our lead statisticians and epidemiologists developed this Sentinel Best System. Sentinel, obviously, the system that came down through Janet Woodcock for safety surveillance in large populations, millions of individuals. Sentinel Best system is one tailored for biologics. It incorporates not only claims-based databases but also access for at least some of those claims to the electronic medical record, which allows one then to not only detect a signal but try to refine it in as rapid a manner as possible. And so, we will continue to work on that Sentinel Best System.

You already heard where we're hoping to head for in terms of a national safety surveillance system. This is really a crucial thing here because we think that with the right partners and with the right technologies, we can really move to the next level of safety surveillance, which would allow us to detect signals in near real time and take action as appropriate.

Those were the questions that were self-interview questions. I will ask myself, that the interviewer's prerogative, and ask myself one more question at the end here before turning it over. That is that one of the questions has come up to us about vaccines: why is it taking us somewhat longer to get some of our Emergency Use Authorizations than it did originally for the original authorizations?

That's because of the complexity of what we are dealing with now. It's not to say that they weren't large files at the beginning, but we

had fewer of them and things were relatively a simpler time back then. We didn't have a host of variants. We didn't have the complexity of having populations that may have been exposed to tons of virus in the middle of trials, etc. So, things were a bit simpler, and it made things – The newer files have become somewhat more complicated.

Also, because we're now dealing with the history of what we know. We know that there are certain safety signals that we have to be very cautious for because we have those data from experience. So, we're in a different place than we were. That's not to say that the agency isn't moving with as much speed as possible on these applications. We are. It's just that we are – There are more of them, and they are more complicated.

And we know we have to get it right because we have seen – Back when we started out with this, the amount of vaccine hesitancy in this country was theoretical. We knew it was there. We didn't know quite how bad it was. Now we know how bad it is, and we know that we have to do our jobs right. Just in case, nothing has changed from our effectiveness standard for these vaccines. They still need to be at least 50 percent effective. Although, it's possible in some populations they might be a little less effective than 50 percent and that could be in the youngest kids, but who knows whether that will be the case or not.

Overall, the vaccines have to be at least 50 percent effective. We will maintain that standard. We will maintain the standard we need for safety follow up and we will try to do what we can to make sure those who end up being on the receiving end of whatever authorizations or approvals that we take can be very confident that we've done the right job there. With that, I will turn this over.

Mary: Dr. Marks, thank so much. That was really great. You are a very good self-interviewer. We particularly are grateful for all of the work across CBER that is represented by all the things you discussed. We also appreciate you really robustly covering a wide range of issues I know many of our members and guests on today's call are interested in. So, now we want to use the Q&A to dive a little deeper into some of those topics.

Before that, I just want to do one moment of housekeeping, which is we would love to have the audience submit questions. I know a few have already come in. Please just do so through the Q&A box

at the bottom of your screen, not the chat box. Please do go ahead and submit your questions to the Q&A box and we'll try to get as many as we can.

So, Dr. Marks, let's start with cell and gene therapy. Certainly, speaking for a rare disease patient population who is eager for a therapy in this space, I know I speak for many of our members and guests with great interest in how CBER is approaching this. You've spoken frequently, including today, about the opportunities and the challenges in this space, a relatively new area of therapeutic development that's teeming with potential and also teeming with an abundance of applications. The volume is just staggering when you look at it and exciting.

I love that you said you think it's an area that requires nurturing and is a priority. And then you also shared that you think some of the hallmarks of success, including in COVID, has been that constant dialogue between FDA review teams and those product sponsors. So, that constant dialogue takes considerable time. Can you speak a little bit more about how you envision the FDA being able to balance that exponential increase in cell and gene therapy product submissions with the need for extensive ongoing pre- and post-IND dialogue? And can you say a bit more about some of the tangible staffing needs, and particularly the culture you'd like to have in this area to facilitate this?

Dr. Marks: Thanks, it's a great question. I think we're going to have to be able to show what we can produce for the resources that we get. I am clearly aware that there are those that would say to us from Congress, "Look, show us what you can do. If we're going to give you resources, we want to see what you're going to do with them. What are we going to get for our money?" So, I'm very interested in seeing what I believe to be true from what my experience has been with the COVID-19 vaccines and the experience with development.

But it's actually not just the COVID-19 vaccines. It has to do with experience in the past, as well, with product development, which is that the back and forth that FDA's able to have with a sponsor can help them. It helps them develop a product in a way that we don't have to change where we are setting the bar. The bar can say where it is for safety and effectiveness. It stays where it is, but our ability to help them along the process can make an incredible difference.

Yes, we won't be able to do this for all sponsors, but it may be that

we can do a pilot project that will help us to see whether placement of additional resources can make a very tangible difference here in moving ahead product development. I think if that's the case, then we would have a justification. And I think we will have the support of patient advocates and, for that matter, hopefully industry in getting additional resources to help with this kind of development moving forward.

For rare disease patients where you have lethal diseases, the most common questions that I've gotten at meetings I've gone to over the past years is: why can't we have our own Operation Warp Speed? So, this to me is a way of trying to answer that with a pilot program to help make that happen. In a way, the analogy here that I've used often is I think early on in product development, we want very robust interaction between FDA and sponsors. I think there's nothing wrong with that. It can be very, very helpful. That robust interaction transitions over into more formal regulatory interactions as the product gets closer and closer to the market.

So, I sometimes describe this as a crescendo-decrescendo. We start very loud with a lot of work with sponsors early on, which then kind of decreases over time and gets softer. And then the regulatory pieces, the more formal regulatory actions crescendo over time. That to me is a way of wanting to have these interactions and I think is what we owe patients if we're going to be humans and not just bureaucrats. Parents of patients of kids who have severe diseases, they don't want to hear about Type A, Type B, and Type C meeting timelines. They want to know what we are doing to truly make a difference in trying to bring something better to their children's lives. So, that to me is what this dialogue is about.

Mary: Let me ask one quick follow-up that just came in through Q&A in the area of cell and gene therapy. Can you speak a bit about how CBER plans to approach diversity targets and equity in this space, especially when we think about really rare disease populations?

Dr. Marks: I think this is really a crucial thing. I have what may seem like an odd approach to it, but part of the way that we democratize gene therapy, and we get the ability to reach more people is by getting more commercial entities interested in gene therapy for small populations. The way we do that is we make it commercially viable by finding manufacturing technologies that make it viable and that allow gene therapy to expand into many diverse areas where it's not going right now because there isn't perhaps a patient advocacy group

that is organized for that particular disease.

I think we want to try to do our best to foster manufacturing advances and other advances in clinical trial and pre-clinical development that will allow that to happen.

Diana: Okay, I have a question. Dr. Marks, it's so great to have you here. You talked a little bit about IT, and we know that's an issue through FDA throughout as many years as I can remember. I guess it would be helpful to us to hear a little bit more about the role of IT in improving information that you can use in adverse event reporting.

Dr. Marks: I think part of our problem is – Look, our information technology systems in general are 10 or 20 years behind industry standard. Let's just start with that. But I'm not just interested in trying to keep our timekeeping systems and our review databases updated. What I'm more interested in doing is starting to actually apply state of the art technology to our mission and have it become integral to what we do. For instance, we receive so many adverse event reports each year. Someone has to look at them. They do a very decent job. But they might actually miss things that could actually be picked up by natural language processing, which could be done using supercomputing in a fraction of the time and could potentially – It's not that you'd eliminate human reviewers, it's that you could reduce, probably by 99 percent of the number of reports that needed to be seen by a human. What's even more important is that the computer could probably identify trends that a human would simply never identify. It might be able to identify in real time that all of the reports or nearly all the reports of a certain adverse event are coming in from women ages 18 to 50 or something like this. That's not something that a reviewer might be able to do until significantly after the fact.

So, I think we need to start to apply systems. Because, unfortunately, IT used to be like a stapler, something that you'd use or that was something on your desk that you'd use. Now, IT is becoming an integral part of the work that – It is how we are working. And so, if we don't incorporate that into what we're doing, I think we're doing a disservice to the population in terms of our ability to have cutting edge safety systems and, for that matter, even being able to branch out into looking at effectiveness and comparative effectiveness of products.

Diana: Thank you. I have one other quick question and that has to do with inspections. Obviously, in person inspections have been a big issue

throughout FDA throughout the pandemic. There's been the need to do remote inspections. But I'm sure there are times when you really want to do in person ones. And I wonder if you could speak to the financial needs to be able to do that.

Dr. Marks: Thanks. We have continued to – Getting inspections done is quite important. I think if people look at the papers today, you'll see what happens when things don't go well in manufacturing. Inspections help detect problems, hopefully before they get out of hand, and lead them to be corrected. It's really important for us to keep up on our inspectional capabilities.

During the pandemic, we did remote inspections in some cases. But they're not a substitute yet for in-person inspections, particularly the initial inspections of facilities for a newly licensed product. Our folks have really put themselves in harm's way in some cases during this pandemic to do those inspections in person. That's really a critical thing. Funding for inspections is really critical because I think we pride ourselves at FDA for having an inspectorate that is second to none, that really finds problems and leads to their correction. That makes a big difference for the medical products that are produced for people.

Diana: Thank you. Kate?

Kate: Thanks, Diana. Dr. Marks, in your introductory remarks and your response to Diana's question, you mentioned modernizing IT capabilities, including the potential for these systems to be used to look at effectiveness. How do you see Real World Evidence being leveraged to support product applications and reviews in the short- to medium-term? And are there specific product areas that CBER thinks are well positioned to use Real World Evidence now?

Dr. Marks: Thanks very much. So, Real World Evidence is something I think we are ready to use now when it is fit for purpose. What does "fit for purpose" look like right now? Products that when used in practice as associated with major endpoints that one can discern easily, one can use Real World Evidence for. It's worked well in oncology, and it's worked well in vaccines. It's now actually a few years old. We were able to pilot a Real World Evidence study of high dose influenza vaccine where one was able to reproduce the results of a randomized clinical trial using Real World Evidence drawn from large databases, in this case the CMS database.

How is that done? Well, it's because these large databases, what you lose in terms of perhaps data about an individual patient, you gain in terms of being able to look at millions of individuals. Sometimes you can look at outcomes that you simply just don't have enough of in clinical trials. For instance, in the high dose influenza case, the study that was done as a randomized trial was able to look at reduction influenza like illness. But it was not able to make big conclusions about a reduction in hospitalization in influenza. However, the Real World Evidence study, which I think, all told between the comparison arm and the high dose influenza arm had about three million individuals in it, was able to actually show a benefit in terms of hospitalization- in terms of reduction of hospitalization.

So, things work when there are clear endpoints, and we see that in oncology. My guess is as we have electronic medical records becoming more trustworthy, we may see finer endpoints be possible. But right now, they're more coarse endpoints. But there's no reason why we shouldn't be using Real World Evidence.

And in vaccines, we are increasingly seeing sponsors coming to us using Real World Evidence. Obviously, the COVID-19 vaccines show some of what can be done with Real World Evidence as well.

Kate: Great, thanks very much. Mary?

Mary: Thanks. So, so much of this is under staffing; the resources that we're talking here are really sophisticated employees at the agency who are able to do all these things you're talking about. Can you speak a little bit more on staffing on some of the impacts on COVID that you talked about some in your opening remarks, and also the ability to work outside of COVID? And particularly, how this has impacted your budget request?

Dr. Marks: We clearly need to staff up very significantly. That's why the PDUFA VII request had a lot of headcount in cell and gene therapy. Our budget request, we really need not just temporary FTEs, we need permanent FTEs increased. That's something that we'll need to work towards over the coming years, having them become part of our base headcount in terms of an increased number of headcount. Remember, it's not just in a given discipline. If we increase in cell and gene therapy, we also have to increase statisticians, we have to increase inspectors, even communications professionals. So, there are a whole host of growth that is required. Without that, we're not

going to be able to meet, I think, the need here.

One can say, "Well, why do you really want to? Can't you just get back to good?" Kind of have the same saying as Metro has, "We'll just get back to good." "We'll get back to 60 days for Type B meetings, 75 days for Type C meetings. Can't we just get back to that?" I don't think that's what we want to do with something that we care about as much as gene therapy. Things that have the potential to be really transformative, things where we in the United States are uniquely the global leader, I think we want to do better than that.

Mary: Diana?

Diana: I guess I just want to in the couple of minutes we have left just want to ask you a little bit about employee retention and morale. I know that's an issue throughout the FDA. Of course, during the pandemic when you were working as hard as you were and long hours, it must have been really difficult. So, I wondered if that is getting any better and if there's anything you can tell us about anything that appropriations can do to help with that.

Dr. Marks: I am incredibly grateful to the Congress for the 21st Century CURES Act because our ability to have the flexibility, to have direct hiring authority, and to have flexibility in pay has made a big difference. It has helped us retain talent that we would have lost otherwise to industry. Granted, the salaries still are not competitive with industry. But at least they are not such that they are an embarrassment in being able to retain someone. That has been incredibly helpful.

The problem is that as we use these higher salaries to recruit and retain, we are going to get budget crunched. It's just coming. It's been very great to have 21st Century hiring authority. I think it would be wonderful to have a more uniform hiring and pay authority across the entire agency. We are lucky to have a 21st Century Cures FDA in the medical products Centers. It has made a huge difference because it's a very big loss when we bring someone on board, train them for several years, and then they leave to go to industry. They leave a hole in the organization. That has to then be filled.

We want to try to make sure that we have salaries as well as other benefits, such as continued training and professional development, that really attract and keep people at the agency. It has been a long haul. I think it's going to be a little bit of a challenge because I

suspect the next year or two, we may see some more attrition than usual because people are fatigued from the pandemic. In our Center, in particular, we have a lot of retirement-eligible people, and some of them may decide that after a very exhausting few years, they may want to take advantage of that. I'm not saying that's definitely going to happen. It's a concern, though, that we have to be prepared for.

We will use- hopefully use our authority as much as we can to get people on board and keep them on board.

Mary: Let's make this our last question and maybe a lightening round. Kate?

Kate: Thanks, Mary. So, we've talked a lot about the need for sufficient funds to hire, train, and retain review staff with specific expertise. But are there policy development efforts to address rapidly evolving therapeutic areas and technologies like those in cell and gene therapy, advance manufacturing, platform approaches, etc. that would benefit from additional funding?

Dr. Marks: Yes, so certainly, our policy shops could always be built out, and indeed, it's not just some of the policy efforts, but probably also some of the science that goes into helping develop those policies.

Mary: Thank you so much, Dr. Marks. We really appreciate you spending the hour with us to cover a wide range of issues that I know are of great interest to the Alliance for Stronger FDA's membership and guests. Thank you all of you who joined for today's webinar. I know we received a question about the availability of this transcript from today's session. It will be available in a future edition of the Alliance for Stronger FDA's Friday news roundup.

Again, thank you so much for everyone joining us today for your time, attention, and great questions. A particular thanks to you, Dr. Marks and the entire CBER staff for all that you do.

Dr. Marks: Thanks so much for having us and thanks for the support. We really appreciate it.

[End of Audio]

Duration: 58 minutes