Todd Sherer: Hi, everyone. I'm Todd Sherer, the CEO of The Michael J. Fox Foundation. Thank you for joining the webinar today. We're really excited to share with you all the momentum happening in Parkinson's disease research and what we see on the horizon for 2021. Just as a quick note, there's a question and answer box. So, please do enter your questions on that box and we will try throughout the hour to get answers to this from our panelists. So, we really appreciate and want this to be interactive and make sure we can cover as many of your questions as we can.

Let me start now by introducing our panelists. I'm really thrilled to have this group here to share their insights with you. First, we have Bret Parker. Bret is the co-chair of our patient council and is the executive director of the New York City Bar Association. Bret was diagnosed with Parkinson's disease in 2007 at the age of 38.

Hi Bret. Thanks for joining.

Bret Parker: Thanks Todd. Thanks for having me.

Todd Sherer: We also have Sohini Chowdhury is the deputy CEO of the Foundation. Today is her birthday, so happy birthday, Sohini.

Sohini Chowdhury: Thank you.

Todd Sherer: Also joining us is Marco Baptista. Marco is the vice president of Research Programs. Thanks Marco for joining today.

Marco Baptista: Thanks for having me.

Todd Sherer: And last but not least we have Alyssa Reimer, who is the senior associate director on our research cohorts team. So thank you, Alyssa, for joining as well.

Alyssa Reimer: Thanks Todd. Glad to be here.

Todd Sherer: As I mentioned, today we're going to talk about all the progress that's been made in developing new treatments for Parkinson's. The trials and innovations that we see on the horizon to both manage symptoms and also target the underlying disease, and other programs the Foundation has launched to overcome challenges in research and care and the development of new treatments for Parkinson's.

So, if we can move ahead to the next slide. We see that there's great momentum in Parkinson's research over the last years. And in fact, in the last six years, 16 new treatments have been improved for Parkinson's. But obviously we want more to be done and we're going to give you an update now on what we think is coming on the horizon and some new areas that the Foundation is focused on.

So, first I just want to start by asking you Sohini, what do you think is behind all of this recent momentum in Parkinson's disease drug development?

Sohini Chowdhury: Yeah, it's extremely exciting, first off, that we have 16 new therapies that were approved in the past six years. And there's a few reasons for the momentum that we're seeing in terms of new drug development. One of that is that we're getting better at understanding the disease. We have researchers, clinicians have a better sense of what the unmet needs are for patients. And so what we're seeing is a plethora of therapies being developed to address a lot of the symptoms that still are not managed well in Parkinson's as well as some therapies that are addressing symptoms that honestly, probably a couple of decades ago were not even thought of as Parkinson's related.

So, part of this is really because we are getting smarter about what the needs are that are unmet for patients. But another component of that is that we're also getting smarter about the science around Parkinson's disease. We have a better understanding about the biology. We have a better understanding about the variability of the disease. So, we recognize that not all therapies are going to be beneficial for everyone and that there's great opportunity to be able to slice and dice things so that you can be able to create therapies that can be targeted to a patient's personal journey with Parkinson's. And so we're all of these reasons, we're beginning to see that industry's extremely excited about investing because they know that there's a market for these therapies and they're pushing this forward. And that's really resulting in not just the new approvals we're seeing, but also the robust pipeline of drug development in the preclinical stage as well.

Todd Sherer: So, you referenced new approvals and in 2020 alone, there've been three new approvals for Parkinson's disease treatment. So, that's really exciting. More options for doctors and patients. Marco, can you give us just an overview of the background on these three new approvals and what they're aiming to accomplish?

Marco Baptista: Sure, Todd, so the first to center around off time and off time is when your medication is not working properly and your symptoms are starting to emerge. And so the first two of these therapies that have been approved address a very important unmet need. Off can happen very suddenly, it could also happen gradually as you're wearing off with your levodopa medication. And it could also happen early in the morning. So, it's very important to have medications that can bring you back on when the medication is then working again.

So, Kynmobi is a very innovative approach of taking a medication called apomorphine, which is a dopamine agonist, and this is designed so that the therapy can be very quick onset. It's like a little Listerine slip type of medication that you put underneath your tongue. And within approximately 30 minutes, you can be back on. With Ongentys, this is what we call a COMT inhibitor, Categorical Omethyl Transferase inhibitor. And this is an enzyme that usually degrades L-DOPA. And so if you have an inhibitor like Ongentys and this then

allows levodopa not to be degraded and you'll have more Levadopa that can get converted into dopamine. And then finally with percept, DBS system, this is a very innovative, personalized way of doing DBS. The deep brain stimulation with this system isn't just providing neuro stimulation to the brain, but it's also taking recordings. And these recordings are then matched with the diary so that you can start to eventually envision a more personalized adaptive form of deep brain stimulation, where you can have this closed loop system where the stimulation will be modulating depending on your brain circuitry and the outputs that come from them.

Todd Sherer: Thanks Marco. So Bret, there's new drugs that have come on the market and one of the things, obviously, that's really critical is understanding how these are being utilized in the patient community, what type of impact they may be having, and as your role in leading the patient council for the Foundation and also a patient yourself, it's always interesting to get your view on what do you think of the momentum in Parkinson's research and the new options that have come to the table with these new drugs and treatments that are available?

Bret Parker: Yeah. It's very different for me now versus when I was diagnosed 13 years ago. When I was diagnosed 13 years ago, there was not the same momentum and frankly, I actually didn't have to pay attention to the drug research pipeline because it was slow. Now of these 16 drugs that have been approved in the past six years, two of them are drugs that I take regularly. They're sort of my primary drug. So, it really is life altering for me. Every time one of these drugs gets approved, speaking of birthdays, it's like a birthday gift. It helps me with another set of symptoms, it helps me manage my disease and the pace of drug development is really very encouraging.

Todd Sherer: But clearly we still have a number of unmet needs for patients, untreated symptoms. And as we go on now to talk about what's coming down the pipe, new trials being launched, we wanted to first start by getting your view on what you see as some of the really continued unmet needs that patients have that should be a priority as we look to develop new treatments.

Bret Parker: You mentioned earlier, Marco mentioned this, this off period. And the off period has been a real unmet need and I'm really pleased that there's some drugs out there now that I can use and in fact, the Foundation has helped support. But there's still other unmet needs. For example, for me, cognition, as I get further along in my disease progression, will become more of a challenge. I'm still working and so cognition is very important to me. I have at times this issue with forgetting names on the tip of my tongue and you sense the cognition symptoms kicking in. So, that's an unmet need that I think will be important. Also every once in a while, I like to do a little bit of running. And so the issues with rigidity and gait and things that interfere with my ability to exercise and keep moving. That's a symptom as well.

And fatigue is another symptom that gets to me sometimes. And there are many, many other symptoms that are not met.

Todd Sherer: As we're moving through, one of the questions I think that people have are what are some of the earliest symptoms that you noticed in your Parkinson's and have those progressed or changed over time?

Bret Parker: When I was first diagnosed, it was a very minor tremor that in fact almost nobody could see except myself. Once I got diagnosed, I realized that there were some other symptoms. My sense of smell was early, sort of dissipated. My handwriting has been terrible for a very long time and my sleep patterns. That plus rigidity on my right side, my arm not swinging as well, my foot not moving as well. It was very subtle, but those were the early symptoms for me that have gotten worse over time.

Todd Sherer: Yeah. And one of the challenges with Parkinson's disease is how variable it is, and some of these symptoms can vary across different patients. The ones that are really impacting people's lives could differ. And it's very informative getting input from you as an individual and the patient council. But I think the biggest insights can come from understanding and getting feedback from a broadest range of Parkinson's patients in really large numbers. And I wanted to now bring Alyssa into the conversation because she's involved in managing a lot of these projects about how we go about really collecting information and data from a wide range of, of patients and how that informed some of the areas that we focus in on development of new treatments.

Alyssa Reimer: Thanks, Todd. The primary way that MJFF really gathers information directly from patients on gaps in care is through our online study called Fox Insight. And two findings from Fox Insight in particular really stand out to me when it comes to illustrating the importance of hearing directly from patients. And they also directly relate back to the therapies that Marco described a few moments ago.

First through Fox insight, we asked patients what their most bothersome symptoms were and many reported gait and balance because of the impact on independence and on safety. And these responses have really led us to prioritize gait and balance through funding programs. Also within Fox Insight, we supported a study that analyzed how PD patients talked about their off periods. Nearly half of the participants in this study described symptoms such as freezing of gait, lack of motivation and memory problems, that would be missed by the tests that are most often used in clinics. So, highlighting these findings for clinicians can really help doctors and patients have better conversations and it can also help us improve scales to optimize existing treatments and therapeutic assessments.

Todd Sherer: Okay. So Marco, we now know there's a number of unmet symptoms that came from this research. What's happening now? What are the new trials that you're tracking that are being launched and that we're expecting results in the near term?

Marco Baptista: Yeah, what's really exciting right now is that there's just so much clinical activity that's occurring. And especially for these types of symptoms. Cognitive

impairment is such a difficult thing for patients to deal with and to talk about and has been traditionally something that's been very under studied and that's been changing and so we're starting to see quite a bit of activity in the clinic.

Recently, there was some top-line results that came from a company called NFX that was looking at that patient's with Parkinson's disease with dementia. And we're starting to see just a growing number of trials. So, the NFX trial is using the sigma one receptor agonist approach. There's also trials that are dealing more with mild cognitive impairment. So, not getting to the point of dementia, but starting to get a little bit milder symptoms, but leading towards down this path of dementia and there's trials there that are taking very innovative approaches that are either going after nicotinic targets or they're going after NMDA targets.

So, there's a lot of diversity and numbers of clinical trials that are emerging for cognition. The same with gait and balance. Again, it's very devastating to have these symptoms because they can lead to really terrible falls. And within gait and balance, there's just been a lot of innovation. Not just with pharmacological approaches. So for example, we've worked with companies like Takeda that have a [inaudible 00:13:51] one positive allosteric modulator approach for gait and individuals that have some cognitive impairment.

But also looking at non-pharmacological approaches. Non-drug approaches and really trying to tap into the innovation that's around technology. And we're starting to see some really out of the box thinking and out of the box clinical trials, where they incorporate wearables, where they incorporate different types of visual cues, where they incorporate different types of tactile stimulation to prevent the freezing of gait, for example. And then finally with dyskinesia, just recently I'm thinking of a trial that's going to be starting soon with a company called Neurolixis. And here they're looking at these unwanted involuntary movements that occur when you're on Levodopa treatment. And they have a very innovative approach. Again, using a very different target. So, we're getting a lot of different shots on goal. Here, they're looking at 5-HT1A agonist. So, a lot of exciting movement that's happening right now with clinical trials for hard to treat symptoms.

Todd Sherer: Before I move on just to the next topic, just to take a step back. I have a PhD in neuroscience, you have a PhD in pharmacology or equivalent. Can you just explain a little bit more to people that maybe don't have those degrees, when you talk about nicotinic, GABA, NMDA, 5-HT1A, whatever you just said. What exactly you're talking about in terms of how people are going about developing treatments for these types of symptoms?

Marco Baptista: Sure. Yeah. And I don't want us to get sort of stuck on the particular terminology that I'm using, but the message that I do want to give is that there are a lot of different approaches now. And because we don't really know exactly where in the brain, what specific brain pathways need to be addressed, we need to see a lot of these different varied approaches. And that's exactly what we're seeing.

So, all of these terms that we were using just simply means there's a lot of novelty, there is a lot of really good experiment-

Marco Baptista: There's a lot of novelty, there's a lot of really good experimentation and good hypothesis that people are following right now in the clinic.

Todd Sherer: Great. The other thing that we're really excited about is that there are now a number of approaches that are looking to not only develop treatments to target the symptoms, but actually to target the underlying disease process itself, with a hope of really slowing or even reversing the underlying disease. And I think that is something that we're all hoping for and working towards that would be really a transformative new direction as none of the available treatments for Parkinson's are able to do that. And as you mentioned, there's a robust pipeline with many different approaches, many different therapeutic targets being looked at. So can you just give us a sense of where you see this field, your level of excitement, and what's coming down the pipe for really targeting the disease itself? Marco.

Marco Baptista: Yeah, so there's a lot of excitement around particular pathways in the brain and in the periphery that we think are involved in Parkinson's and that's captured here on the slide where you see inflammation. We really are getting a much better understanding that there is this uncontrolled inflammation that is occurring. It could occur peripherally, maybe in the gut, and it could also be occurring in the brain. And there are a lot of different companies and different clinical trials that are addressing the uncontrolled inflammation that is occurring in the body. So for example, some of the companies that are working on this. Inflazome has a very exciting approach on how they're targeting neuroinflammation. This is a company that just recently merged with Roche. So we're seeing a lot of excitement with large pharmaceutical companies in tackling inflammation and Parkinson's disease.

There's another company, Alkahest, that has also a different approach, but again, trying to dampen that excessive inflammation that's occurring. There's some very exciting approaches happening at the University of Texas, where they're taking stem cells from bone marrow, and they think that is having an influence on the inflammatory responses in the brain. So yeah, a lot of things around inflammation. Then when we go to alpha-synuclein, we think this is one of the common denominators in all patients that have Parkinson's disease. We think that there is this misfolded aberrant toxic protein, which alpha-synuclein can become. And there are now a lot of different ways to try to tackle and target alpha-synuclein in its toxic forms. We have what are called biological or biologics in that approach. And that approach is either using antibodies or it's either using a vaccine approach, which we know there's a lot of discussion about vaccines right now because of a COVID.

And then also more traditional approaches of using small molecules to specifically target misfolded alpha-synuclein in the brain that we think can cause cell death and cause the progression of the disease. And then we have a lot of

different... Yeah, before I forget, there's just so many trials happening also with regards to biologics or companies like Lundbeck and Biogen that are using this passive immunotherapy approach. That is they're creating these specific antibodies that are going to bind to different parts of toxic alpha-synuclein to try to get them cleared out of the brain.

And then we have a genetic. The whole genetic field within Parkinson's has just exploded and revolutionized how we conduct Parkinson's research. And LRRK2 and GBA mutations in those genes are some of the most common causes of genetic forms of Parkinson's disease. And we're seeing a lot of exciting drug trials that are happening from groups such as Biogen. Groups such as Denali, Prevail for GBA, Sanofi that has their own approach. Again, a lot of different approaches. I'm not going to go into the jargon of all the different targets, but it really shows a robust clinical pipeline that we're very excited about.

Todd Sherer: So Bret, as a patient, how does it make you feel that someone as smart as Marco can't even keep track of all these trials that are going on because there's so many of them [crosstalk 00:04:28].

Bret Parker: I still don't understand all these funny words. I'm sorry.

Todd Sherer: Go ahead, Bret, sorry.

Bret Parker: I was just saying I didn't understand any of the funny, fancy words that he used. So, I'm encouraged. I mean, I'm encouraged. I mean, it's amazing to hear this kind of activity in the area. And we were talking earlier about on and off periods and symptoms, but being able to stop Parkinson's, the actual progression of disease is obviously spectacular. As I think many patients, including myself, are still at the point where if we could freeze our disease right now, even with the symptoms that we have and know that the progression wouldn't continue, I would take that as a win. So, this kind of research is very, very encouraging to me.

Todd Sherer: And as we've learned with all clinical trials and we even see this with the COVID vaccine trials going on, while we all want results as quickly as possible, those results don't happen unless people participate in this research. So Alyssa, what is the role that patients can play in this robust pipeline that we're seeing in therapeutic development?

Alyssa Reimer: You took the words right out of my mouth, Todd. 85% of trials face delays, and 30% actually never even get started because of the chronic shortage of volunteers. So the biggest role that patients can play in this pipeline is by raising their hands to join a study and encouraging others in their community to do the same. And if you've never participated in research before you can find a guidebook to learn the basics of clinical research and the importance of study participation, as well as a tool that will match you with trials in your area, on the MJFF website.

Todd Sherer: Great, and that was actually a specific question we got was where are there resources for people to find out about the trials they could participate in. So as Alyssa said, please go to the website for that information. I now want to pivot and transition a little bit because it's fantastic that there's this robust pipeline, but we still have some challenges in really coming up with the best protocols and procedures for testing the effectiveness of these therapies, particularly in a more rapid timeline. And this is an area the Foundation has made a major investment, which is to try to come up with improved outcome measures, diagnostic tests, to develop better ways to test these therapeutics. Many of you may be familiar with our Parkinson's progression markers initiative but that's a major focus of this initiative, which is to get a handle on the variability of Parkinson's and come up with better protocols and procedures for developing and testing these in clinical trials. So I want to pull Sohini in now to the conversation to remind everyone what the goals are of the PPMI study and what we've learned so far from this initiative.

Sohini Chowdhury: Thanks Todd. Yes, the PPMI is indeed a landmark study for the Foundation. It actually started 10 years ago, it's been a decade since PPMI was launched. And the goal really originally was to develop, as Todd mentioned, outcome measures or biomarkers that could be used in testing therapeutics. Bret mentioned the excitement about being able to slow the disease progression. And there's a lot, as Marco mentioned, there's a lot in the pipeline that's being tested that could potentially slow that disease progression. But just having these potential therapies isn't enough. You need to also be able to have ways to understand the trajectory of the progression and then understand if that trajectory has slowed down or has stopped completely. And that's really at the end of the day what PPMI is about.

It's about following individuals, understanding the nature of the disease, the progression of the disease among up to now 1,400 individuals have participated in PPMI, so understanding the trajectory of the disease in these 1,400 individuals, and then determining whether there are tools or biomarkers or outcome measures that could be utilized in clinical trials that would allow us to know whether the therapies are actually having the intended effect of slowing the disease progression. And this a hard problem to solve. It's something that has been looked at for decades, but the good news 10 years in, is that there are things that are coming out of this study that are extremely valuable and are really pushing the field forward. There have been some preliminary biomarkers identified through PPMI. Many of you are familiar with DaTscan. DaTscan is something that has been looked at in this study. And it has been seen that these brain scans do change over a one and two year timeframe.

There's also been some advances made in understanding whether some blood-based biomarkers can actually first differentiate between people who have Parkinson's disease and people who do not. And then secondly, these blood-based biomarkers are actually showing that they're changing over time in Parkinson's patients. So while it's still early days in terms of really feeling like we have a compelling and robust biomarker that can be used in clinical trials, out of

PPMI, we've definitely seeded and identified a lot of things that are currently undergoing more research to get them to the stage where we have confidence in them. But perhaps what's most exciting about PPMI is the way it's really catalyzed drug development. And early on Todd, you asked me about the momentum that we're seeing right now. I think to go back to that, PPMI has been a huge reason for industry investment in Parkinson's disease and a real generator, or catalyzed, or perhaps is the better way of putting it, of pushing industry to move forward with trials that are looking to slow and stop the disease progression.

The data that has come out of PPMI are informing the trial design, are helping to identify the right patients that ought to be included in these trials, and are helping to identify what are the outcome measures, whether they are exploratory or more robust, what are the outcome measures that should be included. And many of the trials that Marco mentioned, whether they're dealing with alpha-synuclein, LRRK2, or GBA, over 20 trials right now are designed, are informed by PPMI. And so in our mind, this has really been a real sort of game changer for Parkinson's drug development. You asked about the expansion, and so 10 years in, we've learned a lot, it's really catalyzed a field, it's seeded new avenues of research, and it's accelerated existing avenues of research. But one of the things that it has also highlighted is going back to some of the remarks earlier is the challenge of the heterogeneity of the disease.

Michael has always said, "If you meet one Parkinson's patient, you've met one Parkinson's patient." And the fact that every Parkinson's patient journey with PD is slightly different. Does mean that sometimes it's really hard to identify what are trends or areas that we should focus on, and so one of the things that we're looking to do is to expand PPMI to go beyond the 1,400 individuals we're following currently, and actually begin to look at 4,000 individuals. With the idea that if you can really expand the number of people that you're following, you get a better sense of what really matters in the noise. What are the avenues that we want to pursue. The other exciting component of the study is that 10 years in, we followed individuals who were very early-stage in their disease, just diagnosed, and now they're mid and later stage in the disease. And what we want to do is really understand the full spectrum of the disease.

And so, with this study, with this study expansion, what we're going to do is in addition to continuing to enroll individuals at that earlier stage of the disease, we're actually going to try to go even further. We're going to try to find individuals before they are diagnosed with Parkinson's, when they may be at risk for developing the disease. And this is extremely exciting because there's a lot of research that indicates that if you can intervene before the actual symptoms start, there still may be biology that is going on in the body, but it may not be manifesting in the symptoms of the disease yet, that there's a greater likelihood of seeing whether the drug may have an effect. And that's exciting because while this drug may be applicable to all patients, you might be able to really tease out whether that drug is efficacious, if you are able to find people at that early, early stage. And so that's part of the expansion plans too, is

to figure out how do we find people before they manifest the symptoms of Parkinson's disease, but are at risk of developing Parkinson's disease.

Todd Sherer: Just a question that came in if you could expand a little bit more about what the categories of people you're looking for who might be at risk for Parkinson's in the context of PPMI.

Sohini Chowdhury: Sure. I'll caveat this by stating upfront that this concept of at-risk is still in development. There's been research that has identified a few groups that have a higher risk of developing Parkinson's disease. One group was referenced earlier by Marco are individuals who may have genetic mutations, such as LRRK2 or GBA, that indicate they may be at a higher risk of developing Parkinson's disease. So this is one group who could be considered as part of an at-risk population. Another group that data has sort of indicated could be a part of this at-risk population are individuals who have a diagnosis of R.E.M. sleep behavior disorder, or RBD. And RBD basically just means that when you sleep, that ability to have dreams, but not necessarily act them out, your body stays still even though you're dreaming, that connection doesn't work. And so whatever you're dreaming your body is actually doing in the bed. And so if you have an RBD diagnosis, data indicates that one may actually be at an increased risk of developing Parkinson's disease as well.

And certainly I think that there has been a lot of data that has shown that there are some symptoms or lack of symptoms, there are some indications early on that could show that a person may be on track to develop Parkinson's disease. And these things could be constipation, it could be the loss of being able to smell well, et cetera. So they're not specific things, but some of these constellation of constipation, loss of smell, combined together could indicate, again, that an individual has-

Sohini Chowdhury: ... combined together could indicate again, that an individual has a risk of Parkinson's disease. So these are some of the categories that we're looking at to identify who may be eligible for PPMI.

Todd Sherer: Yeah. And I think it's important to point out that this is part of the experiment of the expansion, to see if these hypotheses are true and can this be built into a more robust data set?

Sohini Chowdhury: Exactly. I think that we have a starting off point in understanding what risk means, but I think this study is going to help us really understand who are individuals or what are the things that may confer greater risk on an individual to get PD?

Todd Sherer: Yeah. One of the things that you referenced about one of the outcomes of PPMI is how others are using the data in terms of designing their studies. There's a really unique aspect of PPMI that all of the data is made available in real time to the research community. And I know this is an area that Alyssa spends a lot of

her time working on. So we wanted to just bring her back in to talk a little bit more about why we think it's so important to make the data available. And how does this work kind of in practice for researchers?

Alyssa Reimer: Sure. So when we talk about, for example, the therapeutic pipeline, we often talk about having a multiple shots on goal approach. The more irons that we have in the fire, so to speak, the more chances we have to get new treatments over the finish line. We apply that exact same mindset when it comes to making data available from PPMI and other Fox Foundation sponsored studies. The more qualified researchers we have working with the data, the more chances we have to generate biomarker findings that will accelerate therapeutic development. And in practical terms, as Todd mentioned, this means that the de-identified data collected from PPMI participants are added to the data as quickly as possible, close to real time. And qualified researchers from around the world can access the data days or even hours after applying. We want to make sure it's as easy as possible for researchers to come into the PPMI community to get access to high quality PD data.

Todd Sherer: And we're seeing kind of an exponential impact of that data through that process with hundreds and hundreds of insights being found. So I think this is a really important aspect of the study.

We'll just move to the next slide and topics so that we have time to take all the questions. We've talked a lot about the importance of studying and engaging with large percentages of the Parkinson's population, given the variability in the disease, different types of causes of the disease and different outcomes in terms of response to treatments. And one of the areas the Foundation is established as a goal, is to promote more inclusivity in research for Parkinson's disease. And Sohini, can you just talk a little bit about why this is important and particularly important for improving the current care of Parkinson's, but also the development of new treatments?

Sohini Chowdhury: Sure. So I referenced earlier, sort of, if you've met one Parkinson's patient, you've met one Parkinson's patient, and that's true. But what also is true is that the way we live, our diet, do we live in a rural area? Do we live in an urban area? What is our access to care? What type of doctors we see? All of that has an impact on our health. And if we don't actually have a very diverse population that is participating in research and partnering in this drug development enterprise, then we don't really have a good ability to make sure that what we're developing is meeting the needs of patients across the spectrum.

And secondly, that is actually working in the environment that they live in, with the environment actually playing a role on the way their health is playing out. And so, it's extremely important to make sure that we have a really solid representation in research of making sure that we're aware of all of the aspects that may go into impacting living with Parkinson's, potentially causing Parkinson's, affecting the trajectory of Parkinson's, et cetera. And so, that's why it's extremely important to make sure and to underscore that we want to get as

much of a varied participation and sort of varied kind of perspective on this disease.

Todd Sherer: And to this goal, Alyssa, you're involved in managing an incredibly ambitious project, the Global Parkinson's Genetics Program. So I was wondering if you could talk a little bit more about that program, it's worldwide imprint, but also what's being planned in the United States for 2021.

Alyssa Reimer: Yes. So the Global Parkinson's Genetics Program, or GP2 for short, was launched earlier this year with the goal of bringing together genetic information from 150,000 volunteers across the globe, to better understand the underlying genetics of Parkinson's.

Related to what Sohini said earlier, we can only hope to truly understand the underlying genetics of Parkinson's through this effort, if the volunteers included are representative of the diversity within the Parkinson's community.

As such, the goal of GP2 is for 50,000 of those 150,000 volunteers, to come from populations that have been historically excluded or underrepresented in research. Including volunteers from Latin America, Africa, Asia, and Eastern and Central Europe.

And specifically, in the United States, GP2 is working with clinical sites in the Mid-Atlantic and the South to enroll participants who identify as Black or African American, to build relationships with these communities and to ensure that these populations are represented in GP2.

Todd Sherer: Great. This is, I think, a really important initiative for us and will be a stepping stone for even bigger and better things, I think, in the future, based on the success. I did want to bring Bret in because the patient council you mentioned, that you're part of, and you had told us that has really been talking about this topic as well, around inclusive trial participation. So I was curious if you could just give some insights from those discussions.

Bret Parker: Yeah, thanks. I mean, this has been an area of focus for us. In fact, we had a meeting last week where we talked about this topic. I mean, as Alyssa said earlier, there's a need for patients and control to participate in research. There's just a lot of need for participants. And as a side note, I had to tell you that participating in research is, as a patient, very, very satisfying, because it's one of the few things that we can do to help with the search for a cure. I'm not a scientist, I'm not a researcher, but I'm a patient and I can participate in a trial. So there's a lot of satisfaction that comes from that. So that's a side note and a pitch for people to participate in the clinical trials.

On this issue of diversity inclusion in trials, on the patient council, we talk a lot about the fact that we need to make sure that the whole universe of patients and the public is participating in the research, because the disease is

complicated and there's many different kinds of Parkinson's. And so, if we're going to find the cure that helps everybody, we need to have everybody participating in the research.

And so, I know there's a lot of effort at the patient council to try to get more people from historically underrepresented communities involved in the Foundation, in research, and as part of the discussions and the effort we have to find a cure.

Todd Sherer: Thanks, Bret. I do want to point out that in December we'll be hosting a Spanish language webinar and that information's available on our resource list. So that's something that's coming down in the next month.

There was a question that came in that was relevant to this discussion, about if you live in a rural area, that's far from some of the clinical centers, how could you actually participate in research? Now Sohini, if you want to address that question?

Sohini Chowdhury: Sure. One of the benefits of living in the time that we live in is that we're able to leverage technology to be able to support research participation. And so, I would definitely say that we are seeing a greater number of study opportunities that are able to be done online or through telemedicine.

And so, we've talked about Fox Trial Finder before. Fox Trial Finder's a great way to, which is our sort of platform that highlights trials that are in the PD research arena. Fox Trial Finder's a great way to find out about these research opportunities. And the Fox Foundation, as Alyssa mentioned, does actually have an online study called Fox Insight, where you can participate from your home, from your tablet, your laptop, your phone, et cetera.

So wherever you may live, whether you're close to a research center, whether you're in an urban area, whether you're in a rural area, there's a lot of opportunity now to participate in what we call a virtual fashion in research.

Todd Sherer: And related to this, Marco, you had mentioned technology. And I was just wondering if you could discuss a little bit how technology can be part of research, particularly remote monitoring for people that may be conducting the research outside of the clinical center?

Marco Baptista: Yeah, Todd. I think one big challenge, for example, in Parkinson's diagnosis, is that a lot of it can be quite subjective and we're always looking for more objective ways to be able to diagnose and measure the trajectory of the disease. And I think this ties in to, if we're able to develop better devices and different types of wearables to do remote types of analysis, and this could benefit everyone regardless of where they live.

Todd Sherer: And there was a big push, really, one of... And next thing I want to address, because there've been a number of questions around COVID and one of the... There's been obviously a lot of negatives that have come out of this, but some innovations. So one of the things that really has been pushed forward is telemedicine and tele-research for Parkinson's, kind of at a necessity. And it's something that we've been working with in our policy avenues as well, to make sure to keep pushing on telemedicine. Because it's been, for those who have been able to participate in that, has been quite successful, given the COVID limitations on getting to clinical visits.

In terms of COVID, a couple of questions. One really relates to kind of its impact on research, both clinical trial research and drug development. And I guess I'll throw this over to you, Marco, to just give your views on how had this impacted the momentum and where we see things going forward?

Marco Baptista: Yeah, thanks Todd. So I think when everything started with COVID here in the United States, there was a lot of uncertainty about just how research would progress. And I think what we've seen has been that there have been some delays in doing research and in doing clinical trials, but a lot has transformed into being more innovative, figuring out a little bit more how you could be using remote ways to be doing the measurements for these clinical trials. We're starting to see people returning to do critical experiments in the labs.

So we're starting to see things opening up and certain aspects of the industry haven't slowed down. For example, the smaller biotech companies have continued to move forward. So I think people are getting a little bit more innovative and they're overcoming some of the initial delays that we've seen. So I'm very optimistic about how PD research is looking for the rest of the year.

Todd Sherer: And speaking on this theme, one thing that I think a lot of us are now being encouraged by is the innovation that's happening around vaccines. And we're hopeful that this will be sooner than later.

One of the lessons I've taken from that is really around the collaboration that's been going on in terms of the drug development. And maybe just to get, maybe Alyssa, your thoughts on this as it relates to Parkinson's and even some of the data sharing that you mentioned earlier. And how can we learn, maybe from what's happened with the vaccine development to accelerate some of the discoveries in Parkinson's?

Alyssa Reimer: Absolutely. I think it relates directly back to the previous discussion around open access data. I think one of the key ways to encourage collaboration is to make sure that there's kind of an equal playing field for accessing the highest quality resources out there.

And one thing that I would highlight with the Global Parkinson's Genetics Program or GP2 is a huge emphasis on training, networking, and

communication. So in addition to making the genetic data from GP2 available to qualified researchers as quickly as possible, GP2 is also working to build a network of geneticists, who can come together to work on common areas of interest and common challenges. And we really think that bringing together kind of a meeting of the minds of the best and the brightest in the field is what is going to lead to a new discoveries and eventually new treatments.

Todd Sherer: One of the... Just to wrap up, I guess, the COVID section of our Q&A. This has had a profound impact on the Parkinson's community, just because of those isolations and access to care. One of the questions that came in that I can tell people that we are working on, is from our policy work and bringing together different Parkinson's Foundations and groups to advocate. Obviously, to remind people who are coming up with the vaccine plans that the Parkinson's community, given the underlying condition, we should be towards the top of that list of receiving the vaccines. And that's something that we are working on from a policy perspective.

But just wanted to bring you, Sohini, in to talk about, it's not solely focused on the research, but some of the work the Foundation's done to just provide more support for the community. And I know we have a new initiative around caregiving, that might be in the Buddy Network, that might be of interest to this community. If maybe, you could just talk about quickly and then we'll get to some more of the research questions.

Sohini Chowdhury: Sure. So I think that COVID has had an impact on everyone in the sense that the nature of the isolation that we have to undergo, but specifically, we have reached out to our Parkinson's community over the past months. There's been surveys that we've launched in Fox Insight. There's been Facebook sort of chats, et cetera. And we're well aware that our PD communities is really impacted by COVID and sort of the social distancing, the inability to be able to always get care on an easily accessible basis. And so, one of the, I would say silver linings coming out of this is that it really spurred us over the summer to develop what we're calling the Buddy Network, which is an opportunity to, or platform...

Sohini Chowdhury: We're calling the buddy network which is an opportunity to or platform that would help sort of connect Parkinson's patients with one another in a virtual fashion. To be able to kind of create networks, to create those connections and to have that easily facilitated so that you're not just going on a Facebook chat with hundreds of thousands of people, but you may be able to actually have a more intimate way of connecting with peers. And so we are in the process of building that out. The beta version is going to go live shortly, and we really hope that it will address some of the sort of negative aspects that we know exist right now due to COVID.

Todd Sherer: This is an area I think that's important to highlight also because we've talked a lot about genetics and the role of genetics in Parkinson's. But we do know that there's a pretty significant role of the environment. And I think some of you

referenced this even when we talked about trying to understand the broader diversity of the Parkinson's patient population.

Marco, can you just talk quickly about what we know about the role of environment in Parkinson's and what can be done about that? I can add a little bit into what we're doing about it, but maybe just talk about the science for a second, about what we know.

Marco Baptista: Yeah. The biggest unknown question that we have right now with Parkinson's disease is what's the cause and that's why there's so much excitement around the genetic causes because you can really pinpoint for a subpopulation what the causes are from a genetic point of view. It gets a little trickier when you're looking at the environment because there's so many different confounding variables that you want to want to control for it to really understand if it's a pesticide or if it's air pollution.

So, we're taking a very holistic approach that all the work that we do isn't just genetic and all the work that we're doing in supporting isn't just around the environment, because we do think that there's something in between and it's that interaction between both which makes people probably susceptible to getting Parkinson's disease. We have, for example, launched requests for applications and asked researchers to send in applications that specifically address environmental causes. And we're going through those reviews and picking those types of experiments that we think could really help us better understand what could be environmental causes of the disease, which definitely are real.

Todd Sherer: And one of the things that we've been advocating for through our policy work is that for some of the environmental toxins that have been linked to Parkinson's to try to get these taken out of the environment. And one particularly called paraquat we've been doing a lot of work for, and we're still pushing. So this is an area, I think, where the patient community could help to keep putting pressure on to get some of these toxicants out of the environment that we know could be leading to neurodegenerative diseases like Parkinson's. So, a couple more questions in the remaining time.

Marco, I think you were going to take this one related to Parkinson-isms and how do they all relate PSP Lewy body disease, Parkinson's. A lot of the therapeutic pipeline we're talking about, is there opportunity that some of those drugs could have effects across these different diseases?

Marco Baptista: Thanks, Todd. Yeah, there are opportunities. These Parkinsonians are aspects and symptoms of Parkinson's that are exhibited in individuals that are not officially being diagnosed with Parkinson's disease. And that gets back to just the challenge it is to diagnose and differentiate between someone who has Parkinson's and someone who's showing Parkinsonian symptoms. So, for example, a good way to kind of definitively know if you have Parkinson's is that the Parkinson's treatments such as levodopa are actually working in the

individual and that a diagnosis is made. It's not ideal, but that's a lot of the times how diagnosis are made for Parkinson's. But a lot of these different types of Parkinsonian diseases tap into either common or different types of brain circuitry. And there's a lot of effort at MJFF to try to be able to better measure these.

So, for example, there are certain diseases that are a little bit more linked across that protein which I mentioned earlier called alpha-synuclein so we're trying to make an alpha-synuclein tracer to be able to image that, and that could have benefits for those who have Parkinson's or it could be also beneficial for those that help similar diseases, but not Parkinson's, for example, like MSA. And then the flip side with PSP and with Parkinson's, we're also supporting other types of brain imaging tracers so that we can light up areas of the brain that we think are tapped into those diseases. For example, there's another protein called tau. So these are ways that we're trying to better understand.

Todd Sherer: Great. Alyssa, you mentioned about the worldwide imprint of GP2. What about some of the intervention, the therapeutic trials, are those also happening outside of the United States? What's the status of that?

Alyssa Reimer: Yes, absolutely. I think we see worldwide interest as it relates to therapeutic trials for Parkinson's. And one thing that I would point to to illustrate that is kind of year after year through the MJFF funding programs, we tend to see about one third of our funding going to investigators who are located outside of the United States. So definitely strong interest everywhere. I'll also mention that PPMI is also a global study. About two thirds of the sites are in the U.S., but one third are located outside and that spans sites in Canada, Europe, a site in Australia and a site in Israel.

Todd Sherer: Great. Marco, for the cognition trials you talked about, maybe we could just take a step back first and describe what we mean by cognitive dysfunction in Parkinson's, and at what stage or what level of deficit do people have to have for those trials? What are they targeting?

Marco Baptista: Sure. And it's complex because different trials have different goals. And so you can have trials that are trying to look at more mild impairments in cognition. So for example, difficulties not just a memory, but maybe in planning your day and planning a particular task. It gets back to the challenge of how to measure all of that. So there might be a trial that is more focused on those milder aspects. There are other trials where it's a little bit more definitive that there is true dementia in the patient, where there is really severe memory loss and it's affecting one's functioning in life.

So, that's why I think it's very important in utilizing that tool that was mentioned previously by the panel of the Fox trial finder. Because in trying to find a match for you to the right clinical trial, you can get a better understanding of what we call the inclusion and exclusion criteria for these different trials. And you might not be good fit for one trial because of the goals of that trial. But for another,

for example, cognition trial, you might be a good fit. And the reason that those criteria are there it's to really try to make the results as meaningful as possible by matching the right drug to the right person, if that helps.

Todd Sherer: Yeah. I will mention that sort of understanding the symptoms, the cognitive symptoms of Parkinson's is not straightforward. We are relaunching a guide that we have that describes the symptom in 2021. So I think that's something to keep your eye out. There's some information available on our website as well to get a handle on what really is the aspects of the symptom in Parkinson's. One more question, and then I'm going to ask for some concluding remarks from everyone. DBS is still, we mentioned the new approval, Marco, can you just describe a little bit what DBS is and what types of symptoms that it is a useful therapy for?

Marco Baptista: Right. DBS stands for deep brain stimulation. Obviously this is a surgical procedure where electrodes and leads are dropped deeper into the brain that are tapping into a circuitry of movement. DBS is not something that is necessarily right for everybody and treats all different types of symptoms. It might be good for tremor, but it might not help you with your gait, for example. And, right now where we are with DBS is, again I think I briefly mentioned this, trying to get more to an adaptive DBS. A closed loop system where the actual device itself is listening to your brain and the brain is giving off signals and there can be types of changes to the stimulation so that it can help you.

But DBS is not necessarily something for everyone. It's something that you need to consult with a movement disorder specialist to better understand if you're at that stage where a medication might be working, but it's starting to not work anymore for you and you need to move on to a different type of treatment. But that's a very personal thing that needs to be discussed with your doctor.

Todd Sherer: Great. I want to take a moment to thank the panel. They covered a significant amount of information, thousands of publications in a very short period of time. So, thank you, Marco, Sohini, Alyssa, not only for your work today on the webinar, but all your work that you're doing on behalf of the Parkinson's community and the push for new therapies.

In concluding remarks, I wanted to just bring you in Bret. As someone active in the community and digesting everything you just heard, what's your outlook right now as we end 2020 and go into 2021 on what you think the future might hold for Parkinson's disease treatments.

Bret Parker: First, thanks to you, Todd, and the whole team for everything that you do to help advance this work. It's very important. I'm selfishly interested in it, but there's a whole community of people that appreciate it. I am like Michael an optimist. I feel very positive about the path that I see in front of us. As I said, there are drugs that didn't exist five years ago that are literally helping me have a better life. So, I feel very optimistic. I think we have a lot of shots on goal, as

we've said, irons in the fire and I feel very positive about the future for all the patients in the community.

Todd Sherer: Okay, thank you. I want to thank everybody for taking the time to participate in this webinar. The first step is making sure you're as educated about what's happening, the status of things as you think about the actions that can be taken to improve all of our hopes of accelerating this drug development pipeline and getting to those new treatments as quickly as possible. I want to wish everyone a very happy, healthy, and safe holiday next week for Thanksgiving and 2021 is going to be a better year than 2020. So, thank you all. And again, thanks for your support of the Foundation and participation in the webinar today.