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Speaker 2: Navigating Parkinson's disease can be challenging, but we are here to help. Welcome to the Michael J. Fox Foundation Podcast. Tune in as we discuss what you should know today about Parkinson's research, living well with the disease, and the foundation's mission to speed a cure. Free resources like this podcast are always available at michaeljfox.org.

Maggie Kuhl: Part amazing human body, part science fiction turned real-life, stem cell therapy is a frequently asked-about topic in the Parkinson's community. These special human cells can develop into different cell types and scientists are exploring how they can develop into Parkinson's therapies. I'm Maggie Kuhl, Vice President of Research Engagement at the Michael J. Fox Foundation and host of the Parkinson's Science POV Podcast. This episode is made possible with support from BlueRock Therapeutics. Thank you.

Our founder, Michael J. Fox, has long been an advocate for stem cell research. This is part of his commitment to the aggressive pursuit of all ethical avenues of research toward improved therapies and ultimately, cures for Parkinson's disease and other disorders. This is what Michael said during a US Senate committee hearing in 2000 when the Parkinson's research landscape looked very different with very few of the treatment options that exist today. And at that time, stem cells offered a glimmer of hope. Take a listen.

Michael J. Fox: I'm not here solely to represent the benefits of stem cell research for Parkinson's patients. There are many other promising applications from heart disease to blindness to Alzheimer's, to burn victims to cancer, to HIV/AIDS to stroke to autism to deafness to schizophrenia to diabetes to MS and ALS. I'm confident that the vast majority of you want this research funded, and quickly. I see in these cells a chance for a medical miracle.

Maggie Kuhl: Today, that medical miracle is closer to reality as multiple stem cell therapies are in clinical trials for Parkinson's disease. We'll discuss how stem cells may help scientists replace dopamine, the chemical that's lost in Parkinson's disease. One such trial announced positive safety results earlier this summer. And with us today is the principal investigator of that study and our foundation's Chief Scientific Officer, our CSO, Dr. Brian Fiske, is a frequent panelist with me here on Parkinson's Science POV. And, Brian, thanks for joining me again on the mic.

Brian Fiske: Good to be back.

Maggie Kuhl: And with us today, as I said, is principal investigator of the BlueRock Therapeutics trial of BRT-DA01, which we'll discuss more. Dr. Harini Sarva is also Director of the Parkinson's Disease and Movement Disorder Center, Associate

Professor of clinical Neurology, and lead clinical trialist for movement disorders at Weill Cornell Medicine in New York. Dr. Sarva, thanks for joining us.

Harini Sarva: Thank you for the invitation.

Maggie Kuhl: So let's start with some basics. What is a stem cell? Where do they come from? Dr. Sarva?

Harini Sarva: So stem cells are precursor cells from which all other cells are derived. Commonly, they're produced during embryogenesis when embryos are being created and many of their stem cell trials, the source has been embryonic stem cells.

Maggie Kuhl: What is the current use of stem cells for replacing dopamine lost in Parkinson's disease?

Harini Sarva: So stem cells have been studied in Parkinson's since the early 90s without a lot of success. So really, right now there isn't anything in terms of dopamine replacement therapy from a cell-based standpoint due to a lot of issues with the prior studies. So these potential next-generation studies will offer an opportunity for really cell replacement.

Maggie Kuhl: So, Brian, maybe you could build on that. So dopamine is this chemical that is lost and these stem cells offer a way to perhaps replace that. Tell us more about that approach and how it might work for PD.

Brian Fiske: It's a very, I think, compelling idea when you think again about what we're trying to do. People with Parkinson's, it's not the only brain cell system that's lost, but they've lost these brain cells that produce the neurochemical dopamine. So the idea that you could replace those cells with new cells that can produce that dopamine and restore some of that function that the dopamine cells provide in the brain, obviously, it's a very compelling idea. In the early days, this idea had been played with a little bit with some tissue transplantation approaches and those showed some potential benefits, but they weren't really game-changing yet. They had some issues, there were some complications. They were just messy to work with. So as Dr. Sarva was talking about when stem cells came on the scene and people started playing around with that, one of the first things they started to do really was to try to develop recipes to turn those stem cells into dopamine cells.

And that was something that was a very early bit of work that was done. And actually, some of the first funding that the foundation did in those early days was to actually help support some of that recipe generation to help make those dopamine cells. So the idea now is rather than using messy tissue approaches, can we use stem cells to develop pure populations of dopamine-producing cells that we can then transplant into the brain with the idea that we can then bring back again some of that dopamine into the brain. So again, that idea is really

compelling because it just offers a way to help address some of the movement problems in Parkinson's disease and help restore some of that function.

Maggie Kuhl: So our bodies made dopamine cells at one point. If you have Parkinson's disease, you may have lost those dopamine cells. Can we find new seeds and turn them into dopamine cells and replace what was lost? So we're really harnessing, like I said at the top, the amazing ability of the body to create itself to create more of what people with Parkinson's no longer have. And I want to go back to something that you said, Brian, which is the movement symptoms. So Parkinson's is a very complex disease. It for a very long time was thought to be a dopamine-only condition. And we've learned a lot more about a lot of the systems involved in this condition. So, Harini, maybe you can tell us more again about what we think the dopamine replacement with stem cells would do for a person's function.

Harini Sarva: So normally, when the brain produces dopamine, it's releasing it in a steady rate at a steady stream. And then once that production is reduced and gone because of the loss of the cells, they're not making enough dopamine for coordinated movement. The way we're treating patients right now is that we're not giving them a steady stream of dopamine. We're kind of giving them dopamine replacement through pills at timed intervals. So, it's almost as if we're confusing the brain because it's not used to that kind of interval delivery of dopamine. So, when you put in stem cells that are precursors or immature dopamine cells and they eventually mature and make their connections, they'll be able to produce dopamine at a more physiologic or normal fashion as opposed to this start-stop fashion that we're giving dopamine to our patients. So ideally, it's going back to a more natural state for patients.

Maggie Kuhl: I'm sure that resonates with anyone who has experienced motor fluctuations and the wearing-off after a dose of medication. Brian, were you going to add on?

Brian Fiske: Again, as we think about what these cells are trying to do, again, they're not curing you of your Parkinson's disease in the sense that the disease process may still be continuing in the background, but they really are, again, offering you this additional source of the dopamine in your brain to help address some of these movement problems. In some cases, people may still have to take dopamine medication, maybe they can take less of it or reduce their dosages, which would be obviously beneficial as well. And possibly, in some cases, people may be able to go off medication if the dopamine cells are really working well. But I think it's important to keep in mind what this will offer to people is, again, just an additional way to really address those motor symptoms, hopefully, in a way that would make their quality of life better throughout the day without, again, some of these complications and, again, all the pill taking and all the other things that they would have to normally do to control those movement issues.

Maggie Kuhl: And we're talking about dopamine replacement with stem cells, but there are different stem cell approaches that are both in testing and currently out there in clinics that are advertising themselves to treat everything from Parkinson's to a long list of diseases. So we want to acknowledge that this conversation is not touching on those alternative uses of stem cells or approaches. It is something that the foundation is investigating and testing the validity and the efficacy of, but we urge anyone listening who is interested in Parkinson's stem cell therapies to speak with their physicians and really look closely at the scientific data behind a treatment before adding it to one's treatment plan.

Harini Sarva: And just to piggyback off of what Brian said, this is a piece of the puzzle because as you said, Maggie, dopamine is just the tip of the iceberg and there are a lot of other processes that are happening in the brain and the development of Parkinson's. So, if we're able to successfully show that cell-based therapy can help, again, we're treating the motor symptoms and one piece of the entire puzzle. And hopefully, that'll be a stepping stone for other cell-based approaches for either other chemicals or other nerve cells.

Brian Fiske: And I think that's, for me, the real important point. We're really looking for, I think, a really powerful proof of concept right now in the clinic. And that's why we're excited to see these approaches moving into clinical testing and formal testing because if we could see that signal, we'd be able to really understand the level of benefit these approaches might be able to provide, at least in their current form, be able to compare it against existing therapies like standard medication approaches or some of the other surgical approaches like deep brain stimulation and really be able to compare how these cell replacement approaches could really help people with Parkinson's and what aspects, again, of their movement will be best controlled.

So I think just like we saw with deep brain stimulation where once the first devices were approved and tested, we were able to optimize them further. I could imagine if these cell replacement approaches show some benefits, we'll see that similar innovation happening and people will then really start thinking about additional ways to deliver them or how to deliver them. Or maybe there are additional cell types that could be delivered in addition to the dopamine cells. So I think you'd see a lot of really interesting innovation happening if we can get these first signals in the clinic.

Maggie Kuhl: And we are seeing signals, which is a good transition to our next segment, which is to share the exciting interim but exciting results from one of the first trials which, Dr. Sarva, you led. So please tell us about it.

Harini Sarva: It's a phase one study. It was open-label. There were 12 subjects recruited over three centers, Cornell, UC Irvine. Dr. Henchcliffe is the PI at UC Irvine. And then at Toronto with Dr. Fasano and Dr. Lazano up there. Our surgeon here in the US was Viviane Tabar, who is instrumental in the development of the cells. So far, the safety data looks very good and that's led to continuing as a phase two

study in the coming year. And there's some preliminary suggestion that there's graft survival. So all really good things and an important stepping stone. And I know BlueRock is super excited to present the results at MDS later this month, so I'm not going to steal too much of their thunder. But again, the safety data was really very promising. And when you run a high-risk clinical trial that's a surgical trial, seeing every patient go through the one year without really any major adverse events is really reassuring and heartening and really gives us more confidence in moving this forward.

Brian Fiske: And it's exciting to hear that too. I think for many years, there was so much work to try to optimize these types of stem cell approaches and get the recipe right, "How do you make the right kind of dopamine neuron?" And I remember I used to think about it thinking it along the lines of do they quack like ducks? Do they walk like ducks? Just making sure that really was the right type of dopamine cell because you can make cells from stem cells that resemble the kind of cells you want, but sometimes once you actually put them into the brain, they don't necessarily do what you want them to do. So a lot of really hard work, I think, went into making sure these were the right kinds of cells that once you put them into the brain, they could start showing, hopefully, some meaningful benefits. So it's great to see that initial testing of that is starting to look promising.

Maggie Kuhl: Absolutely. And we want to express our gratitude to the participants who, as you said it, Dr. Sarva, this is a high-risk trial, it's invasive, which I do want to ask you about, but those people who took that first step and raised their hand and said, "I see the benefit. I see the future here and I'm willing to be part of it." That's absolutely critical to these advances. So we thank those participants and anyone else in the future studies to come. I want to clarify a couple of points. You used the words open-label, and I just want to define that for our audience.

Harini Sarva: Open-label essentially means that every participant received therapy, whether it was low-dose therapy or high-dose therapy, there was no randomization, there was no sham procedure done.

Maggie Kuhl: And they all knew that they were receiving the therapy.

Harini Sarva: Yes.

Maggie Kuhl: Which doesn't mean that necessarily alters the results, but it's always just something to consider in comparison.

Harini Sarva: Absolutely.

Maggie Kuhl: And you used the word surgeon and we talked about some of the requirements of this treatment. So it is a brain surgery to implant the dopamine cells.

Harini Sarva: Yes. It's a neurosurgical procedure under general anesthesia.

Maggie Kuhl: And the phase two study of BlueRocks therapy that you are leading is anticipated to begin enrollment in the first half of 2024 as well.

Harini Sarva: Yes. That's what we hope to do, yes.

Maggie Kuhl: So this one trial has reported interim results. What does the landscape look of other stem cell therapies in clinical testing or perhaps close to humans?

Harini Sarva: There's a group out of Sweden that's also developed dopamine precursor stem cells, and that in conjunction with Novo Nordisk will be running their own stem cell trial possibly in the next year as well.

Brian Fiske: And then there's this group in Japan who's been working with a different type of stem cell approach that have also been doing some human testing. So there's definitely some emerging clinical work around these approaches, which is great to see.

Maggie Kuhl: Great. And if you are interested in learning about any recruiting trial or staying close to these and seeing when and where they're opening, then you can visit our foxtrialfinder.org tool to be matched with studies or to search based on interest and eligibility. So let's talk a little bit about the eligibility and the audience for these therapies. You mentioned, I think it was 12 participants were in your first trial. What stage of Parkinson's were those participants? And also maybe just generally this dopamine replacement with stem cells, who would be best for this treatment?

Harini Sarva: The trials in general are looking at patients who've been at least diagnosed for five years, are having to take carbidopa/levodopa, and having motor fluctuations without really bothersome dyskinesia. So this is not something for people who are newly diagnosed or medication naive.

Maggie Kuhl: As, Brian, you said we need something to compare to and we want to have an understanding of the standard trajectory versus something like this.

Brian Fiske: Exactly. Yeah. It's a different world that we live in today than maybe when stem cells first were being looked at a number of years ago where there are all these other options. So we want to be able to, obviously, understand how this approach compares to some of those.

Maggie Kuhl: And these stem cell therapies, these replacement therapies, as we said, we're at the safety stage and just as a primer on how trials work, you recruit a very small number of participants to see safety first and then you move toward efficacy in comparison to standard treatment as you were just discussing. But we do have a lot of other questions to answer, right? Maybe you could just walk us through ones that came to my mind, for example, or how do you know how many dopamine cells made from stem cells to implant and is this a one-time thing or would you need a new dopamine dose after a decade or so?

Harini Sarva: The number of cells are based off of the animal experiments that are done. And in our phase one study, they looked at two separate doses to see what would be safe essentially. Is it a one-time deal or does it need to be repeated later? I don't think we know the answer to that question just yet, but there is some long-term follow-up of patients who've had the original stem cells like 20, 30 years ago, and they've only had it done once. So hopefully, they'll only need to have it once, but that hasn't still been established yet.

Maggie Kuhl: This is a question that we received from a member of our community. If we can transplant new functioning cells but have not altered the underlying disease, won't the new cells also become damaged? We were talking about how there's a lot going on in Parkinson's. This dopamine loss might actually be a result, the sort of downstream effect of things that go wrong well before then. So wouldn't the same happen to these newly implanted dopamine cells? Brian, could you answer that?

Brian Fiske: Yeah. It's just a really interesting question because in some of the first original attempts to use tissue transplantation, which were some of the first attempts to try to replace the dopamine cells, when they looked at some of those individuals a number of years later after they passed away, they actually looked at the transplanted tissue because, obviously, the researchers wanted to know if the transplants had survived or not. They did. First of all, they did see the transplants there, so they seemed to have survived. But they actually found some of the Parkinson's pathology in the transplanted tissue. Why that was interesting at the time was because it was some of the first really suggestive hints that the Parkinson's pathology, in particular, this clumping of this protein called alpha-synuclein, which we've talked about in other podcasts before, might actually be able to spread.

So it might actually spread from the Parkinson's brain into the transplanted tissue. So there was a lot of discussion. So first of all, that opened a whole new realm of research, which had people looking at the spread of alpha-synuclein protein as sort of a part of the pathogenesis of Parkinson's. But it also asked the practical question, would that impact the function of that transplanted tissue, and ultimately, would you have to then replace it, like you said, later on? They couldn't really answer that. It didn't seem the level of pathology would necessarily impact the transplanted tissue. So at least in those individuals who had those transplants, the transplants were still there. So it wasn't like the pathology came in and killed the transplants and they no longer were existing.

So right now, I think it's a slow process. That pathology normally in people accumulates over years. So the idea that it would accumulate in a transplanted piece of tissue that doesn't have that pathology, presumably that would also take many, many years. So my guess is, yes, it might happen. Would it have a really functional impact on the transplanted tissue? Certainly not immediately is my guess. And it may take many years for it to reach a point where it would. So that would be my initial thought on that. But obviously, we don't have the data

on it and Dr. Sarva could certainly probably comment on it further. We would require long-term data to really see if what was the case or not.

Harini Sarva: Yeah, we would have to follow these patients for several years after the initial one or two years in order to really see and obviously ask their permission for autopsies in order to establish if and when and how much has been impacted by the Parkinson's pathology.

Maggie Kuhl: Are you involved in other dopamine replacement trials? Maybe you could tell us what else is out there or upcoming.

Harini Sarva: So there's two cell-based therapy trials that are going to be starting in the next year that we're actually a part of. There's a gene therapy trial that's currently recruiting as well in several centers around the country. And of course, there's continued innovation with focused ultrasound as well as deep brain stimulation.

Maggie Kuhl: But those are not using stem cell approaches, those are alternative.

Harini Sarva: They're alternatives, yes.

Maggie Kuhl: If our audience is interested, we just did a full webinar on gene therapy approaches and we have a wealth of information on our website around some of the other treatments that you discussed, focused ultrasound and deep brain stimulation. Lots to learn for sure, but it sounds, as we said, one trial is moving forward. There are other dopamine replacement approaches in testing. There are other stem cell therapy trials in lab testing moving closer to human testing as well. So a lot of questions still to answer, but I think we said a step, I would call it a giant leap forward, with the findings from this first one. So now we're going to go to what I like to call the lightning round, but it's really just an excuse to ask you a list of questions assembled from my own interests and from members of our community. So, I'm going to take us through these. Brian, what are induced pluripotent stem cells and how are they being used for dopamine replacement?

Brian Fiske: Great, great question. So, the original stem cells that were discovered and represent one source of cells are human cells. They're called embryonic stem cells because they're derived from the earliest stages of embryogenesis. And those were the original human stem cells that were discovered and isolated and provided a wealth of information about stem cell biology. A few years later, a group in Japan developed a technique that allowed you to take other non-stem cell tissue. They initially used skin tissue, but since that time, they've used other types of tissues as well. And using just a handful of recipe factors, they were able to coax those cells to become stem cells or stem cell-like cells.

And the terminology that was used was they were induced to become stem cells. So the term induced pluripotent stem cell just means stem cells that were induced from these initially non-stem cell sources that were made to then

be like stem cells. So these so-called iPS cells, induced pluripotent stem cells, have become an alternative approach for deriving stem cells that can then be used to develop and generate other types of cells. We found that iPS cells are particularly good, especially for research purposes. So we can use iPS cells generated from people with Parkinson's, for example, and generate various cell types from them and study those in the lab to try to better understand the disease. There are some groups who are trying to develop iPS cell-derived dopamine cells for cell replacement purposes as well.

And there's a group in Japan actually affiliated with the original group that discovered iPS cells. There's a group in Japan that's been developing these for therapeutic purposes, including doing some initial clinical trials in Parkinson's. And then we're also aware of some other groups out there that are exploring the use of these so-called iPS-derived dopamine cell approaches as well for Parkinson's that are moving towards the clinic as well. So I think we're going to see a combination of both types of cell sources being used for potential benefits in Parkinson's. We don't know if one is better than the other, that's an open question. We'll have to see how that ultimately plays out in the clinic, but they represent two different approaches for getting dopamine replacement cells.

Maggie Kuhl: It wasn't cool enough to turn a stem cell into a dopamine cell. You had to take another cell and then turn that into a stem cell and then make it into a dopamine cell. Very scientist. Always asking, "What if we did this? Can we do that too?" Harini, we talked a lot about other systems that play in Parkinson's and right now, stem cells into dopamine cells is what we're focused on. Could we have a future of stem cells into other types of cells that are also impacted in PD perhaps to treat symptoms outside of just the movement issues?

Harini Sarva: Well, that's the hope because PD is such a multifaceted disease. Once we've established that these are not only safe, which is really important, but effective as well, that would be a stepping stone to creating cholinergic stem cells. So to improve memory in patients with Parkinson's or serotonergic cells to treat mood disorders or potentially other cells to help with other aspects of Parkinson's, most of which are difficult to treat and we use a smorgasbord of treatments from other specialties to try to combat them, but are the most difficult things to treat.

Maggie Kuhl: I think you get a prize for being our first podcast guest or panelist to use the word smorgasbord, so thank you for that. I'll stick with you. Do you think if someone qualifies for DBS, deep brain stimulation, and has that treatment, especially perhaps earlier on in their disease course as some are exploring its utility, would they be eligible for stem cell treatment for dopamine replacement if that becomes available? Basically, would one cancel out the other?

Harini Sarva: I don't think they would cancel out the other. Right now, the trials are looking at patients who have not had DBS and are essentially good DBS candidates to see if it would basically do what DBS has been established to do over the last 20-plus

years. I could certainly envision a place where in time, that patients who are having some benefit from DBS but may not be from their oral medications either to GI issues or other medication side effects can potentially have benefit from cell-based therapy. But again, it's also having two brain surgeries, and as patients are getting older, what is their surgical risk? So all of those things have to be considered as well as what do they look like in terms of their cognition and overall functionality. But I don't think that they would cancel out each other. In fact, there's definitely a complimentary role. We would just have to look at each patient individually.

Brian Fiske:

And I think that's important, again, just to help listeners understand the distinction between some of these approaches. Again, deep brain stimulation really is about planting these electrodes into parts of the brain impacted by Parkinson's with the idea of helping to modulate the neural activity in those regions and, hopefully, to correct them a little bit so that you can get some good movement control. They're not replacing dopamine. It's not like the deep brain stimulation is giving you back some kind of dopamine signal that is lacking versus the stem cell replacement approaches really is about trying to deliver that dopamine back to you. So I could imagine outside of, again, like you said, having double brain surgery approaches that the two, I agree, could be complimentary. So I think that'd be interesting. Obviously, if we see ultimate approval of these approaches, I could imagine you're going to see attempts to try to combine the two and see if you get even more optimal benefits and things like that.

Maggie Kuhl:

And just to clarify, FUS, I think you shared, which is focused ultrasound, which is a newer therapy that mimics what deep brain stimulation does, but is permanent and is an ablation surgical but non-invasive approach. So again, more information on those different types of approaches and where they are now on our website at michaeljfox.org. Brian, some people may have heard of a breakthrough in dopamine replacement, very early stage, very discovery stage, where one type of cell called an astrocyte can become a dopamine cell in the body. Could you outline for us that finding and the current state of that research?

Brian Fiske:

Yeah. So this is, I would say, a really interesting concept and people have been looking at this idea for a while, but in the last couple of years, there's been at least some research progress that suggest it might be feasible. And again, I would say this is still early days, no one's ready to try this in humans yet, is this idea, using, again, a recipe of factors, can you go directly into the brain and coax cells that are existing in the brain that aren't dopamine cells to become dopamine cells? And there's a particular type of cell type in the brain called an astrocyte. And there's some biological rationale for astrocytes in neurons having a developmental relationship that might make it easy to convert an astrocyte into a neuron. So researchers have looked at this and at least in some model systems in the lab, shown that you can coax these astrocytes to become

dopamine neurons and suggesting that you might actually feasibly be able to do that.

Now, there's a lot of work still to do and there's some ongoing work that we're supporting in partnership with some other groups to try to further explore this idea and see if we can consistently do this and safely do it. There's a lot of big open questions, of course, but this idea again is could you trick the brain into repairing itself I think would be really powerful. And as I think more knowledge is built on this idea, you could imagine then a future where maybe with a cocktail of factors, you could actually help the brain repair and replace the cells that were lost in diseases like Parkinson's. So I think that's still sci-fi to me. I think there's probably still many years to go before anything like that would really be able to be used in humans. A lot of questions you would still have to ask, but I think it would be a very powerful next step, next generation for thinking about cell replacement in diseases like Parkinson's disease.

Maggie Kuhl: Fascinating. Okay, last question. This is a question that we got from the community, it's one we get a lot. What is the timeline? What is the realistic prediction of the timeframe for a regulatory-approved stem cell therapy?

Brian Fiske: How about Harini answer that one?

Harini Sarva: At least another five years, I would say, because the surgical trials have to get off the ground. They have to complete enrollment without any safety concerns. All the data has to be analyzed at least after a year or two of recruitment. And then the next steps have to be decided from theirs, but I would say at least five years, if not more.

Maggie Kuhl: And you said recruitment. One way that people listening can advance those timelines is to volunteer for research both directly for trials or for studies that help us learn more about disease and the ways that we can intervene to stop it or slow it. So again, I'll give a plug for our foxtrialfinder.org tool that helps connect with research opportunities and helps match you with ones that you may be most eligible for volunteers as a resource that money cannot buy, and it's something that all trials desperately need. So again, five years seems a long way off. You can play a role in shortening timelines to new treatments by participating in studies. But I also just want to share the enthusiasm.

Five years for people who are living with Parkinson's and who are waiting for these treatments is a very long time, but in research, that will encompass so much work and so many advancements toward a therapy. So one trial has already reported phase one and is gearing up for phase two. There's more coming behind it. There are a lot of different approaches to achieve this replacement of dopamine and this restoration of movement function, and as we discussed, lots of research into the many other things that go wrong with Parkinson's. So lots of exciting developments. And to keep track of this research and to learn more about all the different aspects of disease that we've discussed

today, you can go to our website, michaeljfox.org. Thank you Dr. Sarva, Dr. Fiske. Any parting words?

Brian Fiske: I think I'm excited. I've been with the foundation for many years and when I started, the idea of stem cells was still new but exciting. There was so much we didn't know about the biology around the stem cells. We still had to figure out how to make the dopamine neurons from the stem cells, and that was some of the early work that we were supporting. And then things took a while to figure out the logistics of how do you actually then make these safe enough to put in people? And that took a long time.

So now that we're seeing these ideas really move into early human testing, it's exciting to me and the rest of the community just because finally we have a real chance to really see if these are going to hold real meaningful benefit. And some of the early signals are suggesting that it's feasible and safe, and that's great, and we'll obviously look eagerly towards the first signals of efficacy. But I think it's exciting times. We say this a lot about the current Parkinson's pipeline being really robust and exciting and a lot of hope in there, and I think this is one of the components of that hope or treatments like this.

Harini Sarva: Absolutely. I think just from a practical clinician standpoint, it's really nice to be able to offer patients alternatives to standard of care, and it's providing a lot of hope for many, many patients

Maggie Kuhl: A smorgasbord of options you'd say.

Harini Sarva: Yes.

Maggie Kuhl: Thank you both and thank you for listening. If you like this podcast, please share it with your friends and family or rate and review us on iTunes and wherever you listen to your podcasts. Until next time.

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