Zoom In on **Dementia & Alzheimer's**

BIO-HERMES-002: Innovative Study to Advance Precise Alzheimer's Diagnosis

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Transcript of Zoom with John Dwyer, President of the Global Alzheimer's Platform Foundation (GAP)

NANCY LYNN KEACH: Good morning and good afternoon to everyone. My name is Nancy Lynn Keach. I am a Senior Vice President at BrightFocus Foundation. BrightFocus Foundation funds research globally for Alzheimer's disease, macular degeneration, and glaucoma, and has invested over $300 million in research worldwide over the last 51 years. And we are delighted to bring you this program, which is made possible in part by educational funding from Biogen, Lilly, and Genentech.

And thanks so much for being here. We have a great study that we're going to be talking about today. As always, a lot of the questions you guys submitted are not necessarily on this topic. So I want to remind everybody that we have all of these other episodes that we've done over the past year and a half. And so if, for example, your questions are about lifestyle interventions, there were several questions about that, you will see that there is an episode from Dr. Laura Baker where she talks about non-drug interventions and all of the science behind lifestyle interventions. And in addition, on January 9, we have one of the world's leaders, Miia Kivipelto, who organized the FINGER study, looking at diet and exercise and sleep

and all kinds of modifiable risk factors for Alzheimer's. That's on January 9th. But again, there are answers to a lot of questions here.

So today, I'm going to introduce our guest, John Dwyer. And John is the President of the Global Alzheimer's Platform Foundation and is a serial health care entrepreneur. He held his first CEO position at the age of 30. And you can see he's now 35 and has held leadership positions in numerous emerging growth companies in the health care industry. John is a co-founder of several Alzheimer's related groups, including UsAgainstAlzheimer's and the Alzheimer's Action Pack. He is a graduate of Marquette University and the Cornell Law School. And John is an outspoken and disruptive in a good way leader in the neurodegenerative space, advocating for greater understanding of how to understand and treat Alzheimer's related dementias and Parkinson's disease. Welcome, John, and thanks so much for giving us your time today.

JOHN DWYER: It's great to be here, Nancy. Really, thank you for the invitation. I've always wanted to be on a podcast with you. I've now can check that off the bucket list.

NANCY LYNN KEACH: Absolutely. And I'm really excited to introduce people to the Bio-Hermes-002 trial. And this is a little complicated, but John is absolutely fantastic. And we're calling each other by first names because we know each other for many years. But John is a great person to explain this in plain English as best as anyone possibly can.

So, John, I'm going to start out, and everybody bear with us, because there's a lot to cover. This is the Bio-Hermes-002 research study. And I understand that there will be approximately 20 to 25 sites for this study across the US. What was Bio-Hermes 1?

JOHN DWYER: So let me start, Nancy, with just one or two sentences about me personally so that the audience understands what I am and what I am not. I was trained in my undergraduate work as a biomedical engineer, never spent a day doing that. So I immediately rushed off to law school. So for those of you that are going to listen to us today, understand I am not a clinician. I am, however, 40, 45 years in the health care system and have a profound family history of the disease. So I have a lot of lived

experience which many of you here today also have had. And that will give you context for why we are doing what we're doing.

Second paragraph, we at GAP were created for establishing a platform and a way of undertaking clinical trials that would make them faster, more effective, and by extension, lower cost than clinical trials were previously conducted. We have been doing this now for about eight years. And in the course of that eight years, we came to understand that we needed more information about how to better conduct studies at the precision person level when we were trying to design and recruit people for clinical trials.

That's how Bio-Hermes 1 came about, Nancy. So COVID starts. And in 2021, we designed and launched Bio-Hermes 1, which was designed to be a 1,000-person study that would look at people that were not demonstrating any clinical impairment or demonstrating mild cognitive impairment or mild Alzheimer's disease. And we had a number of subgoals, including to make it the most diverse clinical trial of its kind, which we did. And we were committed to not closing this study until we had at least 20% of everyone participating in the study coming from communities that were not white Caucasian, which was actually, for the time, a very ambitious goal. We undertook that study with the idea of we weren't going to be involved with the therapy. We were going to put folks through an assessment process where we could give them a battery of digital cognitive tests, retinal exams, and other digital measurements that would indicate either the presence of amyloid plaque or the presence of cognitive impairment, and compare it to traditional cognitive tests, as well as beta amyloid PET, which is the current gold standard for measuring the presence of amyloid, a protein that is considered the foundation for pure Alzheimer's disease. You're going to hear me say ATN a lot, which I'm Nancy said I'm not supposed to do, but—

NANCY LYNN KEACH: Well, what is ATN?

JOHN DWYER: ATN is amyloid or beta amyloid plaque.

NANCY LYNN KEACH: Which is a protein that is associated with Alzheimer's disease that you find clumping in the brain.

JOHN DWYER: We talk about a cascade. So you have beta amyloid plaque as an initiating protein, tau, which follows, and then neuroinflammation, ATN. And the combination of these three things are almost always consistently going to lead to some form of Alzheimer's or related dementia.

So we were trying to measure for that across a broad category of folks that were representative, not just of the communities, but were of an age and character that tend to be the folks plagued by the disease. We took a lot of blood samples in the course of this study, which was really critical because we've seen such and you've seen it. If you come to Nancy's and BrightFocus' podcast, they talk about the blood tests with some regularity. These are minor miracles that there are now neurology tests that can be derived from blood plasma. It provides access and scale and quality of assessments and diagnosis. So we took a lot of blood for the purpose of being able to sample and report out how a variety of blood tests performed relative to beta amyloid PET, but also all these other technologies.

NANCY LYNN KEACH: When John says beta amyloid PET, he is meaning a scan, a scan to see amyloid in the brain.

JOHN DWYER: Correct. It's an FDA-approved diagnostic. And as a consequence, when we put all this information together, and this is the important part about Bio-Hermes 1 now is we concluded the study and finalized the database in '23. So it was a relatively productive study to get 1,000 people in and then close the study and just under two years.

NANCY LYNN KEACH: Wow.

JOHN DWYER: We now have 7,447 biomarkers per participant.

NANCY LYNN KEACH: So because it's really worth dwelling on for a second. So biomarkers are some kind of biological indicator. It can be a protein; it can be genetics. And to really understand Alzheimer's disease, which, frankly, we do not and related dementias, we really don't understand all of the causes and all of what indicates which type of cause there is for any dementia someone is experiencing, these tests, these

studies, collecting every single little bit of precise information about people that science could possibly collect today to know what their status is across literally hundreds, thousands of what we're calling biomarkers.

JOHN DWYER: The only thing I would edit on that, Nancy, is humility dictates that Bio-Hermes hasn't collected every possible biomarker. We did a very thorough job for what we could do at that time. And so Nancy was completely right, we have the full genome on every participant. We have not one, not two, but three different proteomics platforms contributing to the data set, a variety of other data that I've already described, like the retinal imaging data. And we put it all in one place. And now we can look at all of these 1,000 people and ask what was going on with them that led to them either having amyloid positivity consistent with Alzheimer's disease or not having amyloid positivity. And this was one of the outputs of our study is we found a very large subgroup, had all the cognitive impairment signs and symptoms consistent with mild cognitive impairment and mild AD, but no beta amyloid plaque that was consistent with Alzheimer's. So I'll just finish on Bio-Hermes 1 to say we have a study starting that we call the Mohs 300. And I'm smiling.

NANCY LYNN KEACH: That's M-O-H-S.

JOHN DWYER: M-O-H-S. And I'm smiling because those of you who know him, Richard Mohs is a very well-known neurologist, researcher. He used to work at Lilly and Mount Sinai. Now he's our chief science officer. And Richard is now looking for the first time at a group of very well-characterized negative amyloid positive for cognitive impairment at roughly 300, it's actually 297. But 300 sounds more Hollywood. And we are going to analyze what were the elevated proteomics or under expressed proteomics or other proteins or genetic genes that could be influencing these folks that clearly do not have Alzheimer's, but they look like they have Alzheimer's symptoms. They are very well, not just well characterized, but very diverse with a large component of this 300 being Latino and another component being African-American. And of course, the remainder are white.

We are right now grinding through all the data. Hope to have that result by March of next year. But this tells your audience how we look at our

mandate is to go to both sides of the equation, folks that are showing Alzheimer's symptoms and disease and those that aren't, and better understanding the multi-pathologies that scientists are telling us exists in Alzheimer's and dementia but aren't being tracked yet well.

NANCY LYNN KEACH: So I'm going to jump in, John, and bring us to today and bring us to the practical matter now of what Bio-Hermes-002 is and how people who are hearing this on the Zoom or on YouTube thereafter can participate in this study and why it would be useful to them. And I am going to start by saying that while John is clearly putting this in the framework of how this research about all of these biochemistry, as Michael is saying in the chat and I'm going to ask your question in a little bit, how all of that is informing the field so that we better understand what's causing these diseases, why participating in Bio-Hermes-002 will give you as a participant really the state-of-the-art and precise information you could possibly have about your or your loved one's condition at the present moment, which will allow you, if you choose to know the information, the very vast information that this study will collect. And you are allowed to ask for the results, and we'll get into that in a little bit. You will better understand your options for treatment and for the future by having participated in this at no cost.

So I just want to make sure that's really clear, that there is a very personal benefit to participants as well as to the research field by participating in this study. So let's get down to brass tacks here, John. And we are going to put in the chat a website that folks can go to. Actually, maybe we can put that in now. The study is, I believe, not quite up and running yet, but will begin-- when will it begin, John?

JOHN DWYER: Actually, we've started the study. It is currently active in Florida with a couple of sites. And we had first patient in the first week of October.

NANCY LYNN KEACH: So it started up, it's either started or will be starting soon at 20 to 25 or so sites. You can go to this website, globalalzplatform.org/biohermes 002study to see the current sites. It is possible, not guaranteed possible, though, that more sites could be added in the future. And so if you go and you don't see a site really close to you like Carol from Tennessee who asked, how can I join a research group? John was

saying beforehand he was distressed that we don't currently have a site in Tennessee, but there may be one you are willing to drive to or there might be one in the future. So keep checking back if there isn't a site close enough for you to get to. So how many people are you going to be trying to allow into this study, trying to bring into this study?

JOHN DWYER: Minimum of 1,000 up to 1,200.

NANCY LYNN KEACH: Up to 1,200. And my understanding is that you are looking for three different cohorts and cohorts are types of participants with one being people who are not showing any signs of cognitive decline. Is that right?

JOHN DWYER: Yeah. We call them asymptomatic.

NANCY LYNN KEACH: Asymptomatic. So you might have biological markers, but you're not exhibiting any symptoms yet. The second are people who have a diagnosis of mild cognitive impairment. And the third are people who have a diagnosis of mild to moderate Alzheimer's. So if you are anywhere from asymptomatic to mild to moderate, you may be eligible to participate in this study. And John, let's talk a little-- just let's lay out the eligibility criteria broadly.

JOHN DWYER: Well, broadly, we don't have very many.

NANCY LYNN KEACH: That's good.

JOHN DWYER: This study is designed to take all comers that can be safely brought through the study. So there are some very, very narrow exceptions. For example, you might not be appropriate, if you have a heart pacer, you don't want to go into a PET machine and have a magnetic field that could cause you physical harm. That's an example. So let's just assume we're taking all comers with just a handful of very narrow exceptions.

NANCY LYNN KEACH: Well, all comers means right now people who are ages 60 to 90, it's my understanding. Correct? So ages 60 to 90 who have a study partner. And a study partner is defined—

JOHN DWYER: Could ideally-- not ideally, routinely, a sibling, a spouse that works with the participant and knows of their physical condition and can help them if they need it, get transportation to or from the clinical trial site.

NANCY LYNN KEACH: So yeah, I read in your materials that that's defined as at least eight hours of contact per week. So just I want to make sure people understand, yes, it's best if it's somebody who's very close with you, a spouse or an adult child who's living with. But it can be somebody who has eight hours or more contact with you and knows you well and is available to attend the site visits with you.

So let's say they go, and they're considering enrolling. What are the-- I know you can't go into every single little one, but what basically are the tests that people will participate in if they get into this study or if they're trying to qualify for the study?

JOHN DWYER: Yes. So I can give you categories at least. So one part of the study is consistent with every study that's done in Alzheimer's or in research generally, we take a medical history. We ask them about their current condition, ask them about the drugs they're on. And we give them a small battery of traditional paper and pencil cognitive tests.

NANCY LYNN KEACH: So I'm just going to jump in and say, so, Michael, yeah, there are digital and pencil and paper cognitive tests in addition to the biochemistry. Go ahead, John.

JOHN DWYER: And then the next category, which we call digital marker collection comes in a variety of different flavors. And we have many more of these than we did in Bio-Hermes 1, but we will once again be taking retinal exams to see what the eye insights can provide in terms of the accumulation of beta amyloid plaque. We are taking EEG readings in a brand new technology setting to see the correlation between those EEG readings and cognitive impairment. We are also taking several different readings using digital iPad-based measurement mechanisms to also measure for cognitive impairment and subtle differences that paper and pencil can't provide.

And last but certainly not least, we're taking a really interesting approach

where we are asking participants to read a story. And we're measuring the oral measurements of the timber and changes in their voice as a possible indicator of cognitive health. So that's pretty broad.

NANCY LYNN KEACH: That's fantastic. I didn't even read about that. But there are a lot of studies now about how even psychosis or dementias can be detected from speech and linguistics. So it's quite fascinating. I also have that people will come in and have the cognitive testing that you described. They would undergo an MRI brain scan.

JOHN DWYER: We're going to do an MRI brain scan. We will do, once again, a PET imaging for beta amyloid plaque. And we're adding a PET imaging visit for presence of tau.

NANCY LYNN KEACH: Tau proteins, which is great.

JOHN DWYER: Which is about as broad as one can reasonably undertake for our field right now.

NANCY LYNN KEACH: And the blood sampling, John. And then the blood tests you told me would be taken. And can you talk a little bit about that?

JOHN DWYER: Yes. So we're going to be drawing blood, it's about-- there's a total of roughly visits to the site and then the imaging centers. And at several of those visits, we're going to take blood. Those blood samples will be used to generate all these markers we were talking about and including the full genome and the proteomics by spinning them down and using the plasma to see if we can derive an insight into the presence of certain proteins that are either correlated to Alzheimer's or not, and they may be correlated to something else.

Now, what's different about Bio-Hermes, I want your audience to hear this, is that on October 30 of 2023, Dr. Richard Hodes of the National Institute on Aging said in plain English, multi-pathologies causing dementia are the rule, not the exception. Now, Nancy and I've talked about this before, that was news to many of us. I've been doing this for over a decade. And it was always classic Alzheimer's is the majority cause of dementia. And then there are some others important subcategories like

FTD or—

NANCY LYNN KEACH: Lewy body dementia.

JOHN DWYER: Lewy bodies, thank you. But the thing is that get people like Nancy and me, we really were focusing on Alzheimer's as the biggest category in the total of dementia cases. Current research, frankly, changes our view, certainly my view that now, as important as it is and as many advancements as we've made in Alzheimer's, there are other pathologies that are influencing dementia. And Alzheimer's may only be 30% to 40% of all dementia cases, not the majority, but the minority of cases. Still a lot of people, terrible disease. My family's had it in many, many of my aunts and uncles and my father, so I'm not trivializing it at all. But we are duty-bound, I think, in the field to try to open the aperture the way Dr. Hodes opened our aperture to say, what are these other pathologies? How do they express themselves? And how much are they influencing our cognitive conditions?

NANCY LYNN KEACH: And how can we treat them?

JOHN DWYER: First, we have to find them.

NANCY LYNN KEACH: Right. Absolutely.

JOHN DWYER: And once detected, how do we target them and how do we treat them? This is the kind of precision medicine cancer has been pursuing for 30 years. And we're just embarking on it now in Alzheimer's disease and related dementias. So in Bio-Hermes, I'm coming to the point, we are really drilling down on how we can measure the presence of other pathologies that are not routinely measured for in clinical trials.

For example, vascular dementia, which is if you have significant vascular disease, it's understood that that can contribute to dementia separate and distinct from Alzheimer's. Very tough to find, though, actually. The field is not really well-equipped to detect and call out the presence of vascular dementia. So that's why when Nancy was talking about MRI, we're actually trying to use the most advanced protocol we can use in scale to measure for vascular dementia because that's one of the better modalities for

measuring a form of vascular disease.

Similarly, we're in this study taking alpha synuclein measurements. Alpha synuclein, for those of you that the field, is much more pronounced in terms of being analyzed in Parkinson's as compared to Alzheimer's.

NANCY LYNN KEACH: What about alpha synuclein for those that don't know the field, John? What is alpha synuclein?

JOHN DWYER: Well, remember, I'm not doctor. But alpha synuclein is another pathology, a protein causing a pathology that contributes to cognitive impairment that is more routinely-- and other executive function issues more routinely associated with Parkinson's. What a lot of people don't know is that as much as 40% of everyone who is diagnosed with Alzheimer's disease will also have alpha synuclein present.

Now, is that contributing to their condition? Or is it not contributing to their condition? The Bio-Hermes 1 and Bio-Hermes-002 studies will be some of the first to have a very pronounced focus on the presence and progressive nature of alpha synuclein in this population. Just two examples. I'm not going to spend all our time on that, but I want your audience to understand we're taking a very broad approach, so that we can offer the field a more complete picture. And once again, we're going to do that with a very diverse participant pool. Here, we're shooting for 25% to 30% of the panel of participants coming from populations that are not routinely in clinical trials in scale. And we hope that that will further shed light on the differences among us.

NANCY LYNN KEACH: I just was going to say, I think, John is pointing this out. There's a lot of discussion about diverse ancestry in the field. But I think I'm just going to say it in plain old terms, because that's how we-- it's not about being politically correct, but it's about scientifically understanding differences in ancestral-- different conditions are different in people of different ancestries. And scientifically, it's important to understand the differences in order to understand how different populations are affected by diseases or what different causes they have. But I want to go back, John, to the actual participation in Bio-

Hermes-002. And we talked about the cognitive testing, the amyloid and tau PET scans, MRI brain scan, blood sampling, genetic testing. And Beth asked a question that you made a point of telling me yesterday. Beth asked in the chat, in these studies, do you share the results of the amyloid PET and tau PET scans and the blood tests? So you talk to me about this yesterday. Let's let folks know about this.

JOHN DWYER: So we will share that which is clinically proven to be shareable. But I'm not being equivocating. So we have primary investigators and very well tuned in about how to measure—

NANCY LYNN KEACH: Keep it simple, John. Keep it simple.

JOHN DWYER: We're going to tell you what your cognitive condition is from the point of view of a seasoned investigator and using traditional FDA and research-accepted paper and pencil tests. They are not experimental. We'll give you that information if you want it. I want to come back to that. We will give you your tau-- excuse me. We will not give you your tau. We will give you your amyloid PET result, which is an FDA-approved diagnostic test. We will give you that result if you want it.

Remember, I'm a patient advocate and a lawyer. We do not share our clinical trial data on you with your doctor. You share it with your doctor. If you don't want this information in your electronic medical record, we're not putting it in your electronic medical record. We're going to hand you these results. And you can do with it what you may. We hope you will look at it. We hope you will inform yourself about what it tells you and ask us questions. And then in your own consultations with your family and your doctor, pursue a number of options. But the advantage of our process is it's private. It's not in your EMR, and it's certainly not for anyone but you to have and for you to consider. That's a very unique environment in our current situation. And we're proud to help you with it.

NANCY LYNN KEACH: And really important, because a lot of people are quite concerned about any of this information going into their electronic medical records and it affecting their insurance and so on. And so I wanted to point out that I think, correct me if I'm getting this wrong, but I think yesterday you said that for the time being, the blood tests are not FDA-approved.

JOHN DWYER: Correct.

NANCY LYNN KEACH: Although they may be or some of them may be during the course of this trial. So if they are approved, you would be able to share some of the information from the blood testing.

JOHN DWYER: First of all, we are eagerly awaiting an FDA approval of these blood tests as approved diagnostic. And I personally believe that is imminent, like within the next 12 months. When we have approved blood markers, and we are actually using those markers and a participant wants those results, we will provide those results. It may be a year from now before we can release them. But whatever is approved by the FDA, we will make available to you. But we're not going to give you a laboratory developed tests that aren't approved, that are only approved for research use only, because we can't. They're experimental.

NANCY LYNN KEACH: They're experimental. And I think even more to the point, these are such new technologies. And the field is like jumping up and down with excitement because we have these new technologies to see certain proteins and genetic dispositions in the blood. But all tests are not created equal yet, and they're not all fully vetted and tested yet. So until we know that things are as accurate as they need to be and approved by the FDA, you certainly don't want to give people wrong information. You don't want to share information, for example, that would be a false positive from blood.

So I think the accuracy of the blood tests to detect 2017, for example, or other proteins is really high right now in the best tests. And the field has learned a tremendous amount and is moving ahead really at lightning speed on making these tests very accurate, more accurate than anything we've had to date, I would venture, to determine the presence of amyloid and tau especially.

And I will remind us, remind all of us that not that long ago, the only way to detect those things were on autopsy. And now we're talking about being able between scans and blood tests to detect them before you even have symptoms potentially of dementia, so that you can intervene either with a drug or a lifestyle intervention to delay the progression or the onset

of your symptoms. So it's very exciting times. But John is clearly showing caution. And the study design shows caution that. And basically, I think in a nutshell, the Bio-Hermes-002 study will share as much information with you if you want it, as he says, as is legally permitted. And that may change throughout the course of the study because the science is moving so quickly.

So that's interesting. So a YouTube question, can you speak to the ethical implications of insurance/driving capabilities if patients allow EMR record keeping? So I think let's reiterate again that if you participate in this study, your information is not going in automatically to your EMR. But let's say, John, let's say somebody gets their results from Bio-Hermes-002, and it indicates you have the presence of amyloid, you have the presence of tau, you're showing signs of cognitive impairment. So you're going to want to go to your doctor, or neurologist or both and start finding out what you can do or get on one of the approved medications, Leqembi or Kisunla if you're at the right stage and so on. So what are the ethical-- and this is not your specialty I know, but I'm sure you have some opinions that you would share. What are the ethical implications in terms of insurance and driving capabilities and so on? Once you get into this, well, now what? Now what do I do about this?

JOHN DWYER: Right. So the ethical implication is this is your body, this is your information. And as a consequence, if you have a point of view of what you want to learn more about your condition and you go to your doctor, you need to talk to your doctor about what the next steps are and what in terms of the level of invasive information needs to be provided for the doctor to give you a thoughtful answer to what your options are. Doesn't mean it has to go into the EMR. But if the doctor is billing for the visit and he acquires information, he has to put it in the EMR if it supports the visit. So that is the question everyone deals with. California is very aggressive about requiring physicians that have evidence of cognitive impairment reporting it to the DMV for purposes of being able to drive. I don't know the rule precisely because I no longer live in California, but it's a real issue.

So having a frank, open conversation with your doctor about what is

or isn't going to be put into your record, what he can say generically about what your options are without knowing a lot about your current condition, these are all things that you need to explore with your physician. There's a lot of information-- and you need to talk to a medical professional. There is a lot of information out there, though, about your options, particularly, listen again to Nancy's podcast with Miia. The FINGER study that she's going to talk about will explain to you a great deal about lifestyle, how it can make great changes and give real cognitive benefit. So it becomes a time of asking questions and learning more about your condition.

I want to stress one thing. I have a lot of family and friends. Just getting a positive blood test or a positive amyloid PET test does not mean you're going to get Alzheimer's. Just doesn't.

NANCY LYNN KEACH: It's really important. Yeah.

JOHN DWYER: It does mean, you got to think about it, as a higher probability condition that's going to influence your quality of life. And there's a lot of advice out there and learning. One of my favorite answers is if you can keep the literature, this isn't John Dwyer practicing medicine. The literature is clear. If you have hypertension and you can bring your hypertension under control and stay at 120 over 80 on your blood pressure, you are doing as much for your continued vitality and cognitive health as almost anything else you could do. You can still do other things. But the point is the choices are very much broader than people realize. And we encourage people exploring all their choices, not all of which are necessary to go to the doctor for. But you got to get some medical advice for any of these choices.

We would say to you at our clinical trial sites, we know where the current disease modifying therapies are being administered in all our locations. If you want to learn more about those, we can send you to doctors that administer those drugs. If you want to learn more about lifestyle, we can send you to places where they're doing great work and exercise and other lifestyle after you go through our study. And if you want to go into other studies, that is to say real therapeutic studies that are testing either devices or drugs that could make a manifest benefit to you and to society

generally if they work, we have those studies to offer or can tell you where you can go to get those studies. So look at the number of choices you have. And one of the things I always try to stress is the level of hope we have realized in the last six years has gone up exponentially, because we now know more and we know more about what we can do about it.

NANCY LYNN KEACH: John, I'm going to ask you, well, I'm going to ask you something specifically about Bio-Hermes-002 in a second. But Darlene wrote about that her MRI showed that her hippocampus was significantly smaller and she's forgetting past experiences. And I know I said, we're not going to talk about individual medical conditions, but we haven't talked about measurement of hippocampus. Is that part of-- will that be part of what you'll see in Bio-Hermes-002?

And I will also mention, Darlene, please do watch on January 9, because I believe that there are certain lifestyle interventions. And Dr. Sharyn Rossi, who's also on with us, can correct me if I'm wrong, but I believe that there are certain exercises that can slow down the atrophy or shrinkage of different brain areas. So thank you, Sharyn. She did confirm. Dr. Rossi, exercise increases hippocampal volume. So the question for you, Darlene, is going to be and for everybody else who wants to stay healthy, the lifestyle interventions can help increase hippocampal volume and do a lot of other good, as can other lifestyle interventions. So it's a great question.

And I think the connective tissue here is that if you're participating in Bio-Hermes-002, you will know-- you will have the best possible current knowledge of your own condition and be able to monitor it potentially over time in different ways.

JOHN DWYER: Thank you for saying that there is a longitudinal component to Bio-Hermes. We anticipate a minimum of 300 participants being in the study for an additional two years. So we can take measurements of how they proceed. Do they stay healthy? Do they start to progress over that extra two years? Very important.

But I just want to answer that, I didn't answer and won't talk about the hippocampus per se. That is part of the measurement process that the imaging folks use both in the MRI and in the PET imaging process. But

it's all bound up in the result we get from the docks. And so we don't and won't report your hippocampus was broader or narrower. And I thought Sharyn gave you great advice. The more you stimulate blood flow, the better. It's for the whole brain. What's good for your heart is good for your brain. And I firmly believe that. Wish I followed my own advice more.

NANCY LYNN KEACH: There's a YouTube question from Craig. It looks like he's in pharma. Is APOE genotype determination one of the trial endpoints?

JOHN DWYER: We are collecting phenotype APOE status along with the rest of the full genome. Now that's a timing issue. I'm glad you brought it up. What we do is we collect the blood on all 1,000 people. We do not genotype them in a short-- inconsistent with the participants being in the study. We do it later. So we can, if asked, provide their APOE status, but it will be towards the end of the study. It won't be during their actual participation because we batch the entire group and get a consistent genotyping from one vendor.

NANCY LYNN KEACH: Thank you, John. And as the blood tests in general develop and come to market, there will be other ways to assess one's genotype, obviously, than the participation in a study.

JOHN DWYER: Can I say one more thing, a couple things more about the study that show—

NANCY LYNN KEACH: Well, you certainly can. And in fact, John, I'm going to say, we have seven minutes. So you say what is really important here, even though I have lots more I wanted to ask you.

JOHN DWYER: Well, I just want to point out to the audience, one of our missions is-- it does say Global Alzheimer's Platform in the name. So embedded in this study are a couple pieces of technology designed to make whatever we learn more scalable and executable in countries or parts of the United States, for that matter, that are not well-endowed with great medical resources.

One of them is really cool. It's a blood spot technology that's coming out

of Sweden, where you just take a little blood and you literally prick your finger and put it in three different holes in a cardboard device. It seeps the blood and separates the plasma from the red blood cells. And what's so great about that is we believe we're going to validate it, but we know that it's very accurate in giving the same blood tests that we've been talking about, that we're taking big blood draws for, spinning down, and keeping in negative 80 degree freezers. Folks, there's a lot of countries, a lot of parts of the United States that they don't have spinning minus 80 degree freezers to keep blood, much less analyze it. So we really like this technology because if it works, we can do blood tests anywhere for anybody that will help understand their condition from a pathological point of view and inform the doctors who seen some symptoms of some kind of cognitive condition.

We have several like that. As we like to say, can't swing a dead cat without having, now an AI application. So we have four or five different artificial intelligence applications to look at the imaging, to look at the retinal, to look at the cognitive tests on the digital environment. So we're state-of-the-art, and we're also using the most basic technologies we can find, so we can transport our learnings to any part of the globe that can benefit from it.

NANCY LYNN KEACH: And I'm going to give a little shoutout to our friends at RetiSpec, who have been working for years to develop this technology to do retinal scanning. And probably, many of you have heard something about this idea of being able to detect amyloid protein through the eye or other diagnostic hints through the eyes. And the team at RetiSpec has developed some fantastic technology that's now being pioneered in tests around the world that will also help us be able to diagnose in more efficient ways. So I hope I've got that right, John. But I think RetiSpec is the company.

JOHN DWYER: That's right. Someday, these kind of things will all creep into clinical practice. Someday when we all go to get our eyes checked for a new set of glasses, we will be able to get a retinal exam that is seamlessly part of the optimal logical journey and hopefully, provides real information at a more convenient, less onerous way.

NANCY LYNN KEACH: And John, this is going to be, I think, the last question because we're only three minutes out. But it's a great question from Beth. If a person is in another study, not a treatment, not a drug study, but such as ADNI4, which is an imaging study, does that disqualify you?

JOHN DWYER: No. But just so Mike hears me say it, that's the leading godfather of ADNI4. ADNI4 is an important study. It's a great study, but we would happily, if it's convenient for you, we'd happily evaluate you for Bio-Hermes. They are not mutually exclusive.

NANCY LYNN KEACH: That's great. But if you are on Leqembi or Kisunla or something like that, are you eligible?

JOHN DWYER: Actually, Nancy, you are. I don't think you're going to do that because you've already had an MRI and a PET exam to get on Kisunla or Leqembi. But if you want to come in and be evaluated through our protocol and participate in research, we will absolutely-- there's no exclusion for the existing standard of care.

NANCY LYNN KEACH: That is awesome. John, honestly, I could go on for at least another hour on this study, and it's a complex study and obviously a very complex subject. And I want to thank you for laying this out the way that you have in a way that I hope was understandable. And I want to encourage viewers both on YouTube and on the Zoom and who are watching this months from now that if something isn't clear, please go to the website or email us. And we're going to put up our contact information in a second. Because this study will be going on for a year or two years, what, roughly?

JOHN DWYER: Well, we hope to have it fully enrolled in under 14 months.

NANCY LYNN KEACH: Fully enrolled, but then it'll keep—

JOHN DWYER: It will continue. And then the longitudinal piece, I think the whole thing finishes in '27 or '28.

NANCY LYNN KEACH: So there's time for people to get involved.

JOHN DWYER: Absolutely.

NANCY LYNN KEACH: I also want to say that because I think, not only is this pioneering in terms of the complexity of the data that you'll be collecting, and we didn't even get to talking about keeping the blood samples or data storing specimens and things for future use to be able to look at over time and all kinds of fascinating things that GAP is doing in this study. But we hope you'll come back. That's what I'm leading to, maybe when you're fully enrolled or maybe even before that because the field is changing so much to keep us updated on how the study is going and what you're learning and what we're all learning because we're all learning such tremendous amounts right now.

And one of the biggest problems is keeping the public and the health care providers, the doctors and the neurologists, informed about all of this breakthrough research and science that's going on. That's one of the field's big issues right now. And so we hope at BrightFocus and with thanks to GAP, we hope that what we're doing with these monthly and sometimes bi-monthly programs is trying to keep you as best informed as we can along the way as the science becomes really exciting.

So I'm going to ask-- I'm going to thank John Dwyer. Thank you so much, and some of the members of his team who are on, Amanda and Julie. And I'm going to ask Ashley to put up the next slide real quickly. If you would like free resources that are available about Alzheimer's, you can email us at info@brightfocus.org. And I think we had it up before, but to see all the other episodes of Zoom In on Dementia & Alzheimer's and dementia clinical research, you can go to brightfocus.org/zoomin. And the next slide, please.

If there's a topic we haven't covered that you're dying to know about, please email us, reply@brightfocus.org. And the next slide. OK. Yes, so January 9, you'll see, Can Lifestyle Changes Prevent Alzheimer's? What the Research Reveals on January 9, 1:00 PM Eastern, 10:00 AM Pacific, with Dr. Kivipelto, who is absolutely great. So I hope you all can join us.

I want to thank everybody for participating. Again, please feel free to write to us if you have questions that haven't been answered. And we're going

to wish you a fantastic day and a fantastic holiday season and hope that we see you again on January 9th.

JOHN DWYER: So, Nancy, thank you very much. Want to thank you all. But I also want to give a quick shoutout to Stacy Haller, who is a multigenerational leader in the field. And I don't see her today, but I'm sure she's listening. So I just want her to know, I'm thinking about her and very grateful for this opportunity.

NANCY LYNN KEACH: Thank you very much.

Resources:

BIO-HERMES-002: https://globalalzplatform.org/biohermes-002study/