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

**Non-Invasive Light and Sound Stimulation Therapy in Alzheimer's: Update on HOPE Study**
**Thursday, September 18, 2025 | 1 p.m. EDT**
**Transcript of Zoom with Christian Howell, Chief Executive Officer, Cognito Therapeutics**



**NANCY KEACH:** Hello, and welcome to the 32nd episode of BrightFocus Foundation's Zoom In on Dementia & Alzheimer's program. I'm so happy to see everybody here today. And many of you who are coming back for multiple episodes, thank you so much for attending and for your excitement about these new technologies.

My name is Nancy Keach. I am Senior Vice President of Strategic Partnerships at BrightFocus Foundation, which is a nonprofit that funds exceptional scientific research worldwide to understand and treat Alzheimer's disease, macular degeneration, and glaucoma. Over the past 51 years, we have awarded over $310 million for scientific research grants worldwide, and those grants have catalyzed scientific breakthroughs across diseases of mind and sight that have led to novel treatments, prevention strategies, and diagnostic tools.

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these free programs possible.

If you have questions that are not answered today or were not on today's topic, on the screen now is a list of our 31 previous episodes on a wide variety of topics. These have so much information. They are available to you for free. Please enjoy at brightfocus.org or on YouTube.

Today's program is Noninvasive Light and Sound Stimulation Therapy in Alzheimer's: Update on the HOPE Study. Everyone is really excited. We actually did a program on August 1 of 2024 on the HOPE study when it was just enrolling, and we're going to be following this study and these devices all along the way until hopefully they're in all of our hands or on all of our heads. So I'm delighted to introduce our expert today, a fantastic leader in the medical device field, Christian Howell. Hey, Christian.

**CHRISTIAN HOWELL:** Hi, Nancy. How are you?

**NANCY KEACH:** Great to see you. Thank you so much for doing this. Christian is chief executive officer of Cognito Therapeutics, a late-stage clinical neurotech startup pioneering non-invasive neuromodulation therapies to treat Alzheimer's and other neurodegenerative diseases. With more than 20 years of leadership experience across startups and global medtech companies, Christian holds deep expertise in advancing innovative medical technologies from early development through market adoption. Christian began his career as an officer in the US Navy, where he developed a lifelong commitment to mission-driven organizations and work in the service of others, principles that continue to guide his leadership in health care. He has since held senior roles at Medtronic, where he led value-based care initiatives, and at Aetion, where he built partnerships that supported a major growth round. A frequent speaker at institutions, including Harvard, MIT, and the G20, Christian is recognized for his ability to bridge science, business, and policy to expand access to transformative therapies. We are so happy to have you today. Welcome to the program.

**CHRISTIAN HOWELL:** Thank you. I can't wait to meet the guy you just introduced in a way. Seems like a really great guy. But, one, thank you so much for having me. And, two, as you put up the list of previous speakers,

I recognize that I am missing an MD or a PhD in my list. So what I can say for the group is we come at this from a very similar position, which is I am constantly trying to learn about neurodegenerative conditions, Alzheimer's disease, neuroscientists. And so as much as I can try to translate that from oftentimes what can be very scientific and confusing language into much more easily understandable language, please hold me to that. I want to make sure we all walk away really having an understanding of what we're trying to solve here.

**NANCY KEACH:** Well, I'm definitely going to hold you to that with great pleasure. And I'm going to start with the very basics, and then I'm going to ask you about your first trial. Then I'm going to ask you about the HOPE study and the results. So just bear with me, though. I want to go back to the basics. What is your company's device, Spectris? And very basically, how does it work?

**CHRISTIAN HOWELL:** Yeah. So I'll get as basic as possible. So what we've learned over the last 20 years is that an active brain is a healthy brain. And we know when the brain is at particular activity levels, it expresses biology that is incredibly important to protect itself and fortify itself from neurodegenerative conditions. And so what the scientists and neuroscientists at MIT and Harvard and other places learned was that you could stimulate the brain using a non-invasive approach where you use light therapy to stimulate the optic nerve and sound therapy to stimulate the auditory nerve at 40 Hertz. And what it resulted in was a very profound reciprocation of that stimulation across the brain. And so what we know in neurodegenerative conditions like Alzheimer's is that the brain is restricted in its ability to reach these naturally occurring activities levels.

So we're able to stimulate to that. And so patients wear the device an hour a day every day. And, Nancy, as you mentioned, one of the things we're really proud of is that we have made a commitment at Cognito that we want to do very robust clinical research to understand both this technology of Spectris, this idea of using light and sound, and this particular device, which is Spectris AD. So happy to answer any questions about that. But that is it in a nutshell. It's an at-home therapy.

**NANCY KEACH:** This is the device, Spectris.

**CHRISTIAN HOWELL:** Yeah, I have one here.

**NANCY KEACH:** Yep, Christian brought his along.

**CHRISTIAN HOWELL:** Yeah. And you can see that it's a set of goggles. And there is light therapy delivered at the eyes. And then there are earphones in which the sound therapy's delivered, very user friendly. It's incredibly comfortable. In our UX research, we have heard from patients or participants that they feel that it's meditative and comfortable. And I think that's reflected-- and I know we'll talk more about it, but I think that's reflected in the adherence we see in the study. We don't think it's a small ask to ask participants to sit for an hour a day every day. And in our feasibility study, we saw 85% of patients sat for at least 50 minutes at least six days a week. So that tells us that they are incredibly engaged.

**NANCY KEACH:** And I think that's something that the general public doesn't always think about with these clinical trials or devices, that adherence, actually doing what you're asked to do, whether it's a drug or a non-invasive-type device, adherence is a big issue. And your adherence numbers are very, very high, which does indicate that people are enjoying or very committed to using the device. I want to get this out of the way at the beginning because we had two pre-submitted questions. And I see Adel wrote in the chat, would it be suitable for people who are hard of hearing or deaf? And there were two questions from people submitted saying that they had not been able to participate in the trials and that it was unfair. Can you explain, since there was an auditory stimulation here, why that is an issue and whether there's something that people who are hard of hearing can do?

**CHRISTIAN HOWELL:** Yeah. And two just disclaimers as we start. The first one is we are in the middle of a pivotal trial. So I want to be sensitive that we are not doing anything that risks unblinding of that trial because it's a sham-controlled trial, which means we're measuring the impact of the therapy in a group of patients that are receiving an active therapy and then a group that are not receiving an active therapy. So I don't want to do anything to unblind that, but I want to be as open answering questions as I

can.

The other is that we have yet to submit to the FDA. So what I'm going to share with you is what we've learned in our studies and what we have seen in other preclinical work, but we are not yet approved by the FDA. So if it feels like I'm couching my language at all, just know that I want to be sensitive to how the FDA guides companies at our stage to talk about therapies like this.

But it's a very good question in that when we think about designing studies, what we want to do is we want to design the study so that we can get as optimal an outcome as possible and that we can get an outcome that is reflective of what we're going to see in the marketplace. And so when we screen patients, we know that we're going to give patients a visual stimulation, and we know that we're going to give patients an auditory stimulation. And so what would happen if patients couldn't hear the tone, they would adjust volume. And they ended up giving themselves an adverse event in tinnitus. And so what we wanted to make sure was that in our studies, really, what we were measuring is the impact of the therapy. We really want to understand, what is the impact of the therapy in the preservation of function, the preservation of cognition, thinking about things like the preservation of brain volume? And then when we come to market and we start to think about device iteration, and we start to think about new studies that we'll do, I think then we'll start to explore and lower and expand and start to take on some of these other conditions, like how would you address this with a patient that might have significant hearing loss, or how would you address this with a patient that might have complete hearing loss? And I think we're going to continue to explore the science and all that, but this particular design was really meant to make sure that we can measure the impact without interference of the light stimulation and of the sound stimulation.

**NANCY KEACH:** Makes a lot of sense. And it doesn't mean that this won't ultimately be effective for people with hearing loss. But you're doing your best to get this to people, get this approved as soon as humanly possible, which we appreciate.

**CHRISTIAN HOWELL:** That's right.

**NANCY KEACH:** Your first clinical trial using Spectris was the OVERTURE study, which ran, I believe-- correct me if I'm wrong-- 2018 to 2021. And in that trial, you had, I think, about a little over 70 mild and moderate patients, Alzheimer's patients, over the age of 50. And I thought it was really interesting. And again, correct me if I'm wrong, but I read that it was not required that those participants had a lot of amyloid protein in the brain, which is what the drugs that are approved, Kisunla and Leqembi, are targeting is amyloid in the brain. So first, let's just say real briefly, what were the results of the OVERTURE study? And then we're going to talk about the HOPE study.

**CHRISTIAN HOWELL:** Yeah. And I'd love to. So quickly, I'll give you the results because we were incredibly enthusiastic about the results. So one, we measured the preservation of function using a test called the ADCS-ADL. And what we saw was a 77% preservation of function compared to those that received the sham therapy. When we looked at cognition, we used the Mini-Mental State Exam. And what we saw there was a 76% preservation of cognition. And then what we also looked at was brain volume, looking at the MRI. And what we saw there was a 69% preservation of brain volume. And we've also done a series of subanalysis on that, which have been really exciting.

But I think looking at the list of experts that have been here before and thinking about where we've been historically with Alzheimer's disease, I do think it's very important to draw a line and a distinction between a chemistry-based therapy or a drug-based therapy and a physics-based therapy and a medical device and how we test them and how we study them.

So the first thing that we did was a proof-of-concept study, which was really to determine that the therapy was not causing any type of adverse event, that it could be used safely. Then we designed a feasibility study, which is different than what you would see in a phase II, is what you hear in drug therapy. And the reason why is in a device, we want to understand, where are we getting a signal? What are the endpoints in which we're seeing that the therapy is being impactful? And that's what we saw in OVERTURE. And then we did what is called an open-label extension on top of that, which is we took all the patients that wanted to participate on the active and the sham and put them all on active, and we measured that.

That gave us incredibly beneficial signal to say, we know exactly what to measure and what to be looking for now based on this.

And that's how we designed the HOPE study. And so that gave us real clarity to say, we believe that the right way to measure cognition in this patient population is using the MMSE. So we're measuring in hope 15 to 28 on the MMSE. We believe the right way to study function is using the ADCS-ADL. And then, Nancy, you brought up another point, which I do think is really important. What we know from the science from MIT and what we're seeing in our own studies is by stimulating the brain to 40 Hertz, we're seeing this biologic downstream effect. We're seeing synaptic proteins expressed. We're seeing myelin proteins expressed. We're seeing the glymphatic system turned on. We're seeing vaso activity increased. And all of those, this multiple mechanisms of action, create an environment for the brain in which it develops a neuroprotective environment.

What you did not hear me say there is amyloid or tau. We're not specifically targeting amyloid and tau. And why we think that's so important is, as everyone I'm sure on this call knows, is that Alzheimer's disease is what we call a polypathologic disease. There's not one thing that's causing Alzheimer's disease. There are several. And so the idea of just targeting one thing, you're going to see limited impact. But if you have the opportunity to naturally stimulate the brain to drive biology in which you see this broader mechanisms of action expressed in multiple beneficial elements, that's why we think we're seeing such profound clinical impact.

**NANCY KEACH:** I'm going to go a little out of my own order here. And because you're on combination, many people wrote and asked if they have been on Leqembi or Kisunla or if they are taking infusions with Leqembi or Kisunla, when this is available, will those things be able to taken together, or if people have had these treatments or infusions, will they be disqualified from using the device?

**CHRISTIAN HOWELL:** Yeah. The answer is, and I know it's not a great answer, is we don't know. And I say that because we haven't studied it yet. Now, the rationale why we didn't study it and why we didn't permit

the monoclonals or the amyloid targeting therapies is we wanted to make sure that we could identify the treatment effect of Spectris and not confuse what is the treatment effect of Spectris with what might be the treatment effect of other therapies.

So in our OVERTURE study and our HOPE study, we really just studied-- we tried to develop and design a study where we could just see the treatment effect of Spectris. That is the data that we will then take to the Food and Drug Administration and, in our breakthrough designation, work with them to determine how we can get a label to bring this to Alzheimer's patients. Because we believe the device is targeting a different series of mechanism of actions and because we've seen such little adverse-related events associated with the therapy, we are incredibly enthusiastic about the ability to explore this in combination therapy because we think that there's an opportunity-- we have nothing that signals to us yet that this would not be something we can explore. We just can't say conclusively until we study it that it can be. Hear the enthusiasm in my voice that there is nothing signaling to us that this isn't something that we should be exploring and will explore really quickly.

**NANCY KEACH:** Thank you. The HOPE study is now fully enrolled. So for those that asked, can I still volunteer, not right now. But we're going to talk about the timeline. And people are so excited about this, Christian Beth from Colorado Springs, super excited to hear about the study. Karina from Wake Forest, when do I start? It almost has a too-good-to-be-true quality. So the HOPE study, 670 participants, give or take, 50 to 90 years old. We will have the results, the data readout, we call it, around August of 2026.

**CHRISTIAN HOWELL:** That's right.

**NANCY KEACH:** What will we know at that point? And will we be updated in the interim? And I am going to show, by the way-- and we could put the Cognito website into the chat-- you can go to the bottom of Cognito website and subscribe to their newsletter to get updates. Will you be releasing any information before next summer, or is it only next summer? And then what do you expect you'll be reporting on?

**CHRISTIAN HOWELL:** Yeah. So this is not a fair analogy or metaphor,

but just bear with me. I have two little boys that I adore more than any two people in the whole wide world. My job as a parent on one of them is to not screw him up. My job on the other is really to keep him from becoming a screw-up.

**NANCY KEACH:** None of us understand this experience.

**CHRISTIAN HOWELL:** None of us understand that, I'm sure. The HOPE study is the first. Our job was, this is a don't screw it up, meaning the signal we got out of OVERTURE was so substantive, and it was so significant that when we designed HOPE, our thinking was, let's really try to, as best we can, replicate what we found so that we can show it at scale. So to your point, we've just fully enrolled. We're 673 patients in HOPE across 70 sites in the United States. For those of you that don't know, this is the largest medical device study that has ever been done in Alzheimer's disease. So we think it positions us, upon readout, to really understand exactly the impact that this therapy has.

As you mentioned, we are looking at an MMSE between 15 and 28. So we're studying mild to moderate Alzheimer's patients. So we're looking at populations and cohorts of patients that either have not been studied in the past or do not have therapies available to them because of the progression of their disease. What we will know upon readout is, what is the impact as it pertains to the preservation of cognition? What is the impact as it pertains to the preservation of function? How adherent was the population? And we'll also have a sense of what we saw-- we're doing an open-label extension, so we're going to have a sense of, how many patients or participants are progressing to the next study? What I would say is also because what we learned in OVERTURE is we really don't want to do an interim analysis.

I will tell you this is also where I will get outside of my depth as not being a biostatistician quickly. But one of the things you worry about is when you look at data early, you end up what they call burning some of the statistical significance of the study. So the best that you can preserve and keep the data blinded in the study, the best that the study can stay to its original analysis plan. And so we're just really confident in what we've seen out of OVERTURE, what we've seen in the continued subanalysis of

OVERTURE, what we've seen in the hygiene of HOPE that this is, again, a do-no-harm model, which is-- we're going to keep the train rolling all the way through readout in August because we do have, candidly, such confidence in what we're going to see come August that we don't want to do anything that might risk.

**NANCY KEACH:** You mentioned that the participants have mild and moderate Alzheimer's. We had a lot of questions about, and obviously, I'm asking you to predict the future, but is it possible that this will also could be used either preventatively and/or for moderate to late stages of Alzheimer's? We also had a question about functional behavioral variant, FTD. Potentially other neurodegenerative diseases-- ALS, Parkinson's. Again, I know I'm asking you to read the tea leaves, but what can you say as a CEO rather than a scientist about these.

**CHRISTIAN HOWELL:** Somewhere my regulatory officers hair is standing up on the back of his neck. And what I will say is we don't know. We don't know until we study it. Now, the question I think you would ask, maybe asking the CEO is-- is there an interest in studying these others? And is their preclinical signal that gives you confidence that this is something that you should explore? And I can say to that question unequivocally, yes. And this is, I think, one of the things that is most exciting about using a medical technology or a medical device. One is, unlike, I will tell you I spent-- you heard in my bio. I have spent 25 years in medical technologies and medical devices. I have never seen so much preclinical research done around a therapeutic approach or a science. So there is an enormous amount of research that's being done candidly around the world both in preclinical and clinical, on the use of 40-hertz gamma stimulation. And what is the clinical and biomarker impact.

And so we are seeing signal that tells us yes, we should absolutely explore earlier stage impairment. Yes, we should absolutely explore frontal, temporal, and other neurodegenerative conditions like MS and PD. And really what we're trying to do-- you had one of my real heroes on earlier, which was Dr. Ali Rezai from the Rockefeller Neuroscience Institute. And so one of the things that we're trying to do as proactively as possible is build collaboratories, where the science and clinical teams from Cognito

and these leading academic centers can come together and say, what does the preclinical research tell us? What does the clinical research tell us? Where do we think there's good signal? And where should we explore next? And use the benefit of being a medical technology that has been so-- we've had such limited adverse events that it allows us that ability to really lean into that. And so we want to be thoughtful about it, but we also want to be, candidly, I to be ambitious about it because I feel very supported in what I'm seeing in the data and in that we're getting.

**NANCY KEACH:** Yeah, I'm jumping around because we're getting so many questions in the chat, and so many from before. But when the data is read, if it is positive, give us a guesstimate. Again, I know this is reading the tea leaves, will there be another trial? That would be my question-- that people are going to have to enroll in. And somebody did write a question that expressed their frustration with how long do we have to wait for these things? And then in this country at this time, this is how drugs are brought and devices are brought to market. But can you give us some sense of when it might be possible to get FDA approval?

**CHRISTIAN HOWELL:** Yeah.

**NANCY KEACH:** Would it possibly be covered by Medicare or other insurance? Is it a one size all application? Can it be done at home? That I believe the answer is yes.

**CHRISTIAN HOWELL:** Yeah.

**NANCY KEACH:** Because if this was affordable and you could do it at home and accessible, this is in a sense one of the holy grails because people from all walks of life would be able to access it.

**CHRISTIAN HOWELL:** Yeah. So one let me talk to that because I will tell you, that is-- in my bio, you talked about a career of service. And when I tell you I thought the pinnacle of my service was going to be my time in the military until I assumed this role. I feel such a responsibility of service to this community that I want to do absolutely everything possible to make sure because I do believe it has this truly groundbreaking potential

impact.

Speaking of being breaking, we are breakthrough with the Food and Drug Administration. Why that's incredibly important is it allows us to work closely with them now. And we are constantly in communication with our review team and the agency to make sure that we're aligned. Or we understand their disposition about endpoints and study design and when things should be looked at in a composite or so.

What we believe the path forward is, is that we will have topline readout in August. There is some additional work that we will have to do in preparation for a submission, but we expect to submit sometime in the end of 2026. As a breakthrough technology, that time frame can take anywhere between 6 and 9 months. So then we're talking about the middle of 2027, where we really hope and believe we're putting ourselves in the best position possible to have an approval to then bring this to patients.

Now, the other side that you brought up is, will it be covered? Now traditionally, this is where medical devices are different than drug therapies. I used to have the opportunity to work very closely with Dr. Scott Gottlieb, and he mentioned one time that the evidentiary burden for drug therapies is in the premarket. And oftentimes the evidentiary burden for devices is in the post-market. And it's because devices don't generate enough evidence when they come to market to be able to answer both the questions of the FDA and the questions of CMS. And so they put themselves in a position where they then have to answer questions about cost effectiveness once they come to market. And it creates real complication for them. What we are doing is we are generating as much evidence as possible in the pre-market so we are as well prepared as any medtech company in history to have the conversations around cost effectiveness with CMS. And what CMS has said is, look, we're asking for device companies to do really four things. One, do more clinical evidence. Great. So we're doing the largest study, and we've done the overture study and LLE and all of this. Two, make the studies representative of the population in which you want the device covered in, which we know this is going to be a Medicare population. So we've done that in the inclusion criteria of the study. Three, have the studies be diverse. This is why we developed the study that's going to go across 70 sites in the United States.

And four, engage us early, which is what we've done. And so they have a program that's called TCET I won't go into the specifics, but what it's meant to do is for truly breakthrough medical devices that can bring data and substantiate not only the effect they can have on patients, but the cost effectiveness of the therapy. That program allows for concurrent coverage, so you receive a national coverage determination relatively concurrently within six months of receiving your FDA approval. Just to give a sense, the average medical device spends about 5 and 1/2 years between an FDA approval and a coverage decision from CMS. Our goal is to do everything we can now to make that as narrow as possible.

One other thing you said at the end of your comment that I do think is really important, which also speaks to why I think medical devices and medical technologies are so important here is one of the things that happens for participants in our study is we do the MMSE to confirm that they can participate. We also do a confirmatory blood test, which is really required for the diagnosis of Alzheimer's disease. Patients then come in and they go through what we call a tolerance and a gamma response. Tolerance is we give them the headset, we put it on, and we make sure that patients can tolerate the light and the sound therapy. Greater than 95% of patients have no issue with the light therapy. We then put the therapy on under an EEG, and we confirm that we can get a gamma response. In probably 92, 93% of patients were able to get a gamma response. And those that we're not is usually to your first question about hearing loss. They can't hear. But what participants then know is they're going home with a therapy that has one, been personalized to them. And 2, they know their brain is responding to. That we are able to evoke the gamma oscillations. And I think that is the big driver for adherence.

I think oftentimes as patients, we sit with hope that a therapy is going to work for us. But we don't know. To know that you're getting a therapy that you have confirmation that your brain has responded to it. I think that lends a great deal of confidence. And I think it gives a lot of empowerment to patients. And that's what we hear most from our participants in the studies, I feel empowered to take on my disease.

**NANCY KEACH:** Thank you. And I'm going to address Rochelle and

Bill's comments and several that I received in advance. And forgive me because I too get emotional. But Rochelle writes, five years will be too late for me. Bill says, maybe me too. And Rochelle is asking and we got several questions in advance about-- is there anything else we can use in the meanwhile? And we are also getting a lot of questions, which I'll try to go back to about how this works. But I'm just going to run through several of them. It's an addition to Rochelle's and Bill's because, obviously, there are millions of people who want something today. So Barbara from Statesville, North Carolina, what are the other non-invasive approaches to dementia? George from Nokomis, Florida. Any comments on the AlzLife product using an iPad pro and headphones to generate 40 Hertz light and sound for an AD patient until a more advanced project is on the market? Is something better than nothing? Ailsa from London. How long each day do you watch? And here I use a light bulb flashing at 40 hertz, plus sound from my iPad via earphones. Will this have any effect? A couple more. Joe from Bay Village, Ohio. Is the ValAsta variable light emitting device a good product? I did note when I went out to look that up, it was $495, which seems like a lot of money to me. Steven wrote there are a lot of red light units out there that claim to be helpful. Are there any consumer models worth considering? The last one. Rosanna from Springfield, Illinois. What about PEMF, which I learned was Pulsed Electromagnetic Field Therapy. Has this been studied? So the overarching question what else is out there that people can use today?

**CHRISTIAN HOWELL:** Yeah so and maybe just to Rochelle and the others. One is I can't tell you the amount of sympathy and empathy I have for this sense of time. And as the CEO of the company, I really talk about, our North Star is really the patients, right. And fidelity to the mission of delivering this therapy to patients in as responsible, candidly, and as validated a way as possible. And so what it perceives is that it's boy, it goes slowly. But what I can say is slow is smooth, and smooth is fast. Meaning let's make sure we run as sound a study as possible so that when we read out in August, we are as well positioned as possible to go to the Food and Drug Administration right away. And then we are as well positioned then to keep our review teams so that we can have this therapy to patients as early as early 2027. But that clinical validation is what needs to happen.

I think it's incredibly exciting that there is this list of alternatives really, what's called physics-based approaches. Because I think what we've all seen is oftentimes the brain can be very difficult to treat using chemistry. The blood brain barrier creates real challenges. I know Dr. Rezai talked to the team about that. Oftentimes, drug therapies can be indiscriminate. If I target amyloid on the neuron, I don't know if it's amyloid in the neuron or amyloid in the blood vessel. So that can cause risk. And by using physics or by using a medical technology, the central nervous system creates this really elegant on ramp for us. So we can use the CNS to access regions of the brain and then drive stimulation, but we have to study it. And so I think it's great that there are companies that have taken the learnings of MIT and the Picower Institute and said, OK, let's do something and give people something they can order on Amazon. But we just don't know if they're effective because they haven't been studied. There have been some studies that have come out that said, there are definitely environmental factors and that you have to really think and we can share that about these readily available music or sound, that it's not just one or the other. There really is value to the combination, but they just haven't been clinically validated yet. They haven't been studied.

**NANCY KEACH:** So what I believe I'm hearing you say is we don't know about the devices I mentioned because they haven't been studied to the appropriate extent, but obviously, people are using these devices, some of these devices that they find on the web. We don't know how effective they are.

And I just want to also tell the audience that I have been speaking with the CEOs of other startup companies working on similar but not identical technologies. And I asked Christian if he might be willing to host a group session where he and a group of these other CEOs from other device companies came together to talk to you. And he graciously said, yes. So they're all supporting each other. And that gives me a lot of joy that rather than being competitive, they are being supportive of each other and are willing to come on and talk to us all together. And so if that would be of interest to you, I'd ask you just to maybe type yes in the chat so that we know that that's something you would like us to do. That would be a bit of a departure from our normal format as it is having a CEO. Thank you. The

yeses are pouring in.

**CHRISTIAN HOWELL:** I see them coming through.

**NANCY KEACH:** Because we are a foundation that funds scientific research, we're very careful that most of our speakers have been the greatest expert scientists. But we believe we would be doing the public and our parents and our families a disservice if we weren't additionally bringing these noninvasive and non pharmacologic solutions to people and letting them know where they are in the pipeline of being delivered to the marketplace.

**CHRISTIAN HOWELL:** Nancy, maybe if I can just make a comment on that. And just as a community, I'm sure of potentially patients or caregivers or loved ones that are struggling with this, what I would want, nothing more is I would want to know that evidence and ideas and solutions are happening in a community, not in private. And obviously, companies have to be protective of IP and they have to. But I have not seen in my career a community as focused on bringing solutions as the Alzheimer's community. Meaning the drug therapy companies are as open to talking to us as we are in talking to them. Companies that are also thinking about brain activation therapies, whether they're using trans magnetic or whether they're using alternating current or electricity, there is this idea of it is all hands on deck moment. And the rising tide will lift all boats. We will learn from each other. And so I can tell you that has just been my read of the community, is that I'm sure that there are disease states and conditions in the world where people are really focusing and acting in isolation, and that is not this community. I have been incredibly impressed. And so as a member of it, I want to continue to be supportive of that and really try to learn from others and make sure that we're sharing our learnings so we can bring solutions as rapidly as possible to the market.

**NANCY KEACH:** I'm going to double down on your comments here because I think everybody knows we're at a time when government funding for scientific research is being pulled back significantly. So it is incumbent upon us, the philanthropists and you, the private sector, to make sure everybody is doing research in as collaborative and efficient a way as possible. So I think all of us are very much grateful to the private

sector for these types of efforts. I'm going to just keep jumping into a bunch of the questions because they're coming in hard and fast. We had a couple, Linda from Buffalo, and Jania from San Jose, California. Does this also potentially help with insomnia or to get better REM sleep? Know a lot of people with mild cognitive impairment and more advanced Alzheimer's have a lot of sleep issues.

**CHRISTIAN HOWELL:** Yeah. So again not to hit the repeat: to be studied. So for me to be able to say that conclusively, we're going to have to study it. But what I can tell you is that there is very clear signal coming from the preclinical state, that 40-hertz gamma stimulation one has a profound impact on the glymphatic system, which is why deep sleep is so important, because the glymphatic system serves as a sort of a car wash for our brain. When we're asleep, it floods our brain and it removes inflammation and neurotoxins. And so knowing that we're prompting that. And 2, I think there has always been a real interest in the clinical and scientific community to study 40 hertz as it pertains to the impact to sleep. And again, something that I think we are incredibly excited that post our HOPE readout in our submission to the FDA, we will have the opportunity to really accelerate additional research. Our intent is to be-- I say to the team all the time, we have to be as focused on data and evidence as we are on adoption. And so I want to make sure that we are always thinking about how we are capturing data with health systems and with patients, so that we can get signal to inform us on where we should be studying this, and then where we should be taking that evidence to the agency to make sure that we can be appropriately labeled and available to patients.

**NANCY KEACH:** Julie in the chat asked, does this treatment relate at all to TMS treatments that are being explored-- Transcranial Magnetic Stimulation?

**CHRISTIAN HOWELL:** Yeah. So I would say that they're related but different in the context that what TMS is trying to do is TMS is trying to drive brain activity. But what is it does it in a much more localized way, and it doesn't currently do it to the gamma band. So it is doing it at a lower level of hertz frequency within the brain. But the central premise of

using a physics-based intervention to drive activity in the brain, so that the brain then expresses naturally occurring biology to address a condition that is very similar. But again, where it's different is localized. Currently, it is required to be done inpatient. It has not been studied in Alzheimer's or neurodegenerative conditions versus we're using sensory stimulation. We're going to be used in the home. And we obviously are doing our lead research in Alzheimer's.

**NANCY KEACH:** Elsa from London. In your trial, how long do you need to watch and hear each day?

**CHRISTIAN HOWELL:** Yeah, it's a great question. So

**NANCY KEACH:** Any details also about the intensity of the light? I use a light bulb flashing at 40 hertz, plus sound from my iPad via earphones. Will this have any effect?

**CHRISTIAN HOWELL:** Again, I don't know that answer. I just don't. What we ask of patients is for an hour a day, every day. Now that is what the preclinical research has told us. It's what we learned in overture to the point earlier. We saw such profound effect in overture that we wanted to replicate that in the HOPE trial. What we will do moving forward is we will continue to think about, ironically, the term is dosage. And so we'll think about dosage, and we will explore. Is it an hour a day? Is it every day? But what we know is-- or what we've seen, I should say, is in our OVERTURE Study, that an hour, a day, every day is what allowed us to see those profound treatment effects. And so we wanted to replicate that.

**NANCY KEACH:** Mary from Ponte Vedra, Florida. Can people with a history of vertigo use this therapies described in this presentation?

**CHRISTIAN HOWELL:** It's a good question. We had vertigo as an exclusion criteria in our study. So we don't have any data on the impact of the therapy with patients with vertigo. But again, I'm sure it is something that we will look to explore or an investigator will initiate to explore as well. But candidly, the answer there is we don't know because we excluded it from the study.

**NANCY KEACH:** And I know you're going to have the same or similar answer and Dr. Rossi, who I want to thank, our scientific affairs Alzheimer's director is the person answering all of your questions in the chat. Dr. Rossi, thank you, Dr. Rossi. And she's texting me the other questions: what about people who are APOE4 positive, have vascular dementia, have epilepsy. I know you're, again, going to say it depends if we have studied these or not. But any comments?

**CHRISTIAN HOWELL:** Yeah I will say for us, again, the APOE4 is a disposition toward amyloid. Our inclusion criteria was an MMSE score and a confirmatory blood test. So there was not an inclusion or exclusion based on the genetic disposition toward APOE4. And candidly, why we think that's so exciting is because we were looking at an MMSE score and a confirmatory P-tau. What if things go as we hope they go? We would expect to have a very large number of patients eligible for the therapy because we would not have many of the restrictions that I think we're all experiencing with some of the amyloid-targeting therapies.

**NANCY KEACH:** Yeah. And further to that point, and Dr. Rossi just answered it in the chat, but Julie wrote, do brain bleeds preclude or impact incomes or is it too soon to tell? And I've had several people ask the question about brain bleeds and this therapy. And we'll just recap that brain bleeds or ARIA are a potential side effect of the infusion drugs that are targeting amyloid. So I think people are not only asking, does this cause, they're asking if they've had them or will that interfere?

**CHRISTIAN HOWELL:** Yeah. So it's a very important distinction that I want to be very clear about. One is, there was the existence of brain bleeds as an inclusion/exclusion criteria, again, because we wanted to study a population where there wasn't interference to the potential signal. That being said, we know that when we think about ARIA H&E, those are amyloid-related imaging abnormalities. Meaning the targeting of amyloid is resulting in the removal of amyloid in structures that are causing bleeds. Because we're not targeting amyloid, we have not seen any instance of ARIA in any of our studies to date.

**NANCY KEACH:** I hope everyone is finding this hopeful. If also frustrating that we don't have these approved covered technologies in our hands

today, but we have about seven minutes left. So I just want to mention if you have a burning question, if you really want to ask something before we tie up, please do it now. You can either raise your hand or write it into the chat. And I'm just going to run through a couple of questions.

**CHRISTIAN HOWELL:** Sorry, Nancy, can I just make just one comment?

**NANCY KEACH:** Please.

**CHRISTIAN HOWELL:** So I'm hoping over the course of the hour, what you've heard from us is that we're trying to be as transparent as possible. And I want to continue that transparency through the HOPE readout, through our regulatory submission, through our work with CMS. And so whether it-- I think we have a newsletter on our website that folks can follow, whether it's following us on LinkedIn. But to the conversation earlier about community, I think it's unbelievably important to share what we're learning. Not just as we bring the first non-invasive therapy for Alzheimer's to market, but also as a company of this size in this space. And so that's a little bit of the commitment you'll hear from me today, which is I really want to make sure that we are as far as we can really push the envelope. Being very transparent about what we're experiencing, what we're learning, what we're seeing, what we're thinking. Because I do think that type of candor is what is needed now because I think so much of what I'm hearing in the course is this anxiety of I just don't know. And so we want to do the best we can to share what we know so that even if it's not the exact right answer, at least we really are-- you understand how we're thinking about because we think we have this enormous responsibility in our hands that this therapy really is a generational therapy. And we want to make sure that we are as responsible stewards of it as we can be.

**NANCY KEACH:** I'm so happy, Rebecca just put in the chat. She said, I've been following the development for years now. I've been using 40 hertz and Leqembi for 18 months. Gone from frequent amyloid plaque to 0. So, Christian I didn't make you say anything positive, but that's a very encouraging and hopeful. We're almost out of time so I'm going to wrap up. And I'm going to, first of all, promise everyone we're going to stay very close to Christian and the other CEOs. Thank you for all your responses.

We will have that, probably very early in the 2026, because we do have these episodes booked through the end of this year, which is fantastic. But we'll keep you very closely informed on as these technologies are being developed. If you want to sign up for Cognito's newsletter again, here is the website cognitotx.com, and you can get updates on the HOPE study.

BrightFocus, as always, offers tons of free resources on all aspects of Alzheimer's disease and macular degeneration and glaucoma. You can get free publications at this email, reply@BrightFocus.org. All of the episodes of Zoom In are available at BrightFocus.org/ZoomIn.

If this program was helpful to you and you think it would be helpful to other people, please share this link with friends. The program is growing wildly, which is fantastic. But we know with the millions of people who have neurodegenerative diseases today, it's only reaching a tiny fraction of people. So please share the link BrightFocus.org/ZoomIn.

And just to let you know, on October 2, Thursday at 1 o'clock Eastern, 10 Pacific, we're going to have Dr. Laura Baker on to discuss the results of the US POINTER study, which studied structured lifestyle interventions. So this too, I know there's tremendous interest about diet, exercise, sleep, brain games, social interaction all the things we're supposed to do. How do they work? Do they really work? We're going to have the results of the most rigorous study in the US to date on these episodes, and then we have another great treat, gut microbiome and Alzheimer's disease with Dr. Beau Ances.

I want to end by speaking. I don't know if she's still here, to Rochelle and everyone, just to say you are not alone. The 149 questions I received, I have things like how do I help my mom? How do I know if her moments of anger are directed at me? How do I deal with hallucinations? I'm 70. I was diagnosed a year ago. Is there hope for me? We're here for you and with you all. My mom has MCI. She's 95, so she's still knows who I am, and I'm very grateful for that. But we just want you to know that we understand what you're going through. We're trying to bring you as much information as we possibly can, and we're trying to fund as much science as we possibly can at present. And we want to make ourselves available to you. We want you to feel like you have access to people who can help you

navigate this because it is so difficult. And while it's not on topic, and I'm really over time, I'm just going to say before I thank Christian with every ounce of my being. Suzanne from Washington wrote, I'm 83 years old and have Alzheimer's. What are the most important things I should be doing to limit the impact on my life? Christian, I don't know if you want to answer some of that. I know Dr. Rossi and I would love to jump in. But let me give you a second.

**CHRISTIAN HOWELL:** No. This is a time and place moment. I think Dr. Rossi is in a much better position to answer that than I am, so I defer to you.

**NANCY KEACH:** Sharyn, why don't you go first and I'm going to give my two cents.

SHARYN ROSSI: Sure, sure. Well, we all know eating healthy, exercising, and staying social is really important. I just had a conversation with one of my grantees, and I think as we age, our circle gets a little bit smaller. So the more that you guys can work on just expanding that in any way, shape, or form-- taking on a new activity or instrument or language or just exposing yourself to new things I think are really important. And Nancy, if you want to take it from there.

**NANCY KEACH:** I'll add a few other things that if you can limit sugar and alcohol intake, that's always a good thing. Sugar is inflammatory and we all eat a lot of it. Sleep is extremely important. Trying to get good sleep, staying and exercising. Try to keep moving. There's chair-exercise videos available that are absolutely awesome. And in the US POINTER study episode, we're going to talk in much more depth about how to keep-- But mostly, I want to say to Suzanne that we had once on a woman, a caregiver whose mother had gotten Alzheimer's, and she discussed what she did as a caregiver to try to help her mom and all of the things she did, and all of the conversations she tried to have and all the interventions she tried to do. And then after her mother passed, her dad developed Alzheimer's. And we asked her, was there anything different that you did with your dad having gone through it with your mom? And she said yes. She said, I tend to sit on the porch with him and just be with him and talk. And so I don't know if you all will agree with me or not, but I think just

spending that time. My mom came across the country to visit recently. I told you, she's 95, and we lay on the bed and we just talked. And I was shocked because her brain has changed, she started to speak to me in a way she never had through her whole life. And so I think the way when she writes to limit the impact on my life is to have that quality time, to have those quality conversations.

I always close the show by saying, life is short. Hug the people that you love and keep them close. So I'll say that again today. But there are moments to be had given these conditions if we still just wake up and share with each other. Beth is reminding us six pillars of brain health. And you can google that. And you'll find it with us on the POINTER study conversation. So sorry, I've gone over and thank you for staying. For those of you who have. And Christian and everyone at Cognito, your entire team, thank you so much. Thank you for being as candid as you have been today, and as committed as you are to developing these technologies to help people. And thank you for your service.

And again, thank you all for being with us today. Please come back. Please share the program. We're just starting to look at developing this as a podcast as well. So we just want to try to bring this to as many people as possible. And your help would be deeply appreciated. Thank you all for coming and staying and participating and for all of your comments. I'll applaud you back. Thank you, Julie. We'd love to see you, and that's why we don't do this in a webinar format. We want to see your faces, and be able to speak with you directly. And let your voices be heard. Have a great rest of the week, a great weekend. We'll see you in a couple of weeks.

**Resources:**

- Glymphatic system = drainage of toxic substances from brain
- Myelination = restoring the fatty connective substance that allows brain cells (neurons) to survive, function, and communicate
- Vascular changes = reduce inflammation at vascular interfaces and

perhaps even increase vascularization (providing more blood flow to the brain)

- Cognito website: https://www.cognitotx.com/
- Cognito LinkedIn: https://www.linkedin.com/company/cognito-therapeutics-inc/
- Topline results of the OVERTURE Study: https://www.cognitotx.com/clinical-studies

**Q&A from Live Program Chatbox:**

- Q: Are there any patients with specific brain conditions who could be harmed by flickering light at 40 hz or 20 hz?
- A: That is an interesting question. I think it is rare for any brain condition to be analyzed or even characterized on a level of brain function/activity like that. We know that epilepsy is associated with hyperactivity in brain circuits, and Alzheimer's disease is associated with an excitatory/inhibitory imbalance – but the whole idea of Spectris is to get these unbalanced 'waveforms' back on board and entrained. I think this intervention is considered very safe – if anything – it may be less effective under certain conditions.
- Q: Is this device considered a significant risk or non-significant risk device?
- A: Phase I showed that this is very safe. I think perhaps a headache was the most reported side effect.
- Q: Does the person have to be awake while using the device?
- A: Yes, it relies on stimulating receptors in your eyes (and ears), so you need to make sure those 'portals' are open.
- Q: Do you expect this to be complementary to current best of class

treatments like Kisunla and Leqembi and could it be used while being treated with those drugs?

- A: Yes, because this is a completely different 'target' we are thinking this has a lot of potential for combinatorial treatments
- Q: I see items for sale using sound and light therapy for AD quite often. Are these items "scam products"?
- A: We can't speak to any specific device but we would assume if it hasn't undergone rigorous scientific testing, you can't speak to its effectiveness.
- Q: Can't 40hz light and sound be delivered with a tablet and headphones?
- A: It is about the pattern and timing of delivery. We are surrounded by 40Hz all the time, but it has to do with the delivery and how it is entraining.