Speaker 1:

Welcome to the Eye on the Cure Podcast, the podcast about winning the fight against retinal disease from the Foundation Fighting Blindness.

Ben Shaberman:

Welcome everyone to the Eye on the Cure podcast. I'm your host, Ben Shaberman from the Foundation Fighting Blindness, and I am very pleased to have as my guest today, Paul Bresge. He's the CEO and co-founder of Ray Therapeutics, a company focused on optogenetic therapies for retinal diseases. Welcome to the podcast, Paul.

Paul Bresge:

Thank you so much, Ben. Appreciate all the fantastic work that the Foundation does and that you do, and appreciate that you invited me to be your guest today.

Ben Shaberman:

Well, it's my pleasure and privilege, and just to let our listeners know a little bit about Paul. You have an interesting background. You started off your career, if I understand correctly, in generic pharmaceuticals. You moved out of that space, you moved out of the pharma biotech space entirely, and then you moved back in as CEO of jCyte, which is developing a cell-based therapy for retinitis pigmentosa and potentially other conditions. I know some of our listeners are familiar with jCyte.

But then after a successful run there, you helped launch Ray Therapeutics, which again is focused on optogenetics. I want to talk more about Ray and jCyte, and I know in the Eye on the Cure podcast, we've talked about optogenetics a few times already. But I think it's helpful for our listeners to understand what it is, how does it work, and what are the opportunities in terms of vision restoration and what are some of the challenges?

Paul Bresge:

Ben, in terms of just very broadly, how does optogenetics work? It's been known for decades that single cell microbes have the ability to move towards light, and that's because they've evolved the channel protein called channel rhodopsins on their cell surface, which are actually activated by light. In more recent years, molecular biologists have been able to optimize these channel rhodopsins, express them in neurons, and make the neurons responsive to light.

What we've done at Ray Therapeutics is we've taken the best channel rhodopsin that's actually found in nature, and then we've further engineered and optimized it for characteristics that will specifically improve vision. Then for retinitis pigmentosa, we're targeting the retinal ganglion cell, which is the appropriate cell and the last remaining cell in the retina, hence bringing promise to patients at the end stage of disease who have no remaining photoreceptor function.

Ben Shaberman:

Right, and just to clarify, I know, you meaning Ray Therapeutics has done some work engineering it to be even more light sensitive, but does it come from algae like some of the other channel rhodopsins?

Paul Bresge:

Yes, it does.

Ben Shaberman:

Okay, great. What are some of the challenges with optogenetics and I guess the specific challenges that Ray is driving to overcome?

Paul Bresge:

Let's focus on the opportunities first. I like to think of challenges as opportunities as well, but in terms of what this can potentially translate in for patients is very, very important. We need to keep in mind that we're targeting patients, as I mentioned earlier, at the end stage of disease. These are patients who are blind, already blind, and to some extent, this patient population has been left out. I mean, there's incredibly exciting work going on in cell therapy, neuroprotection, traditional gene therapy and gene editing, but all target patients really at earlier stages of disease. In gene therapy, traditional gene therapy requires targeting causative gene.

Our approach is independent of genetic mutation and it aims actually at reversing blindness, not slowing down or stopping the progression of disease. I think that's where the opportunity lies. In terms of challenges and of course emerging technologies, there's always challenges because we're learning on the go, but we do have a very experienced world-class team actually with decades of experience in regen medicine for ocular indications.

I think that we've appropriately identified the challenges and we strategized around them. I mean, one challenge of course in drug development universally is that it takes time and this is so frustrating and upsetting to patients, but we are really moving as quickly as possible. In context, the company was formed exactly two years ago and will be in clinic this year, which I think is remarkably fast, and that's because we're very excited about getting our therapy to patients really as soon as possible.

Ben Shaberman:

Yeah, that's great. Obviously with our folks out there with retinal diseases who have lost all their vision, we can't get them the opportunities for vision restoration soon enough.

Speaking of challenges, I know with some optogenetic therapies there's a limitation in terms of what spectrum of light they will operate well in. But if I understand correctly, you've addressed that challenge, or at least you think you have pretty well. Can you talk about that?

Paul Bresge:

Yeah, I mean, again, this protein has been specifically engineered for a pretty broad spectrum of light, so we think that that's a big advantage of our program over some of the others as well. It's a great question actually.

Ben Shaberman:

Sure. What retinal diseases do you think your approach will apply toward?

Paul Bresge:

I mean, we're targeting retinitis pigmentosa as the first indication, and we are very, very grateful to some of the other programs that have already shown proof of concept in RP such as jCyte. But we do believe that this therapy will also be beneficial to patients with other inherited retinal diseases and geographic atrophy. That's because the same principle applies to these patients who no longer have functioning photoreceptors.

What we do is we target the appropriate and remaining cells to restore vision. We plan to initiate our Stargardt study actually very shortly after we begin our study in RP. The fact that Stargardt's is a juvenile form of macular degeneration, it should provide a very nice proof of concept for us to then move into GA. Then of course, we're interested in addressing the other inherited retinal diseases as well.

Ben Shaberman:

Right. GA, just for our listeners, meaning geographic atrophy.

Paul Bresge:

Correct.

Ben Shaberman:

The advanced form of dry age-related macular degeneration.

Paul Bresge:

Exactly.

Ben Shaberman:

That's great. You're gene agnostic, and to some maybe saying disease agnostic would be going a little too far, but you've got broad potential applicability, let's say that.

Paul Bresge:

That's correct.

Ben Shaberman:

That's pretty fair. One question I have, and I'm always amazed how companies begin. It's not easy to launch a company. There are a lot of things that one has to do. You have to find the talent and the money. Can you talk about, since you are a co-founder, how Ray Therapeutics came about?

Paul Bresge:

Sure. I mean, I think it's the progression from jCyte to Ray Therapeutics was a very natural progression. I spent many years devoted to the jCyte program, and I'm very, very excited about the potential for that therapy for patients. Then when moving on to Ray Therapeutics, what I loved was that it was so complimentary to the work that I did at jCyte. The work at jCyte is targeting patients at the earlier stage of disease to stop the progression of disease, to restore some vision, but the data suggests that it works better in patients at the earlier stage of the disease because those patients still have existing photoreceptors.

How I got involved at Ray was I knew some of the people who were the co-founders and founders of RetroSense, which was really the first optogenetic program that was bought into clinic, later purchased by AbbVie Allergan. This group was licensing the next generation of optogenetics from Dr. Pan's lab, Dr. Pang being the scientific founder of the work behind RetroSense.

When I saw the data that was produced by Dr. Pan and the potential for the translatability of that into patients, I was absolutely blown away and joined the co-founding team, and of course took on the CEO position.

Ben Shaberman:

That's great. Your company is only, what, about two years old?

Paul Bresge:

Yeah, yeah, it's two years old. There's been a lot of excitement about optogenetics, and again, I referenced jCyte earlier. I think that what is important to point out in our estimation anyway, is that we truly have a next generation product. That's not only because I mentioned earlier about the fact that we believe that we have the most light sensitive protein found in nature, but also because it's specifically been engineered, as I mentioned, for optimization for visual function.

Again, the jCyte data is extremely exciting. They've had some remarkable results in patients, but because their protein is less light sensitive than ours, their patients have to wear these light enhancing goggles. I know patients at the end stage of disease, they'll do anything understandably so, and if wearing goggles is required, they'll do so, but it can make the regulatory and commercial process potentially more challenging.

Our data suggests that the patients will not have to wear goggles because the light is activated in very dim settings. We've also, for the first time actually been able to see robust visual acuity data in our animal models, and again, we believe that that will translate as well or even better to humans.

Ben Shaberman:

That visual acuity is such an important component for the treatment for vision restoration. Do you have a sense at all of how much visual acuity might be restored, or is that just difficult to extrapolate from animals to humans because animals can't read?

Paul Bresge:

I mean, that's why we're so excited to get into our trials and see, or should I say more properly, have the patient see. But there are some papers out there that suggest, or one paper for sure that I read recently that suggests that even the first generation of optogenetics can potentially restore vision to as something as remarkable as 20/70, which is I think legal driving in some states. Very, very exciting potential.

Ben Shaberman:

Yes, that would be awesome I'm sure for just about everyone affected. I want to switch gears a little bit because one of the things that I think is so interesting about your story is some of your personal connections to the eye and the retinal space. Wasn't your father in the pharmaceutical industry when you were growing up?

Paul Bresge:

Yeah, my dad was the founder of a Canadian division of a generic pharmaceutical company. I grew up in that space and started my career there, and then in contract manufacturing for the pharmaceutical, generic and cosmetic industries.

But I left that space for a long time, and then life actually took me back in shortly after my middle daughter was diagnosed with retinitis pigmentosa in 2010. That was obviously a very pivotal moment in all of our lives, as you can imagine, my daughter's the most. But that set me on this journey to find the

most promising science out there and do what I could personally to support that science, bring it to patients.

That was when I had the opportunity of meeting Henry Klassen and Jing Yang, who are absolutely brilliant scientists, and they had created jCell, and then again, we formed the company. This is back in 2012, which became jCyte. But yes, behind all of this, is a very, very personal mission here to get these therapies to patients, and very personally and very specifically to my daughter as well. That's why we continue to work hard and do everything that we can to get this to the patients as quickly as possible.

Ben Shaberman:

Yeah, I think that connection to your daughter is, well, obviously it's very personal, but it really amps up the urgency of the mission for you. Can you talk a bit about your daughter, because she's taken some interesting educational and career focuses.

Paul Bresge:

Yeah, of course. I mean, it's her story, so I always prefer that she's the one who tells it. She recently did a fantastic TED Talk, which I think is available online. Her name is Tamar, and the same last name as me. I remember that when she was diagnosed, the doctor who diagnosed her, she had just turned 15 two weeks prior to her diagnosis. The doctor right in that session told her, "You know, you should think about what you're going to study." Fast-forward, what are we, 12, 13 years later, she actually has a master's in Fine Arts from Tufts University, and she teaches at Tufts and does some other work there. She's just an incredibly talented and brilliant artist.

She certainly followed her passion and she's done remarkably well doing exactly that, so I just couldn't be more proud of her. Now, she's working very specifically in an area of understanding the cross section between art and creative writing, and I think that she's already, but she'll continue to be enormously successful.

Ben Shaberman:

That's great. She must have such a strong appreciation and unique perspective on the visual world given her situation, but I think that's something she could use to her benefit in terms of expressing herself and coming up with new ideas and views of the visual world. I'm curious, when you moved into the biotech space after she was diagnosed, how did she react to that? What does she think of what you do professionally?

Paul Bresge:

That's a great question, one that I'm going to specifically ask her after this podcast, because I've never actually asked her that question very specifically. But I think she's a very strong and level-headed young woman, and she has a very good understanding of the work that I'm doing and that we're all doing in the field. She's incredibly supportive, as you can imagine. She's very hopeful as she should be, and all patients should be.

I mean, this is an absolutely remarkable time in science and drug development, and it will result in treatments for patients. I think she has a very good balance of going about her life in the boldest way, in reference to a statement that you made a couple of minutes ago about her vision. She lives the reality as patients do with these inherited retinal diseases and all retinal diseases is really understanding how precious her vision is. But I think that she's very well-balanced in navigating the world as she does so well with the vision that she has and also being very hopeful for these treatments for the future.

Ben Shaberman:

That's great. Well, I know our entire community is appreciative of the work you're doing and Ray Therapeutics is doing to get some exciting treatments out there and hopefully across the finish line. Paul, I appreciate you taking time out of your busy schedule to tell us about your work and a bit about your personal story. Thank you. Thank you for sharing your activities and your perspective.

Paul Bresge:

The thank you belongs to you. FFB is playing a really critical role I think in educating patients to understand their conditions, to ask the right questions to their clinicians, to understand opportunities for appropriate trials. This is a team effort. The biotechs and pharma companies, FFB, physicians, patients. We're all working together for successful outcomes, and I'm very confident that Ray will be one of those successful outcomes. So yeah, I think there again is a lot of hope for patients, and again, happy to support everything that FFB is doing.

Ben Shaberman:

Thank you again, Paul, for being an important part of that hope, and thank you to all our listeners. We appreciate you tuning in for another episode of Eye on the Cure. Thank you for all you do to support our mission and to drive the research, and we look forward to having you all back in a couple of weeks for the next episode.

Speaker 1:

This has been Eye On the Cure. To help us win the fight, please donate at foundationfightingblindness.org.