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:

Hello everyone. Welcome to the inaugural episode of the Eye on the Cure Podcast. I'm Ben Shaberman. I'm the senior director of scientific outreach at the Foundation Fighting Blindness, and I'm glad to be your host. And while I am the host of the podcast, I plan to occasionally include some guests so we can keep things fresh and interesting. In addition to guests, I'll feature news, information and even some occasional humor and ephemera about the retina and vision. But of course, since we're connected to the Foundation Fighting Blindness, we'll have a special focus on retinal degenerative diseases. But for episode one, it's just me. And I'll be discussing today why the retina is such a desirable target for researchers, including those focused on conditions that affect other parts of the body, including the brain and central nervous system. And after that, I'll be providing an update on some clinical trials, and I think you'll find that interesting as well.

So let's get started. As many of you know, the retina, that magical piece of tissue that lines the back of the eye is really important because it makes vision possible. Without this light sensing tissue, we can't see. No retinas, no vision. We often make the comparison of the retina to film in a camera or digital sensors in a camera. But retinas are also an extension of the brain. Retinas are neural tissue. It's kind of creepy when you think about it, but our retinas are actually the parts of our brains that extend outside of our skulls. So compared to the rest of our brain, which is inside our skulls, retinas are relatively accessible neural tissue. Though most of us don't like the idea of procedures or injections on our eyes, it is more accessible than doing procedures on your brain. Also, the retina is a relatively small piece of tissue, so you don't need a lot of gene therapy or perhaps a stem cell treatment to potentially address a condition.

Another nice thing about retinas is that we have two of them. So if scientists are evaluating a treatment in a clinical trial, they can treat one eye or one retina and compare it to the untreated eye or what we call the control and see if the treated eye does better. So for all these reasons, retinas are a really good research and therapy target. And as I mentioned before, what may work for the retina might also work for conditions that affect other parts of the body, like the brain and the central nervous system. And finally, it's important to remember that inherited retinal diseases such as retinitis pigmentosa, Usher Syndrome, and Stargardt disease are all caused by mutations in a single gene. So that makes these retinal conditions clear targets for developers of genetic therapies. And what's exciting now is that we now have more than 40 clinical trials underway for emerging therapies to save or restore vision for people with these inherited retinal conditions.

And as many of you know, the Foundation Fighting Blindness is strongly focused on moving more therapies through clinical trials and getting them out to the people who need them. So now let's switch gears a little bit, and I want to give you an update on a couple of clinical trials that have recently reported some new results. And one is for an RNA therapy being developed by a company called ProQR out of the Netherlands. And this therapy is known as an antisense oligonucleotide. And for short, we call it an AON and don't get too intimidated by the long terminology. An AON is simply a small piece of genetic material that can mask a disease causing mutation in RNA. So it covers up the mutation in RNA. And RNA are the genetic messages that our cells read to make proteins. And so when we can mask that mutation, the cell can then read that genetic information and make a normal protein.

So ProQR recently reported some pretty good results from their phase one, two clinical trial for people with mutations in the exon region of the gene USH2A. So exon 13 is a part of the USH2A gene that's a

hotspot of mutations. And these mutations can either cause Usher Syndrome type two A or non syndromic retinitis pigmentosa, just regular RP without the hearing loss. Now, the company reported results for 14 patients and very encouragingly the treatment improved visual acuity for the six people with the most advanced disease, and it improved peripheral sensitivity for the eight patients with early to moderate disease. And thanks to these very promising results, ProQR is now planning to move this therapy into a phase two, three trial later this year. And just so you know, ProQR also has clinical trials underway for a mutation and CEP290, which causes LCA10, that's had some good results in its early clinical trial, and now is in a phase two, three.

And they're also targeting the rhodopsin gene, which when mutated causes RP, a specific mutation called P23H. That's still in an early clinical trial, and they haven't reported results for that yet, but lots of great work going on for ProQR. So the other treatment I wanted to mention is a GUCY2D gene therapy being developed by Atsena Therapeutics. This treatment came out of the lab of Shannon Boye at University of Florida, and she's a co-founder of the company. Now, mutations in GUCY2D cause severe vision loss due to leber congenital amaurosis or LCA, specifically LCA type one. And the condition causes severe or significant vision loss at birth. However, people with mutations in this gene often have some remaining retinal structure, which makes them good candidates for gene therapy. Now, the Atsena trial is in an early stage.

It's in a phase one, two stage at University of Pennsylvania. And they recently reported results for the first three patients, all of whom are adults who received the lowest dose. And most important, the treatment had a favorable safety profile, which is the most critical aspect of the study at this early stage. However, there were also signs of efficacy. Two patients showed improved light sensitivity as measured by a test called full field sensitivity or FST, which is a general measure of rod function. Rods give us vision in dim settings, they give us peripheral vision, and this test is good for somebody with advanced vision loss who can't fixate well. Now, the third patient in this trial had improved visual acuity. This person improved from 2400 to 2200. And again, the folks in this trial have very advanced vision loss. So it's nice to see that there is some visual improvement shown at this early stage, but we are looking forward to results as they move into higher doses with additional patients.

And one thing I'd like to note is that both Atsena and the ProQR research projects that I mentioned are funded by the Foundation's RD fund. It's our venture philanthropy fund that's focused on moving treatments into and through early stage clinical trials. So it's nice to see some success for these investments. So I mentioned earlier I'm going to try to inject some humor into these podcasts. And so I actually have a vision related joke for you, and I have to credit this joke to Richard Fabian, our director of development in Denver. So here's your first Eye on the Cure joke. So a blind gentleman with his guide dog, they walk into a bar and they walk into the bar and they stop just after a few steps moving in. And the bar is somewhat full. There's a lot of people, and everybody gets quiet because they're looking at this gentleman and his guide dog.

But this gentleman proceeds to take his guide dog and lift the guide dog above his head, and then he slowly revolves around. He turns around in a circle with this dog over his head. And when he completes the 360 degree revolution, he puts the dog back down and continues to just stand there. And everybody's kind of in awe at what this guy is doing. And the bartender decides to ask and says, Sir, why did you just lift your dog above your head like that and turn around? And the blind gentleman says, I was scanning the room.

So that's your first Eye on the Cure joke. So okay, again, Richard Fabian gets credit for that joke whether you liked it or not. Thank you, Richard. So to keep this podcast interactive and fresh, we appreciate your comments and your questions. If you have any ideas for stories or jokes, we could really use some jokes, feel free to send an email to podcast@fightingblindness.org. Again, that's

podcast@fightingblindness.org. So that concludes our first Eye on the Cure Podcast. Thanks for joining me, and we look forward to having you with us for the next episode.

Speaker 1:

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