

Speaker 1: Welcome to the Eye on the Cure Podcast, the podcast about winning the fight against retinal disease from the Foundation Fighting Blindness.

Speaker 2: Welcome everyone to the Eye on the Cure podcast. I am your host, Ben Shaberman, VP of Science Communications at the Foundation Fighting Blindness, and happy New Year. I hope you had a great holiday season and your 2023 is off to a great start.

This episode, which happens to be episode 38, will be a special New Year's review provided by yours truly, of clinical research advances made in 2022, and which position us for a very promising 2023. So without further ado, let's get started.

And the first company I wanted to talk about, the first emerging therapy, is being developed by Sparing Vision. They're a French company, they're part of the foundation's RD fund, our venture philanthropy fund, and they are developing a therapy to preserve cones. So what researchers have observed for many years is that patients with retinitis pigmentosa, usher syndrome and related conditions, they lose their rods first, but after the rods are gone, the cones degenerate.

And so what their therapy is designed to do is preserve cones. And in case you don't know or didn't remember, cones are really important for our vision. They provide visual acuity, the ability to read, recognize faces. They give us color vision, they give us vision in lighted settings, they give us central vision. So if we can just preserve some cones for people with retinal diseases, that will go a long way toward maintaining their independence and mobility.

So this therapy is aptly named Rod-Derived Cone Viability Factor, or RDCVF. And the exciting news from Sparing Vision is they received authorization from the US Food and Drug Administration to launch a clinical trial for RDCVF, and that will likely happen early next year. They received the authorization in early December. This will be a phase one two trial. It'll occur at the University of Pittsburgh Medical Center, and the company will also hopefully launch a trial in Paris, France. They're working with the European Medicines Agency to get authorization to launch a trial there.

This emerging therapy has been in development for decades. The foundation has funded a lot of lab research to make this possible, and the foundation has provided more than seven and a half million euros in the clinical development of this therapy as well as part of its RD fund investment. So very exciting. This is a gene agnostic therapy and we're looking forward to seeing it move into trials and hopefully get some initial results within about a year or so.

Now, another company that got authorization to launch a clinical trial is called Opus Genetics. Now, what's special about Opus Genetics is there a company that was actually launched by the Foundation Fighting Blindness. Our senior leadership actually were the first, what I call de facto employees. They got the company off the ground. They hired senior staff to get the company running.

And excitingly, Opus has received authorization to launch its first clinical trial for a gene therapy for people with LCA5, which is caused by mutations in lebercilin. And the company also has gene therapies in the pipeline for LCA caused by RDH12 mutations and LCA caused by NMNAT1 mutations. But again, LCA5 will be the first to move into a clinical trial.

Now, Opus is focused on gene therapies for rarer retinal conditions, those conditions that aren't being addressed by other companies. The CEO of Opus is former FFB, Foundation Fighting Blindness CEO, Ben Yerxa. Its scientific co-founders include Jean Bennett, the visionary behind Luxturna at University of Pennsylvania, and Eric Pierce, also a very well respected, well renowned researcher up at Mass Eye and Ear. He was chair of our scientific advisory board for 10 years.

So we have a lot of great personnel and scientific know-how behind Opus. Their goal is to launch a new clinical trial just about every year if they can. So it's an ambitious goal, but we're excited about this company's potential.

This company too is part of our venture philanthropy fund, the RD Fund. We made a substantial investment in its launch and its continued operation. We look forward for results from this first trial, which will occur at the University of Pennsylvania and start in early 2023.

Next, I'm excited to tell you about the progress being made at Atsena Therapeutics. This is a company founded by University of Florida science folks, Shannon Boye and her husband, Sanford Boye. Shannon is a longtime gene therapy developer funded by the foundation, one of our leading innovators. This company, more than a year ago, launched a clinical trial of a gene therapy for LCA1, which is caused by mutations in the gene GUCY2D. And excitingly, they announced results for the first 15 participants in that LCA1 trial.

And first of all, they reported that the gene therapy was well tolerated, which is always important. You want to confirm that the therapy is relatively safe. But the first nine patients which received the highest dose of this gene therapy had clinically meaningful vision improvements as measured by a full field stimulus test. That's a test that measures the general sensitivity of rods and cones.

And also they had clinically meaningful vision improvements in their ability to navigate a multi-luminance mobility course. So very encouraging results. And now Atsena is planning a phase three trial for this LCA1 gene therapy. Stay tuned as they talk with the FDA about the design and potential launch date of the phase three.

Excitingly, Atsena is also planning a phase one two clinical trial for a gene therapy targeting x-linked retinoschisis. They plan to seek authorization to launch that trial in early 2023. So stay tuned for that. And it's important to note that also in their development pipeline, they are working on a gene therapy for people with Usher Syndrome type 1B. Usher 1B, the gene is a bigger gene. That gene, MYO7A, won't fit into the traditional gene therapy delivery system that most researchers and companies

are using. So Atsena is coming up with a dual vector system to deliver that USH1B gene in two different containers. So it's an important technological project. They're making good progress and development of that dual vector gene therapy and we hope they can move that into a clinical trial.

So next, I would like to move into a discussion of two emerging therapies for the dry form of age-related macular degeneration. Specifically, the advanced form of dry AMD known as geographic atrophy.

Geographic atrophy is when there's been actual cell loss near or in the center of the retina. So there's not only cell loss, there's vision loss. And two companies have completed phase three clinical trials to slow the progression of geographic atrophy or in short, GA. Those two companies are Apellis and IVERIC Bio. And both are seeking FDA approval of their drugs so that they can be made available to patients with GA.

Now, both therapies target the innate immune system. Researchers many years ago observed that the innate immune system is overactive in people with all forms of a AMD and that overactivity leads to damage to the retina. So by tempering the innate immune system, they believe they can slow progression of this disease. Now, Apellis is targeting a specific factor called complement factor three or C3. And in their two clinical trials, both phase three, one is called Derby, one is called Oaks, over 24 months, their C3 inhibitor slowed disease progression. It slowed the growth of the lesions associated with geographic atrophy.

In the Derby trial, monthly injections of their treatment, monthly intravitreal injections slowed GA lesion growth by 19%. In their Oaks trial, monthly injections slowed lesion growth by 22%. Now, Apellis has already submitted an application to the FDA to get authorization, and they are due to hear back from the FDA in late February to determine if their treatment has been approved and will be made available to geographic atrophy patients in the United States.

Now, IVERIC Bio has also completed phase three trials. Their therapy also targets the complement system. They are targeting a different factor called complement factor five. They too are looking to slow the lesion associated with geographic atrophy. In their two clinical trials after 12 months, one trial's called Gather One, the other trial's called Gather Two, their treatment slowed disease progression by 35% and 18% respectively. In Gather One again, 35% reduction in GA lesion growth. In Gather Two, 18%.

They have just completed submission of their new drug application to the FDA. So hopefully sometime not too far into 2023, they will get an answer from the FDA to their application submission. So hopefully in 2023, we will have at least one, maybe two treatments for geographic atrophy approved by the Food and Drug Administration. That would be awesome because geographic atrophy, the advanced form of dry AMD, is a significant unmet need. We definitely need to get something across the finish line.

Now, I'd like to shift into Stargardt disease. And to help you understand a couple therapies that are in the pipeline for Stargardt disease, I want to explain what the

underlying cause of vision loss is in Stargardt disease. Basically what happens is in Stargardt disease, there's an accumulation of toxic byproducts that cause cell loss. And these byproducts are the result of vitamin A metabolism.

Now all of us to see, for our retinas to be light sensitive, need vitamin A, and most of us in developed countries get plenty of vitamin A from a normal diet. Even if we don't eat a lot of fruits and vegetables, we still get plenty of vitamin A. And again, vitamin A helps our retinas work. It helps them become light sensitive. I like to think of vitamin A as like a fuel. And like a fuel, when vitamin A is metabolized, there are byproducts. There are what we call metabolites that are produced, and these metabolites are toxic.

In a healthy retina, in a normal retina, these metabolites are cleared. But in people with Stargardt disease, these toxins accumulate. They accumulate in deposits called lipofuscin. Over time, as these lipofuscin develop underneath the retina, they cause the atrophy and the vision loss.

So two companies are targeting the development of these toxic byproducts, the accumulation of lipofuscin. One of these companies is called Alkeus, and they've had a phase two trial underway for more than a year. And excitingly, earlier in 2022, they reported that their therapy reduced the growth of the lesions associated with Stargardt disease by 30%.

Now, Alkeus's therapy is a modified form of vitamin A. It's called deuterated vitamin A. And that's what patients take orally. And what Alkeus has shown pre-clinically, and they think is happening in humans, is this modified form of vitamin A metabolizes more cleanly than the vitamin A we get from our diets. And that 30% reduction in growth of the Stargardt lesions is great evidence that it's working. And we hope they will continue to see these encouraging results as their phase two trial progresses.

Now, another company targeting the vitamin A metabolism pathway is called Belite Bio. Now, instead of providing a modified form of vitamin A, Belite has a drug that is blocking the uptake of vitamin A into the retina. Their treatment is called an RBP4 inhibitor. And excitingly, they've launched a phase three trial for their therapy in adolescence, people 12 to 18 years of age, with Stargardt's disease. They believe this population is going to be the group of patients most likely to respond to this approach in a clinical trial. So that's why they're enrolling adolescents.

And we hope at some point in 2023 they report results. And of course we hope those results will provide some promise that their drug can slow disease progression. They too will be looking at the growth of the area of atrophy, that lesion that I was talking about, which causes vision loss in people with Stargardt disease.

So next I'd like to talk about an approach for advanced retinal disease called optogenetics. So people who have lost all their vision have by definition lost most or all of their photoreceptors, all their rods and cones, the cells that make vision possible. But what some very clever researchers have observed is that there are other cells in the

retina that survive in people with advanced retinal diseases. And these cells are known as ganglion cells and bipolar cells.

And what these very clever researchers have done is they deliver a therapy to these ganglion cells and bipolar cells that makes them light sensitive. Normally these cells aren't light sensitive, but essentially what's happening is these ganglion cells and or bipolar cells are working like a backup system for photoreceptors. So with optogenetics, excitingly, we have three clinical trials underway from BionicSite, GeneSite, and also Nanoscope. All three trials are still in phase one two, but all three trials have reported some encouraging early results. People can see shapes and motion. In the BionicSite trial, one gentleman was able to see dog running in the snow. So we're hoping as these trials move forward, the vision improvements will be even greater.

So excitingly, another company has moved into this space and their therapy isn't exactly optogenetics. It's optogenetic-like, but instead of using a gene therapy to express light sensitive proteins, they have a small molecule. And excitingly, their small molecule received authorization to move into a clinical trial in Australia for people with RP and they've dosed their first patient with RP.

Unlike the other trials that I mentioned, GeneSite, BionicSite, and Nanoscope, the Cura treatment will be injected on a monthly basis into the eyes of patients. It's an intravitreal injection. With the optogenetic therapies, those are one-time injections. Now, what's nice about the Cura approach, while it may not be as convenient to get monthly injections, you have a better opportunity to modify the therapy to adjust the dosing or try a new and better therapy if desired down the road. Because with the small molecule therapy, it washes out, it diminishes over time. That's why it needs to be re-injected.

So stay tuned as Cura doses more patients in 2023. I will add that the Cura therapy was made possible by some funding that we provided to Richard Kramer at UC Berkeley for his lab work on the photo switch, as we call it, that has moved into the Cura clinical trial.

And last but not least, I wanted to mention some exciting progress that is being made in X-linked retinitis pigmentosa. Two of our partners, MeiraGTx and Applied Genetic Technologies Corporation, AGTC, reported encouraging results in phase one two trials, some encouraging vision improvements. MeiraGTx has moved into phase three. AGTC was recently acquired by the company Syncona. They continue their phase two expansion trial and are planning a phase three trial.

So exciting progress being made for X-linked retinitis pigmentosa. A third company, 4D Molecular Therapeutics, has a phase one two trial underway. So we're hoping to report more exciting progress from all three companies in 2023.

So that, my friends, wraps up the 2022 highlights. There is much more going on I might add that I wasn't able to cover in a single podcast episode. Visit [fightingblindness.org](http://fightingblindness.org) to learn about other great research projects that are underway for addressing the entire spectrum of retinal degenerations.

This transcript was exported on May 10, 2023 - view latest version [here](#).

Thanks as always for listening to the podcast. It's great to have the guests that I have to share the great progress that's being made in research and share their stories of addressing the many challenges of retinal degenerations.

And again, thanks to you for listening and for supporting the mission of the foundation. I wish you and your loved ones a happy 2023 and look forward to having you back for the next episode of Eye on the Cure in a couple of weeks. Take care.

Speaker 1: This has been Eye on the Cure. To help us win the fight, please donate at [foundationfightingblindness.org](http://foundationfightingblindness.org).