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 everybody to another installment of the Eye on the Cure podcast. I am Ben Shaberman, senior director of scientific outreach at the foundation, and really glad you could join us for another episode of the podcast. And I'm delighted that for this episode we have Jill Dolgin from AGTC, Applied Genetic Technologies Corporation, and Jill is the head of patient advocacy. And if you didn't know, AGTC is very active in our space. They are a clinical stage biotech and they're developing groundbreaking gene therapies for rare diseases. And in our space we're excited because they have gene therapy clinical trials underway for both X-linked RP and achromatopsia. A little more about Jill.

She leads the patient and professional engagement strategy to drive disease awareness and clinical trial recruitment efforts for the AGTC pipeline. She has more than 20 years of global bio pharmaceutical experience in medical affairs, corporate communications, patient and professional advocacy and public policy. Jill earned her Pharm D from the University of the Sciences at Philadelphia, and she earned her bachelor's of science in pharmacy from the Ohio State University. Go Buckeyes. Really glad that you could join us, Jill. And I was thinking as we were getting ready to record, you've been with AGTC now for quite a few years. How long has it been exactly?

Jill Dolgin:

Ben, it's been four and a half years. Time has just flow by.

Ben Shaberman:

It really has. It doesn't seem all that long ago when you began, but I was thinking when you began there really weren't any clinical trials underway for AGTC. So it's really exciting to see your work moving forward in the clinic and you're going to tell us more about that in just a little bit. But to start off, I was hoping you could tell us more about what it means to be a patient advocate. What do you do in that role?

Jill Dolgin:

I think just as the quick summary of my role is to be responsible for ensuring that I understand the issues and challenges of our constituents. In other words we need to understand that patient journey, not just the individual, but the journey of the family as they're dealing with these rare conditions. And so my role is to engage with those organizations as well as individuals, to educate me, to educate them about the condition and help them make some informed decisions. In other words, the more they know about their condition, whether it's getting that genetic test or whether it's being the right specialist, the more empowered they can be with that knowledge to make some decisions about going forward, including a clinical trial.

Ben Shaberman:

Right and I think with clinical trials it's really important because people are anxious to get into clinical trials, but often they don't understand the risks, the commitment. It's not a trivial thing to be in a clinical trial for an emerging therapy. So I was wondering, how long have you actually been in patient advocacy? Did you do that before you came to AGTC?

Jill Dolgin:

Well, as a matter of fact, starting in my early days as a clinical pharmacist I would say that I've always been a patient advocate. I mean a pharmacist's job is to educate their patients about their medication so that they understand how to take it. So I would say that as early as my pharmacy days and understanding pharmacology and explaining it to my patients, it motivates those individuals to continue with their care when they understand why it's important for them and for their condition to continue with their therapy. So it goes back many, many years as a clinical pharmacist, and I actually ran a regional poison center so I can say that I've advocated for individuals and families by handling one phone call, one patient at a time.

But over the years in working in bio pharmaceuticals and engaging with patient organizations like FFB, I feel like I'm impacting or helping more than one patient at a time. By working with FFB, you are educating and learning about what we're doing you can in turn interpret that information and explain it to your constituents. So having this dialogue and understanding the science and understanding the clinical trials that we're conducting, you can be that voice, the credible voice for those physicians as well as those patients and families to help them understand what's coming in the future.

Ben Shaberman:

Right. Well, we do our best to keep people informed about what's happening on the research front, but something you said really caught my attention. You worked in, did you call it a poison control center?

Jill Dolgin:

Yes.

Ben Shaberman:

So were you answering calls from people who were concerned or in fact poisoned or taken a poison?

Jill Dolgin:

Yes. Yes. So my post-doctoral work was in clinical toxicology. And so my role was twofold. At the Children's Hospital Buffalo I was the clinical pharmacist for a 200 bed pediatric high risk maternity hospital, but I was also the administrative director for a regional poison center covering about 3 million individuals in western New York. And those calls ranged from sort of non-toxic, child swallowed a penny to major overdoses and actually animals as well as human overdoses. So interesting. Plant exposures, venomous creature exposures, as well as medicinal so I was there for about 10 years.

Ben Shaberman:

Wow, that sounds extremely intense.

Jill Dolgin:

It was.

Ben Shaberman:

High pressure when you have somebody on the phone. Wow. You think that work has helped inform your overall patient advocacy work?

Jill Dolgin:

Oh, absolutely. When you're in that high pressure situation and you have to make some decisions based on sometimes just animal data alone and you're making a clinical decision for a human that's in serious condition, I think it underscores the importance of the patients, families, and doctors to fully understand the information in front of them and empower them to make some decisions. So absolutely, I think it's made me a better advocate.

Ben Shaberman:

That's really interesting. And so you've been obviously now working as an advocate at AGTC for a while. Are there any memorable moments that come to mind for patients and families that you've been working with for the XLRP or achromatopsia trials?

Jill Dolgin:

There have been so many over the last four years. We recently had two families with children who were waiting years to join the achromatopsia trials and one of the families was in Canada and they were trying to get to one of our Boston sites, and we ran into some COVID challenges. Surprise. One of the things we had to do was contact border control. We contacted Fighting Blindness Canada, trying to get a medical exemption for the two week quarantine that they were going to have to undergo. This is one of those things where you just try to get as much information as possible to help them make a decision. And COVID was an unusual situation.

Ben Shaberman:

Right. It presented new challenges in your advocacy role, I'm sure. So one thing I wanted to have you explain to our listeners, I know a lot of people know what RP is and X-linked RP, it's just one of the common forms of RP. Can you tell people what achromatopsia is?

Jill Dolgin:

Sure. Achromatopsia is an inherited retinal disorder, its fairly rare. There's about 20,000 cases in the US. It is caused by one of six genetic mutations, most commonly caused by mutation in the CNGA3 or CNGB3 gene. These individuals are born blind, are born with a poor visual acuity, legally blind. They also, it's a disease of the cones. So their close up vision, their fine motor skills are affected. So they have poor visual acuity. They're very light sensitive in the sense that they need very dark glasses or contacts to manage in bright sunlight. And they also lack the ability to perceive color. And those are the three major signs and symptoms of achromatopsia.

Ben Shaberman:

Right. I guess thinking about it's almost the reverse of RP.

Jill Dolgin:

Correct.

Ben Shaberman:

With RP a lot of people maintain some central vision. They have problems seeing in dim or dark settings where achromatopsia, it's just the opposite.

Jill Dolgin:

Exactly. Exactly. The difference is that achromatopsia is not progressive. I mean, there may be some deterioration of cones over time, but they're born with this and so it's not a matter of having great vision when they're born and then getting worse over time, as you see with RP that they're actually born legally blind.

Ben Shaberman:

Right. And isn't one of the end points that you're evaluating in the achromatopsia trial light sensitivity, but unlike improving somebody's light sensitivity, in achromatopsia you're actually trying to make them less light sensitive so they're not so uncomfortable. Isn't that correct?

Jill Dolgin:

Correct. Correct.

Ben Shaberman:

Because my understanding is that people with achromatopsia, it can actually be painful for them to be in a brightly lit situation.

Jill Dolgin:

Yes. Actually outside in the bright sun.

Ben Shaberman:

Seek out dark settings. Yeah. I always have a tough time wrapping my head around that because I'm so used to talking to RP patients who again want better light perception. So can you give us a quick update on what's going on in both the XLRP and achromatopsia gene therapy trials?

Jill Dolgin:

Sure. So with achromatopsia we have completed the phase one and phase two for adults. And as you know, phase one is where we demonstrate that it's safe. And phase two we in a larger number of individuals are trying to see if there's a biologic signal to see if it works. So we always start with adults. And we've now, the results so far have been encouraging in both safety and in efficacy. We recently have reported the first improvements in visual sensitivity or light discomfort. And according to our patient research those are the most bothersome aspects of the condition, that light discomfort. And they've also shown that there's some sustained improvements in their visual sensitivity. And at this point we're about 12 months out, so we're given that good safety profile and some encouraging efficacy results. We've now started treating, we've just now have been enrolling children aged four to eight, so adults first, then pediatrics. So we're still finishing up those phase one to four for children and we'll have some additional readouts and efficacy results later this summer.

Ben Shaberman:

That's great. And we'll be sure to report on those. We [inaudible 00:13:33] the Foundation Fighting Blindness so we look forward to hearing those results. And so what's the latest on XLRP?

Jill Dolgin:

So with XLRP we recently reported that we continue to see a favorable safety profile. We had no dose limiting toxicity in all patients across our six dosing groups. And at the 12 months time point we just reported those who were treated centrally. We saw measurable improvements in visual sensitivity as well as the majority showing stable or improvement in their visual acuity as well. We've initiated two additional trials. The first one called, they're both called the Scenic trials, but the first one is called Skyline. We're already enrolling in this one where we're randomizing 12 patients to one of two dosing groups. Both of those doses have demonstrated some benefit in the earlier trial. And then later this year we'll begin screening for Vista, which is our phase 2/3 trial. That will be a larger trial in which individuals will be randomized to one of three groups. Two of the groups will be treated in one eye initially, and then the third group is our control group, meaning that they'll be observed for a year before they receive treatment.

Ben Shaberman:

Yeah, the launch of the phase 2/3 is really exciting because if that goes well then there's a reasonable chance that you'll go to the FDA for approval. But we're getting ahead of ourselves. We need to get it the treatment-

Jill Dolgin:

Exactly.

Ben Shaberman:

... into and through the phase 2/3. Can you talk about anything else that is in the AGTC pipeline? I know people can't see, but Jill's shaking her head no, but she [inaudible 00:15:35] me a hard time.

Jill Dolgin:

Absolutely. I mean, so in addition to our achromatopsia and XLRP trials, we have some preclinical programs and optogenetics, some other ophthalmology programs, our CNS, Central Nervous System program, as well as otology, which is obviously the ear. Our optogenetics program is being developed in collaboration with Bionic Sight and they are managing their clinical trial. We are just a partner in that. And our otology program is partnered with Otonomy. So in addition to our product pipeline we've got significant intellectual property portfolio and experience in the design of gene therapy products, including capsids, promoters, et cetera, which we're also partnering with other companies to share our expertise.

Ben Shaberman:

That's great. I know that developing the actual gene therapy, engineering that virus is not a trivial thing. I know when we talk about gene therapy we say it's an injection of the healthy gene underneath the eye or underneath the retina, and it sounds so simple, but to develop that actual vector to do that is quite complicated.

Jill Dolgin:

It is the biggest challenge that all gene therapy companies have. I mean, gene therapy, manufacturing and development is the number one challenge for these types of regenerative treatments, if you will.

Ben Shaberman:

Right. So I know a lot of people out there are interested in clinical trials, whether they're interested in AGTCs trials or another sponsor's trials. Can you talk about what people should expect or think about if they're interested in a clinical trial?

Jill Dolgin:

Absolutely. I think that's, as I had mentioned earlier my role is to help patients understand what the expectations are in order for them to make an informed decision. And I think the most important consideration is the time commitment. Certainly adverse events, et cetera are important. But more, I think, important for them to consider whether they're going to join a trial is to understand that time commitment. The IRD trials, not just ours, but others are generally five years or longer in some studies, meaning that the most time being that they spend at the trial site is about 12 visits in the first year. After that it's an annual visit up to five years. But on average it's a huge time commitment, not just for the individual who's undergoing that treatment, but for the family as well. They have to take time off from school or work, find daycare for other kids, et cetera so the time commitment is certainly the biggest issue.

Ben Shaberman:

And if people need to travel, in other words get on a plane or maybe stay at a hotel, AGTC normally picks up those expenses, correct?

Jill Dolgin:

In our case, yes. I would not say that, that's the case for every trial out there. In some cases I've seen where the companies are not paying for those types of visits, certainly the medical costs associated with it, every company will cover. AGTC does cover the travel, the lodging, the food, not just for that individual, but for a companion. We don't expect a visually impaired individual to travel by themselves so we will take care of that for the family for every visit that they have to attend.

Ben Shaberman:

That's great, that's very helpful. As you said there's the time commitment, but the money, the support sure helps as well. So I just want to remind our listeners that if they're interested in information about these trials, we stay up to date on the news and you can visit fightingblindness.org to get the latest news on these trials and other trials. If you have a question or a comment related to the podcast itself, you can send an email to podcast@fightingblindness.org. And Jill, I just want to thank you for taking a little time out of your busy day to talk about your role, talk about the trials. I know patients and families out there are always eager for information and to learn, and this was a very helpful exercise in educating our community. So thank you.

Jill Dolgin:

Well, thank you. And if they want to learn more about our trials, please come to agtc.com, send us a question and we'll provide them with direction on how they can get involved.

Ben Shaberman:

And I'll echo that. I know you have a great website with a lot of good information. So thank you again, Jill, and thanks everyone out there for joining us, and please tune in for our next podcast.

Speaker 1:

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