

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 another episode of the Eye on the Cure Podcast. I am your host Ben Shaberman with the Foundation Fighting Blindness, and I'm pleased to have as my guest for this episode, Brian Strem. He is CEO of Kiora Pharmaceuticals and Kiora has just launched a clinical trial for a promising small molecule that's designed to restore vision to people with advanced vision loss from retinitis pigmentosa and maybe other conditions. So welcome to the podcast Brian. It's great to have you.

Brian Strem:

Ben, pleasure to chat with you today and thank you for having me on.

Ben Shaberman:

You are most welcome. So before we begin our conversation, I'd like to give you a little background on Brian. He received a PhD in Biomedical Engineering from UCLA, a Bachelor of Science in Bioengineering from Cornell. And Brian has worked at a few different pharmaceutical companies, Sound Pharmaceuticals, Allergan and Shire, and he was responsible for business development and corporate strategy and ophthalmology, otology and regenerative medicine. Now Brian, in researching your background, I also saw that you co-founded two ophthalmology companies, Bayon Therapeutics and Okogen. Can you briefly tell us about those before we talk about Kiora?

Brian Strem:

Yeah, it'd be my pleasure. So after leaving Allergan in, I think it was 2015 at the time, right when we got acquired by a company called Activists, I actually decided to take some time away from corporate life and spent some time with the family and just enjoy what I thought was going to be a summer off, at which point in time a colleague of mine came over a cup of coffee and told me about this asset that he was starting to help a company out with. That was a very promising antiviral and while at companies like Shire and Allergan, we were always looking for a good antiviral to treat Adenoviral conjunctivitis or the viral form of pink eye. And so instead of having a summer off and spending more time with the family and the new puppy we just got, ended up starting Okogen, which was really focused on developing this promising antiviral asset in adenoviral conjunctivitis patients.

And so we ended up receiving or closing a series A financing round, actually from a VC out of Australia and moved that program into a phase two clinical trial where we actually saw some really exciting promising efficacy and safety around the ability to eradicate viruses on the ocular surface that do cause this type of infection. Unfortunately, that directly overlapped then with Covid, which as we all know, really put a hamper on a lot of the clinical trial activities. And so that company, which I still remain on the board of, I did hand off the CEO reigns to the new CEO Joshua Moriarty, who's taking that into later stage clinical trials. Towards in the middle of Covid or so we actually ended up founding Bayon Therapeutics, which is actually the genesis of the retina program that we will talk about at Kiora.

And so we can definitely spend a lot more time talking about this, but actually in Adelaide, Australia, we met Russ Van Gelder who gave a keynote lecture at one of their local ophthalmology conferences called RANZCO and he was telling us about these small molecule photo switches that to me just was fascinating science and a really exciting approach to helping patients get restored vision in the case of

retinal degeneration. So conversations moved very quickly because I knew this is something I wanted to be a part of, knowing how large of an unmet need there was, especially in retinitis pigmentosa patients and not just trying to slow disease, but how can we actually restore vision that was already lost. So that was really the genesis of Bayon Therapeutics, which then got acquired by what was at the time EyeGate pharmaceuticals where I took over a CEO and then we rebranded it into Kiora Pharmaceuticals.

Ben Shaberman:

Interesting. Thanks for sharing the stories of both companies and the journeys for these emerging therapies and the companies developing them are always interesting. They're usually not that straightforward. There's a circuitous path, but I'm really glad that Kiora is moving forward with its clinical trial for this small molecule. So tell our listeners about the small molecule and what it's designed to do.

Brian Strem:

So without going too science heavy, basically this is a molecule that was custom built in the sense that the core of the molecule is based around something called an Azobenzene. And the reason I bring that up is because Azobenzene are notorious for shape shifting and oftentimes different types of stimuli can cause these isomeric shape shifts. And so the way the molecule was completed then was in a way that would actually alter certain ion channels. And in this case what we see was in a non-permanent way, the molecule is able to actually go inside of retinal ganglion cells, rather specifically those that are no longer connected to upstream photo receptors. So basically they have degeneration in their retina in certain locations. We know this isn't just a quick disease that goes from full vision to no vision, it is a progressive disease and in the areas where there is cell death of those photo receptors, those downstream retinal ganglion cells take up our molecule and then the molecule literally sits on the intracellular domain of these potassium and HCN voltage gated ion channels.

And when light then touches those cells, the molecule does its shape shifting and that causes a physical blockage of those ion channels. When that happens, that neuron essentially goes through a depolarization state and signals the brain that light is present. And the exciting part obviously is when you take the light stimulus away, it reverts back to its lower energy state, the molecule, allowing the cell to repolarize and therefore stop signaling the brain as to the presence of light. So that's why we call them photo switches. Light is the activation source and it literally can switch back and forth faster than our native vision even works.

Ben Shaberman:

That's so interesting. And I guess to summarize what this molecule, this photo switch, is doing is it's harnessing ganglion cells for vision, it's making them light sensitive in the specific regions where photo receptors have degenerate.

Brian Strem:

That's correct.

Ben Shaberman:

So my first question is how does it know to go to the areas where there's degeneration?

Brian Strem:

That's a great question and really one of the first questions I asked as well when I was doing my homework around this because as a patient is losing their vision, what any therapy does not want to do is interfere with the residual vision they have. And so that's a really important thing that there is not this crosstalk and interference of interpretation of light. Interestingly, in cases of retinal degeneration, for instance with RP where the photoreceptors are degenerating, those retinal gang cells and some of their other machinery within the retina itself actually remains alive for a very long time, but they don't stay exactly how they were. They are going through this "remodeling".

Part of that remodeling essentially in search of new input, they open up this P2X7 pore, which is a transmembrane protein that enables or allows our molecule to gain entry into the cell. And so we've been able to demonstrate specifically that these P2X7 pores are only open in these remodeling retinal ganglion cells due to the lack of the upstream photo receptors. So that is essentially the specificity that enables our molecule to only target really sections of the retina that do have degeneration.

Ben Shaberman:

That's so cool. It's like some of the cells welcome the molecule with open arms, so to speak, and then the other cells that are still working with photoreceptors are not. That's really, really cool. And I want our listeners to know that early generations of this photo switch came out of the lab of a researcher named Richard Kramer at UC Berkeley, and we funded his work for actually several years. I think we've invested more than a million dollars in the work on photo switches that he did. And it's wonderful to see this moving into a clinical trial and we'll talk about the clinical trial in a moment. But what I wanted to ask you about Brian is on this podcast and in other articles we posted to our website, we've talked a lot about optogenetics and this is similar in some ways to optogenetics, but it is distinctly different. Can you compare and contrast this chemical photo switch, if you will, with optogenetics.

Brian Strem:

Absolutely, but firstly I would just like to also thank the FFB because if you guys never funded that work with Rich Kramer at Berkeley, none of this is where we are today. So my appreciation obviously to the foundation for the ability to identify promising research projects at the academic level that are able to translate into now corporate settings and actually clinical trials. But with respect to your second question there on how do we differ from optogenetics, and I think optogenetics are incredibly exciting space and I'm really hopeful to see some more data coming out of the companies that are currently running studies with their optogenetics, but there certainly are, as you mentioned, some key distinct differences. First and foremost, we all know that optogenetics is essentially a gene therapy approach, which is really a "permanent" approach towards trying to insert new light sensitive proteins into similar cells like we are targeting the retinal ganglion cells or even the bipolar cells.

And we know that that's going to last probably between a decade, two decades if not more. We're still learning as a society as to what it's really going to be like, but we also don't really understand fully what is happening all the way down to the individual patient level and how are they functioning and how is this performing for them. So one key difference is that ours is not a "permanent" therapy and I think that's a really good thing because if something does go wrong with any of these approaches, ours will actually just dissipate as all small molecules do in our bodies with respect to just dosing frequencies. Whereas the gene therapies will clearly not be just eliminated over time. And so what that also provides though is as a medical group, none of us are stopping innovating, but if someone received a gene therapy and a few years later a new technology or a new therapy becomes available, that is even better, that patient likely will not be eligible to receive that new therapy.

Whereas those patients that are on a small molecule, once that molecule is fully eliminated from the body, which we think takes about 30 days from a single injection from us, then they should be eligible for next generation therapy. So we see some big differences from that regard as well as the fact that ours is a small molecule, much cheaper to make, much cheaper to actually deliver to patients and to get to patients. We're not talking about a million dollar therapy like these gene therapies are likely going to be pricing at and causing a pretty substantial strain on the overall healthcare system.

Ben Shaberman:

That's interesting. Thanks for again comparing and contrasting the two approaches. Now with optogenetics, some of the companies, their therapies require really bright light and because of that, their approaches also involve use of glasses or goggles to amplify the light coming into the eye, but you're not incorporating any additional devices or glasses or anything like that. Is that correct? Do you think the treatment will work well in natural light for people?

Brian Strem:

Yeah, so what you're asking really comes down to how much light intensity or how many light photons are actually hitting those target proteins or molecules like ours and how much is needed to cause this activation to occur. And so all the data that we have shows walking outside in normal daylight provides more than enough photons to cause our isomeric shift or our photo switch to occur, which tells us we do not need to amplify or focus that light intensity at a higher level, which is what those goggles are really doing. They're acting essentially as projectors to take an image from a camera and then projecting that in a very bright way onto the retina. Again, a lot of those proteins that are being explored with the optogenetics approaches are requiring that type of intensity, light intensity, whereas our molecule we do not believe will need anywhere near that amount of photon flux to actually cause the activation to occur, which means we don't need the goggles. We believe, obviously the data will tell us everything we need to see, but that's how we are approaching this based upon the underlying science.

Ben Shaberman:

Got it. Thanks for explaining that. So as you and I are speaking in early July 2022, Kiora just received authorization to launch that phase 1/2 trial in Australia. You haven't dosed anybody yet as we're speaking, hopefully that'll happen relatively soon. So why did you choose Australia? You did reference earlier in our conversations Russ Van Gelder and maybe that's the connection that he's in Australia. And since we have a lot of listeners in other parts of the world, many in the US, do you hope to move to a US site or another site outside of Australia sometime in the future if things go well in the phase 1/2?

Brian Strem:

Yeah, so just to be perfectly clear, Russ Van Gelder is actually the Chair of Ophthalmology at the University of Washington up in Seattle. He was just invited out to that Australia conference to give a keynote lecture. He's also the previous President of the American Academy of Ophthalmology and I believe now is the Editor-in-chief of the research journal Ophthalmology. So he is certainly a very US focused and based individual or should I say a global individual and we just happen to meet him in Australia. So why go to Australia for this first study? There's actually multiple reasons. Number one, they have a first world, first in class healthcare system just like we have here in the States. So there is from a quality perspective of running clinical trials and just conducting medicine, they are on par if not even better than I think most countries in this world.

They do provide though a regulatory framework that enables earlier stage or smaller companies such as Kiora to actually move forward with clinical studies without as much in terms of the non-clinical packages required to actually get approval to start those studies. And that's not to say that what we're doing is being a cowboy in any stretch. We obviously have all the data that we feel very comfortable with and it does go through a full ethics review committees who actually give the approval. So there is still pretty strict regulatory assessments and questions being asked from regulatory bodies, but they just provide a faster approach to actually getting started in the clinic. And it's also a little bit cheaper, frankly. So again, being a small company helps us a little bit in that regard and we absolutely intend to take this molecule with positive proof of concept data from this first study back here to the US where I am currently based as well and continue our development work, not just here in the US but really our goal is to get this thing to be a global therapy with positive data. So our intention is certainly to come back to the United States and to continue our clinical development again on a global setting.

Ben Shaberman:

Got it. Sounds like a good strategy. And I'll let our listeners know we're funding a company called Acuity. They're a US company who's developed an antioxidant that is also in a clinical trial in Australia, and they hope to move that to the US. So Australia seems to be a good place these days to get some early stage clinical research going. So the trial that you are about to launch, you're targeting people with retinitis pigmentosa. And I want to note that the approach, this photo switch, is gene agnostic. We don't care what the underlying gene mutation is for the people with RP. And while you're targeting RP patients early on, do you think that this molecule could help people with other inherited retinal diseases, maybe something like Stargardt disease or maybe even AMD?

Brian Strem:

Yeah, and that's a great question and I absolutely believe that this approach can be very helpful for multiple different clinical indications. Obviously we wanted to start with a disease that we as a society understand really well and RP is certainly one of those, but we do believe that there could be utility in some of these other retinal degenerative diseases, whether it is inherited or age related. Now that being said, this is a switch. So this is an on off of individual retinal ganglion cells on the presence or absence of light. What that isn't, is going to be able to restore things like color vision.

So if you think about some of the diseases that are more cone focused diseases and cause more cone degeneration solely, that's probably not going to be an area that I think our therapy will be able to help in, just because we're not able to restore again that wavelength specific, if you will, activation. So we do believe, though again, there are a lot of unmet diseases out there that are caused, like I said, by various forms of retinal degeneration. And after getting proof of concept, we'll certainly start exploring hopefully a lot more and a lot quicker, some of those other indications that we can then apply our therapy to.

Ben Shaberman:

Great. Thanks for explaining that. So my last question, it's the big question that I'm sure a lot of listeners out there are wondering what or how much vision do you think this molecule has the potential to restore?

Brian Strem:

Yeah, that's a fabulous question and we have certainly thought about different animal experiments that we could run to try to understand that even better. But the reality is until you can get a dog or a mouse to actually speak English to us and tell us what they see, it's just really hard to know. And I can promise you the way that we have built our study is that we will be assessing and asking a lot of questions and trying to understand what type of vision is being restored and is it meaningful? Is it helping a patient, whether it is walking down the street and restoring peripheral vision or central vision that may be lost based upon their disease progression. And these are exactly the types of things that we are going to be asking and keeping our fingers crossed that we can really help as many patients as possible.

Ben Shaberman:

And I know for people, especially with advanced vision loss who are down to let's say light perception or hand motion, really any improvement in vision can be a pretty big deal. So obviously we hope the vision improvement can be dramatic, at least in some cases, but even a little vision improvement would go a long way for many people. So Brian, this has been a really compelling and interesting discussion. I'm always excited about therapies. Well, I'm excited about all therapies, but especially those that are gene agnostic and targeting people who have advanced vision loss. I know they bring people a lot of hope and we wish you the best as this trial gets underway. Folks, stay tuned to our website fightingblindness.org. As the trial gets underway and we hear results, we will definitely report those there. In the meantime, Brian, thanks for taking time out of your day to tell us about Kiora and your photo switch. It's been a lot of fun and very interesting.

Brian Strem:

My pleasure, Ben. It's been great speaking with you and certainly look forward to keeping you guys updated on our progress.

Ben Shaberman:

We appreciate it. And listeners, as always, thanks for tuning into Eye on the Cure and we look forward to having you back for the next episode. Take care.

Speaker 1:

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