

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. I'm very pleased today to have with us, Ash Jayagopal, who is the chief scientific officer of Opus Genetics. Opus is a company, actually, launched by the Foundation Fighting Blindness. We launched it in September 2021 with the expressed purpose of developing treatments for retinal diseases that aren't being addressed by other groups. Welcome to Eye On the Cure, Ash. It's great to have you.

Ash Jayagopal:

Thanks for having me, Ben.

Ben Shaberman:

Before we get started, I wanted to give our audience a little background on you. Ash has both a PhD and an MBA. He's a bioengineer by training and has had over a decade of experience in leading multidisciplinary research teams focused on research and development of therapeutics, drug delivery platforms and biomarkers for retinal diseases. Ash came to Opus from Kodiak Sciences, where he served as executive director of Discovery Medicine. Prior to Kodiak, he was the head of molecular pharmacology and biomarkers in ophthalmology at Hoffmann-La Roche. Then, before that you were in academia. You were an assistant professor in the Department of Ophthalmology and Visual Sciences at Vanderbilt in Nashville. Again, it's great to have you with us, Ash. To get things started, when did you join Opus and tell us a little bit about your role as the chief scientific officer.

Ash Jayagopal:

Sure. I joined Opus in October 2021, so roughly around the same time that our work was getting started being launched out of the Foundation Fighting Blindness and its venture arm of RD Fund. As a CSO, I see my role at Opus as really being accountable for developing and sustaining the Opus portfolio of gene therapies so that we can bring as many scientifically validated gene therapies to the clinic to treat IRD patients as possible. We also want to build a strong internal gene therapy discovery team to develop new gene therapies, De Novo in-house for IRDs. To do this, I've been recruiting and building a team of talented scientists and scientific and clinical collaborators, many of whom are already part of the FFB Research and Clinical Trial network. Collectively, we're trying to identify the most promising gene therapy approaches for the various forms of inherited retinal degenerations and to prioritize their development and get more of these medicines to the finish line.

And so, generally, as CSO, I'm trying to align the corporate goals of Opus with the scientific goals and helping our team align the resources and capabilities to direct dedicated IRD gene therapy programs. Furthermore, I also play a role in representing the Opus Scientific Organization to the community at large, and that's including patient advocacy groups, investors, scientists and clinicians in the IRD space. It's really important to stay up-to-date for Opus on the most recent advances in the research community but also, we need to stay in tune with the patient and families community that we're working for. Making sure we're hearing their needs and responding to them in the best way we can as a

pharmaceutical company. It's something I'm truly enjoying and I'm really fortunate and grateful to be here in this role.

Ben Shaberman:

Well again, it's great to have you in that role, and I didn't realize how broad your role really is. You're working on both the science side really clinical development and then the patient advocacy side. That's a lot of work, especially with a startup company, where you're bringing so many new people on board. I presume you're staying pretty darn busy?

Ash Jayagopal:

Well, to develop these gene therapy medicines, it takes a village, of course. We need input from all the stakeholders. We need the patients to tell us what their IRD experience is like. For the clinicians, to tell us how they're treating and managing these patients now so that we can develop a medicine that's tailored to the patient population.

Ben Shaberman:

Right, exactly. That's very important. Tell us what Opus is focused on now, therapeutically speaking, what gene therapies are in development?

Ash Jayagopal:

Sure. Our initial programs, our first three programs or medicines are based on the work of our scientific founders. The first two are based on Jean Bennett and Junwei Sun's work at the University of Pennsylvania. The third program is based on the work of Eric Pierce of Harvard, Massachusetts Eye and Ear Institute. Jean's work, as many folks know, was instrumental in achieving FDA approval of the first ocular gene therapy for IRDs called Luxturna, which addresses a type of IRD called Leber congenital amaurosis or what we call LCA. Building on the success of Luxturna, Jean Bennett's lab actually developed a number of additional gene therapies for other forms of LCA. But unfortunately, a general lack of interest in ultra rare disease programs like this from the pharmaceutical industry led to a lot of difficulties getting these other gene therapies to the clinic. Opus was really founded to get more of these medicines to the finish line so that patients can benefit from all of this groundbreaking science.

A lot of which was funded by the FFB itself. Our founders, our leadership and our relationship with the patient community through the FFB and RD Fund is really enabling us to move swiftly in identifying and progressing the new therapeutics, which I can now summarize briefly. Our first three programs target these different forms of LCA that I was just talking about. Our lead program, which we call OPGx-001 or our first program, is designed to address mutations in the LCA5 gene. This encodes for the Lebercilin protein. OPGx-001 utilizes an adeno-associated virus, an AAV8. Not too unlike Luxturna, an AAV vector to precisely deliver a functional LCA5 gene to the photoreceptors in the patient's retina. OPGx-002 or our second program focuses on restoration of protein expression and halting functional deterioration in patients with retinal dystrophy caused by mutations in the retinal dehydrogenase gene, also called RDH12.

Our second program also leverages the same vector used in the first program, an AAV. Transporting, again, a functional gene to photoreceptors in the retina to hopefully result in visual functional improvement. Those first two programs are from the University of Pennsylvania and Jean Bennett who led these discoveries is very active as a scientific founder of our company and is a member of our board of directors and scientific advisory board. It's great to lean on Jean as a resource to make sure we're

doing everything we can to get these medicines to the clinic. The third program from Massachusetts Eye and Ear is designed to correct deficiencies caused by mutations in the NMNAT1 gene. NMNAT1 is an enzyme essential for retinal metabolism and it governs essential cellular processes needed for vision. Our OPGx-003 uses an AAV gene therapy, essentially to do the same thing, to structurally rescue this retinal tissue that is deficient in this gene. We hope to announce several additional programs soon, while we're building out our earlier stage development work. More to come.

Ben Shaberman:

Now, that's a great initial set of targets. In case our listeners don't know, again, as you said, all of these are targeting LCA. LCA affects kids really at birth or very early on. LCA is pretty severe in the effects it has on the retina. It's exciting that you're working on therapies to help kids, ultimately, with some pretty challenging conditions. LCA5, if I understand correctly, the first one you mentioned, will be the first to move into a clinical trial, or at least that's the plan. What's the timetable on that?

Ash Jayagopal:

We expect to initiate the LCA5 phase one clinical trial before the end of this year. Second half of 2022. It will be a safety trial evaluating AAV gene therapy for LCA5 in first, adults and subsequently, pediatric patients. This trial will be conducted at the University of Pennsylvania.

Ben Shaberman:

To reiterate a point you made, it's really great to be able to work with Jean Bennett, who is really a world-class pioneer in developing gene therapies with all the work that she and her team did with Luxturna. I'm curious, you have an interesting background, you've worked in both industry and academia, and then along comes this company that's~ launched by a nonprofit foundation. What drew you to Opus?

Ash Jayagopal:

Sure, yeah. A great question. As we build our team and try to recruit talented people to join us on the Opus mission, it's always exciting for me to share my perspective on what drew me to Opus so to recruit others to join us as well. I've been involved with the Foundation Fighting Blindness in several activities on the research side of things for several years. First, as a grant reviewer, and then a volunteer. I was mostly aware of the FFB's significant role in improving patient quality of life through establishment of the groundbreaking research programs, support for the clinical centers of excellence for treating IRDs and AMD and various patient advocacy and support programs. I had an idea of what the FFB was about. But I felt that at this incredible time for scientific progress with all of this fantastic research funded by the FFB along with other institutions such as the NIH towards bringing innovative therapies to patients with IRDs, it was just really unfortunate to see that many of these wonderful research projects with compelling preclinical evidence to support clinical applications, they just don't make it to the clinic where they can benefit patients.

Talking with the FFB, they agreed with this. They decided to take a proactive role and address this lack of clinical translation for so many promising research advances by stepping up and actually forming a company designed by and for patients to get more of these innovative gene therapies to the clinic so that we can treat patients that have been waiting for these therapies for a long time. That was really attractive to me, seeing a company such as Opus backed by a determined group of leaders, but also patients and their families, who all collectively want to address the lack of new therapies for IRDs. It's just incredible and rare to see the alignment of all the stakeholders behind the Opus family. You have

the investors, the patients and their caregivers. You have the clinicians and the scientists we collaborate with and work with in-house all towards the same goal.

To achieve something so ambitious, which is essentially to treat every IRD that we can that isn't being addressed by approved therapies or therapies under investigation and clinical trials, it's really going to be critical that we have that alignment that I'm talking about. That everyone's united toward the same goal. As a scientist, it's just really important to me because our sense of purpose is then crystal clear and we all get closer to our goals as a team. Then, you really feel like this isn't really a job, perhaps it's more of a calling to help people. It drives you to work really hard for something that's greater than your personal ambitions and goals. This is really a different company, and it was clear early on that Opus was a great fit for me.

Ben Shaberman:

Well, that's all so well put, Ash. We appreciate you diving in, taking the leap to be in this foundation startup. I'm thinking it's almost May now, this will probably air in May. You joined in October. What's it been like to be with this startup gene therapy company that's really growing by leaps and pounds very quickly? Has it been challenging, heartening? What's it been like for you?

Ash Jayagopal:

Oh boy, yeah. Every day has been so exciting. You come into work knowing that there are a number of challenges in rare disease drug development to overcome, especially regarding IRDs. But yet you look beside yourself and see your team nevertheless dedicated to supporting one another to overcome these obstacles one by one. It's important in a company at our stage to be courageous and creative. As you tackle the problems, you do your best to stay focus on the overall main goal and the end game, which is getting a medicine to patients as efficiently as possible. And so, the first goal, of course, was to build a team with world-class talent. With the founding FFB team that established Opus, we knew we were already starting on the right path as the FFB leadership team has decades of combined experiments in drug development already, including company creation.

We had experts setting us up for success. From that foundation, we were able to recruit promising scientists and clinicians and other key team members to really build that broad base of expertise that you need. As soon as you recruit that talent, then you need to find and develop world-class science into medicines. Fortunately, again, FFB supported this research for decades and have developed the careers of so many fantastic scientists who can then feed the results of their research into Opus, so we can help them turn their concept into a medicine for patients. That's what we did with Jean Bennett and Eric Pierce, our founders. Really for Opus to be a vehicle for clinical translation of these approaches for LCA. They've dedicated their careers to establishing the animal models we've needed to study and elucidate these IRDs, which were once really poorly understood and really shedding light onto what clinically relevant treatment approaches are likely to work.

The last challenge has always been fundraising. It's always important in a company of our stage to fuel that engine of drug discovery and drug development, which is through clinical trials and the FDA regulatory process. RD Fund has really played a strong leadership role in providing us with the needed funding to get started with our first clinical program this year that is LCA5, while also helping us propel the other two programs, RDH12 and NMNAT1 through the regulatory review and approval process. In summary, it's been a really exciting and challenging time to be at Opus, but I absolutely love it.

Ben Shaberman:

Well, again, really well put. For our listeners, you mentioned the RD Fund, I wanted to explain that's a special fund that was created by the foundation to raise bigger dollars to move treatments into clinical trials. It's called a venture philanthropy fund. Unlike a venture capital fund, where returns on investments are returned to the investors with the RD Fund as a venture philanthropy fund, all the returns are put back into research. That's very exciting. When you have some success, you're actually boosting your ability to fund more research. One thing that I know I don't appreciate it enough because it's an important part of getting a therapy into a clinical trial is the manufacturing side. We always talk about the research, whether the treatment works or not in animal models and getting the clinical trial off the ground. But the especially gene therapies are a pretty challenging technology to manufacture. Opus recently announced a partnership with a manufacturer called Resilience. Can you tell us more about why that partnership is so important and what Resilience will do for Opus?

Ash Jayagopal:

Yeah. Our strategic partnership with Resilience is really critical for our goal and our commitment toward the efficient development of gene therapies for these unaddressed IRDs. Achieving our goal requires a very specific manufacturing approach that enables the right size, small scale, yet high quality batches of AAV gene therapies tailored to our patient population, which is often numbering in the hundreds to a few thousands. As opposed to more prevalent diseases toward, which manufacturing in the pharmaceutical industry is geared towards. Manufacturing usually is tailored towards large production volumes for hundreds of thousands of patients or more, not the case with IRDs. And so, that requires actually special expertise and dedication. And so, finding the right partner in Resilience, ones that really understands our efficient, unique, small scale approach and can streamline this work was the right call for Opus.

Because the idea about Opus is not about one big blockbuster drug program, it's about building an engine to solve as many IRDs as possible by leveraging scale and consistent manufacturing processes to the extent possible. And so, manufacturing is the key to our success, and the concept of manufacturing scale is not traditional given what you think in terms of volume of drug production. But rather, we're focusing on developing the capabilities and managing the cadence of our clinical timelines to produce therapeutics most efficiently year after year, until we can treat all the IRDs that we've set out to treat.

Ben Shaberman:

Right. You can have a great therapy that works really well in the lab and does what you hope it does, but if you don't manufacture it well, then you're not going to succeed. Manufacturing is huge and it's exciting to have this partnership established and announced. To close off our discussion, I want to get back to you a little bit, Ash, because when I was looking up your bio and where you came from, you really started off, if I understand correctly, in academia and then you moved into the commercial sector and here you are in our unique company, Opus. When you started off out of school, what did you envision for yourself? Did you always know that you wanted to move into a broader role beyond, let's say, bench science?

Ash Jayagopal:

Early in my academic career, starting at the Vanderbilt Eye Institute, where I worked on retinal drug discovery research. My goal was always to translate concepts in the lab to solutions for patients. And so, the goal was always what we called translational research, and of course, with the goal of making an impact on patient lives. Much of the work we generated was published or patented and received funding to develop these programs, which I'm very grateful for. But in the process, I didn't really fully

understand how to take a concept, build financing, structure around it and pitch it to investors and create a product or company. I was seeing the difficulties in academia of establishing a vehicle for turning laboratory concepts to clinical realities.

And so, I wanted to develop a skill set beyond science in order to have a seat at the table to translate these concepts to the clinic. It was evident that I needed to develop business acumen along with scientific acumen to have a key role in translating academic research to medicines. That's where the management training can really help scientists, really. Help them speak in a business development sense alongside being a scientific champion of your work. That's where really, when you have more power and capabilities to bring a concept full circle and make a difference in the lives of patients. Opus is a great place to apply what I've learned and what I've been trained to do.

Ben Shaberman:

Right, exactly. It's almost poetic that what you set out to do early in your career really fits well with your role at Opus. Again, very glad you were here. Ash, this has been very enlightening. It's been a great conversation. Again, we're delighted to have you at Opus and pleased that you took a little time out of your busy day to tell us about what you're doing. Again, thanks for joining us.

Ash Jayagopal:

It was a pleasure, Ben. Thanks for having me.

Ben Shaberman:

To all our listeners, thank you as always for joining our podcast. We look forward to having you for our next episode. Take care everyone.

Speaker 1:

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