

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 the Eye on the Cure podcast. I'm your host, Ben Shaberman, with the Foundation Fighting Blindness. I'm very excited to have as my guest for this episode Dr. Aaron Osborne. He's the Chief Medical Officer and the Chief Development Officer at Nanoscope, which is a biotech company with emerging optogenetic therapies. Optogenetics is a promising and exciting therapeutic approach for restoring vision to people with advanced vision loss from inherited retinal diseases. Aaron and I will be talking about some encouraging results from clinical trials for their optogenetics approach. That'll happen later in the interview. Aaron, welcome to Eye on the Cure.

Dr. Aaron Osborne:

Well, thank you, Ben. Thank you so much for the invitation to be part of the podcast, and thank you for all the work you and the FFB are doing to advance therapies that can help improve vision for people with severe vision impairment.

Ben Shaberman:

Well, delighted to have you and thank you for all that Nanoscope is doing. I'm going to give a little more background, Aaron, before we start the Q&A. Aaron began his career as an ophthalmologist, having trained at Queen's Medical Center in Nottingham in the UK, and he earned his medical degree at University College London. He has extensive experience in the biopharmaceutical space, having worked in clinical development and medical affairs in companies such as Alcon, Bayer, and Novartis. Notably, he worked as a development leader for the recently approved treatment Vabysmo for wet AMD and diabetic macular edema.

Aaron, you have some impressive experience with your roles in some large biotech companies. What drew you to Nanoscope?

Dr. Aaron Osborne:

I was really fortunate, Ben. Once I joined the industry, I joined with the advent of some very exciting new therapies in the ophthalmology space, particularly the anti-VEGF drugs. That's really where I spent a lot of my career, was working on the development and approvals in multiple indications for those drugs. Some of those drugs include Lucentis, Eylea, and most recently Vabysmo. What we saw really with those drugs is transformative improvements in vision. They were able to restore vision in patients that had lost vision due to wet AMD basically by drying up the exudative process. Wet AMD, whilst it represents only about 20% of the total macular degeneration population, it represents about 80% of the AMD associated blindness. With really the advent of these therapies, we've been able to dramatically reduce the amount of people that go blind due to wet AMD really around the world.

So I think it was a really exciting start to my career, and I've really been looking for new therapies that can potentially lead to similar or even better outcomes in other diseases. That was really a big part of why I joined Nanoscope Therapeutics. There's treatments now for wet age related macular degeneration, and there are even treatments that can slow down the progression of dry age related macular degeneration, or geographic atrophy.

The leading cause of blindness in working age people at this point is actually inherited retinal diseases, or so suggests research coming from Australia and from other countries. As you know, that can be due to a huge amount of different genetic causes. But generally, they have a common final pathway, which is destruction of photoreceptors. There's lots of different therapeutic approaches that are aiming to slow down that destructive process, or even reverse it somewhat. But optogenetics is a really exciting approach because it is independent of the genetic mutation, and it can also work even when those photoreceptors are beyond rescue. That's because what it's doing is it's providing light sensitive properties to existing inner retinal cells that are already there.

The approach of optogenetics is incredibly exciting and it's something I've been excited about for a long period of time. But where Nanoscope Therapeutics was is that they already had preclinical proof of concept data and also had exciting clinical data. So me, as a clinician, I felt that this was a situation to which I could add value and to help accelerate the clinical program to generate more evidence that could potentially lead to a therapy that could get approved and benefit many, many patients.

Ben Shaberman:

Certainly. Certainly. We, as a community, are very excited about the potential that optogenetics holds for restoring vision to people who have such advanced vision loss. So you joined Nanoscope, you're the Chief Medical Officer and the Chief Development Officer. Can you tell us what you actually do, what your roles are?

Dr. Aaron Osborne:

Of course. Nanoscope Therapeutics was founded in 2017. The co-founders, Samar Mohanty and Sulagna Bhattacharya, had really been developing the MCO-010 program, really in stealth for a while before that. It's a small team. Really, their expertise, particularly Samar's, is in biomedical engineering and light as well as in gene therapy. So I joined the team. It's a small team, we're into the clinic, and I'm the first ophthalmologist that has joined the team full-time. Really, my role as both Chief Medical Officer and Chief Development Officer is to guide the clinical development programs, and really maximize those programs to ensure we've got the right strategies, right trial design, and that we've got the people in place to be able to execute those trials and then to report the data. All of that goes into regulatory interactions and advancing the therapy forward to the next stage.

What's so exciting about this is that MCO-010 program is by far the most clinically advanced optogenetic therapy that there is. We recently have shared Phase 2B data from a randomized controlled trial, I believe the first randomized controlled trial in optogenetic therapy, and we already have Phase 1/2 data that supported that. So we have two trials that have reported, and also a third trial in Stargardt disease where we have preliminary data as well. So despite Nanoscope being a small company, there has been great progression on the clinical side to be generating clinical evidence in these patients with advanced RP and Stargardt disease.

Ben Shaberman:

Right. It's very encouraging to hear results from these trials and the vision restoration that's occurring. Before we talk about the trials, tell us exactly how MCO-010 works. What's the approach?

Dr. Aaron Osborne:

MCO-010 is a intravitreal injection, so differently to some gene therapies that require subretinal administration and the associated procedure. This is a gene therapy that's administered as a single eye injection that can be administered in the office. The reason for that is that the gene therapy is

transducing cells on the inner retina and really aiming specifically for bipolar cells, which are the next neuron up from photoreceptors, and can preserve the most potential vision function of any retinal cell because they're the closest to photoreceptors.

So we have a gene therapy that's administered intravitreally. It has a cell specific promoter enhancer that guides it towards these bipolar cells. Once it's in those bipolar cells, it expresses a transgene called the multi-characteristic opsin. As the name suggests, this is a somewhat unusual opsin in that rather than just having one light sensitive component, this highly engineered protein contains multiple light sensitive components, which enable it to be sensitive across the entire visual bandwidth of light whilst also preserving fast response time, which is really important in order to minimize any blur, and also to have high light sensitivity as well so it can function in ambient light. What this means is that in order to work, this approach does not require any external device to be worn by the patient, and it means that it can function really in day-to-day light conditions and to provide meaningful benefits in day-to-day life for these patients.

Ben Shaberman:

Right, right. That's very exciting. The question I have is, the patients you're enrolling, they have pretty advanced vision loss, if I understand correctly. What kind of vision, if any, do they have remaining before they get the treatment in the clinical trial?

Dr. Aaron Osborne:

That's a great question. We have similar eligibility requirements and similar patients in both the Phase 1/2 trial as well as in the Phase 2B trial. We have a total of 38 patients that have been enrolled into one of those two trials. With regards to visual acuity, we do not specify a lower limit. So hypothetically, we could have enrolled patients that had no light perception even, but all of our patients did have light perception. They range basically from light perception at the poorest end of vision to around the counting fingers range at the better end.

We use a special visual acuity chart, which is designed for poorer vision, called the Freiburg Computerized Assessment of Visual Acuity, and the best vision that they're allowed in order to enter the study corresponds with logMAR 1.9. This is around counting fingers vision. If you were to test it at a meter, at best, these patients can count fingers. At worst, they really just have perception of light. It's an important question because it's noticeably poorer. For example, patients who were enrolled in the Luxturna clinical trial for gene replacement therapy, these patients have extremely poor vision in our trials, and that's due to advanced retinitis pigmentosa. They're generally very highly reliant on caregivers in order to be able to even guide them into the clinic.

Ben Shaberman:

Tell us about the results from your two clinical trials for RP. What did you observe in patients who received the therapy?

Dr. Aaron Osborne:

Well, what I mentioned is that the trials were very similar in terms of the patients, in terms of their vision at baseline. The first trial was performed in India, the second trial was at multiple centers in the US and included a placebo arm. But we have pretty similar reports and actually quite very comparable and consistent data between the two trials. Really, it was the patient experiences and videos of that patient experience that really excited me the most about the trial in India. What we heard from patients and their caregivers was that many of these patients, their lives really had been transformed since

receiving the treatment. For example, you had patients who, rather than be guided into the clinic, they were able to independently navigate the stairs into the clinic room and sit down, whereas that was something that they hadn't done before.

Again, in the India study, we had reports of a patient being able to prepare vegetables, for example, in a way that they hadn't done for many, many years. Able to chop carrots and other items in a way that hadn't been feasible to them in the recent past. Another one had gone back to working in a shop, and able to see and identify individual items of confectionery. And another one improving so much on the site chart that was able to read not just newspaper headlines, but also some of the text.

In the US study, we've seen multiple similar experiences as well with particularly the RP patients, who have very poor vision at baseline, improving on their navigational vision, some reporting seeing faces again of relatives or other people, and others reporting improved vision and greater sensitivity to different light conditions.

Recently, we put up on the Nanoscope website a video from the open label STARLIGHT trial of a patient with Stargardt disease, predominantly macular degeneration. This patient had much better vision at baseline, but she has improved in terms of her central vision and ability to do a number of tasks, for example, operating a phone or operating a calculator. I think it's dependent somewhat on the vision that the patient comes in at. This also goes to the number of different tests that we have to detect these changes in vision.

These are the types of changes that we've seen in both the India study and in the US study. The results are actually very similar between those two studies when we look at the outcome measures. Besides those patient reported measures, we use two key tests, one of which is a vision guided mobility test, and another one is looking at visual acuity with the Freiburg chart. In the Phase 1/2 trial, we saw that the majority of patients, nine of 11 patients, either improved by two light levels on the navigation task or by a substantial amount of 0.3 logMAR. That's sort of a halving of the visual angle or doubling of your visual acuity on the sight chart.

We see similar numbers showing improvements in the randomized control trial. I think what's in that trial as well, which makes the results more compelling, is obviously there's a sham arm, so we have a comparison there. If you look at the number of patients who experience an improvement on either visual acuity or on vision guided mobility, all of the patients improved on one of those three measures receiving MCO-010, whereas around half did on shams. So we're seeing consistent improvements that are similar to the Phase 1/2, but also separated from what we see with the sham treated patients. That's important. There's a lot of variability in performance in patients with these severe vision impairment due to inherited retinal diseases. And to see that there's still a difference, despite a relatively small study, is hugely encouraging. I think the consistency between the two studies is very exciting as well.

I think the final thing just to put into this brief recap is the safety profile has been reassuring in both the Phase 1/2 as well as in the restore Phase 2B. We've seen no serious adverse events. Again, it's delivered as a simple intravitreal injection. Some patients do experience some post-injection inflammation, but that has all been managed with eye drops. The safety profile seems very, very reassuring as well. So extremely exciting results for MCO-010 in both of those trials.

Ben Shaberman:

That's great. Very encouraging. Very encouraging results. You're in the process of completing these earlier stage trials, and I presume the hope is to move into later stage trials. If that's the case, what do you think you can do to restore potentially even more vision in patients? What are the next steps in advancing MCO-010?

Dr. Aaron Osborne:

At this stage, Ben, we've now dosed 37 patients in the two RP trials, as well as another six patients in the Stargardt trial, which I mentioned there. We actually have a fairly substantial amount of evidence which is consistent across the trials and with that favorable safety profile. So before considering further trials, which may well be needed to take this through to registration, we plan to sit with the regulatory authorities and discuss what could be the most expeditious route to towards getting this to patients. Retinitis pigmentosa is a serious disease. These patients have no treatments available for them. There are no treatments that are coming forward for patients that have such severe site loss that can restore vision probably other than other optogenetic approaches, which are potentially several years behind the Nanoscope approach. Given the potentially transformative benefits that a number of these patients are getting and the consistent data, we want to discuss as to how we can make this available as soon as possible for patients.

Ben Shaberman:

Got it. Well, we're excited about these initial encouraging results. Best wishes moving forward. We hope we can get this out to patients more broadly. That would be great. Thanks again for taking time out of your day to tell us about what's happening at Nanoscope and the encouraging results of your optogenetics trials. We look forward to hearing more about advancing this treatment further to patients and families. It's been great to have you on the podcast.

Dr. Aaron Osborne:

Absolutely, Ben. Great to be here. Excited to be able to share these updates on the Nanoscope program and look forward to sharing more in the future. Thanks again.

Ben Shaberman:

Thank you, Aaron. And thanks to our listeners for tuning into another episode of Eye on the Cure. We look forward to having you back for the next episode.

Speaker 1:

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