GUY EAKIN: Hello, everyone, and welcome to our monthly BrightFocus Chat, presented by the BrightFocus Foundation. My name is Guy Eakin; I’m the Vice President of Scientific Affairs at BrightFocus.

Today we are delighted to be able to talk with Dr. Josh Dunaief from the University of Pennsylvania’s Perelman School of Medicine. Josh specializes in the study of age-related macular degeneration.

He is also a BrightFocus Foundation grantee and is a volunteer for the organization. He writes our monthly Insights articles, which address questions that people with macular degeneration have about their disease. Copies of those can be found on our website or by calling into the Foundation. I will give the number for the Foundation a number of times over the course of the call. Every month we have a different topic for Chats, and today we will be discussing the latest in research discoveries.

If you would like to submit a question at any time during today’s call, please press *3 to submit your question to an operator. If for some reason you are disconnected from the call, the number to call back is 877-229-8493. They will ask you for an ID code, which is 112435. So that’s 877-229-8493, followed by the 112435 code.

Without further ado, I would like to get started. Josh, thank you for joining us today on the call. Could you give us a little statement about where you are and what you do in your clinical and research duties?
JOSHUA DUNAIEF: Thank you for inviting me, Guy. It is a pleasure to speak to all of you today. Over the years, I have been caring for patients with macular degeneration and also running a laboratory that is studying the disease to try to develop new treatments for it.

GUY EAKIN: The idea of research is something that is a funny concept, and it covers a lot of ground. We talk about discovery sciences or what might be called basic research. We also learn, in our work, about clinical trials, and we hear ultimately about the phase clinical trials of what go on to become drugs. I’m curious—I think in our education we learn about the path it takes for a bill to become a law, but I’m curious if you could give us an idea about how an idea or an observation in the laboratory goes on to become a drug or a cure for the disease.

JOSHUA DUNAIEF: Sure, Guy. Typically, we will first learn something new about macular degeneration [from a scientists] from his or her basic research. Then, they will test the idea in the laboratory—usually first in cells that are grown in plastic dishes. We can grow cells from the retina in plastic dishes and test how they behave, test them with drugs to see if they can be protected, and then, if they are protected in these cultured cells, we will typically test them in mice. The mice are very powerful, because they can be genetically engineered to simulate some features of macular degeneration. Then, if the drug still looks promising in mice, we can do some extensive safety testing, and then test the drug in human clinical trials.

The first phase of clinical trials, called Phase I, is really focused on safety— to make sure, in a very small number of patients, that this drug is not going to do any harm.

Then, if it passes that test, it will go onto Phase II, which is kind of a combination of both safety and a little bit of efficacy. It will ask in a larger group of people, “Will this drug potentially work?”

Finally, if the drug passes Phase II, it can go onto Phase III, which is primarily an efficacy test. This will be in a large number of patients—
typically hundreds, maybe even thousands of patients—to see if the drug is going to work and whether it is going to reverse the process of macular degeneration or prevent its progression.

**GUY EAKIN:** The phases you mentioned, these are typically related to our government—our FDA’s regulatory oversight. They are the ones that control Phase I, II, and III. There is a pipeline of drugs all along the timeline that you described.

There has been a lot of advancement in macular degeneration over the past couple of years, but if we take a step back and go back even a decade, the therapies that most people are currently using were not available yet. These are the anti-VEGF drugs that have saved so much vision.

There are a lot of other different technologies in the works. I was wondering if you could give us a summary of some of the recent discoveries that you believe would make a positive impact in the years to come and maybe give us a sense of what is the timeline in that statement of years to come.

**JOSHUA DUNAIEF:** Sure, Guy. The discovery of anti-VEGF drugs has really been tremendous for people with wet macular degeneration. VEGF, or Vascular Endothelial Growth Factor, is a protein that promotes blood vessel growth and leakage in wet macular degeneration. The drugs that were developed to inhibit VEGF—like Lucentis, Avastin, and Eylea—are antibodies that can bind to VEGF and prevent it, for a period of a month or two, from promoting the blood vessel growth and leakage.

The process of discovering that VEGF was important until the time of development of the treatment, took about 10 to 15 years. That is what I expect will be the time frame for new treatments. Now that’s not to say that we won’t see any new treatments for another 15 years, because there are several drugs that are in the pipeline now and a couple that are very close to coming out the end of the pipe.
One is called Lampalizumab. This is another antibody that can be injected into the eye, and in Phase II trial it looked quite promising for people with the other form of advanced macular degeneration, which is called geographic atrophy.

There are two forms of advanced macular degeneration. One is called wet macular degeneration and the other is called geographic atrophy. Either one can happen in people with the early form of macular degeneration. That is to say, people with the early form of macular degeneration or drusen could progress to either geographic atrophy or wet macular degeneration, or both. They could also remain stable and develop neither, which is what we hope will be the case for each person. But should the wet macular degeneration or geographic atrophy develop, we want to have drugs to offer to slow the progression or stop it. Lampalizumab is looking promising and it has just entered Phase III trials now.

Another drug that is fairly close to finishing Phase III trials is called Fovista. This is a drug that can be used for wet macular degeneration in combination with anti-VEGF drugs. I think within about a year or two, if the trials are successful, ophthalmologists may be able to offer an injection of this drug in combination with one of the anti-VEGF drugs. That may work even better than the anti-VEGF drugs alone.

**GUY EAKIN:** I want to pause just a second before I let you go on with some of the other drugs. You mentioned something that may be coming on the market in a time that many of the people on the call may have an interest in it. Some of these names are rather complicated. Fovista is F-O-V-I-S-T-A. I want to point out that we are going to have a transcript of this conversation, this Chat that we are having, that will be made available through our website and it will also be made available if you were to call into our organization. I will give the phone number. The telephone number is 1-800-437-2423 and if you missed it now I will say it again a little bit later.

Josh, I don’t want to interrupt you too much. So, you have been telling us about Fovista and the timeline of maybe one to two years for it to get
through these Phase III clinical trials. Are there other drugs that you are watching?

JOSHUA DUNAIEF: Well, the Lampalizumab and the Fovista are really the ones that are closest to coming through the pipeline. Others that are in earlier phases of development are other drugs that inhibit the same pathway as Lampalizumab but at different points in the pathway. This pathway is called a complement. Complement is an arm of the immune system that goes wrong in macular degeneration and causes inflammation, kind of like what happens in arthritis. Inhibiting the complement system in animal models is really quite effective, and in this Phase II study that I mentioned, it did slow the progression of geographic atrophy. I think we are going to be seeing other complement inhibitory drugs come on the market after Lampalizumab.

Also, Guy, I just wanted to mention that my patients and those of you who have received intraocular injections of anti-VEGF drugs would love it if the injections could be less frequent. I think that this is coming. There are extended release formulations that are being tested that I think could last maybe 3 months initially and up to 6 months after that. Then, maybe even up to a year.

Another thing that is being tested is gene therapy. Gene therapy has become extremely efficient in the eyes. My colleague at Penn, Dr. Jean Bennett, has worked out a way to express genes in the eye for years after a single injection. One study that she is running has shown that children who are born blind can see following a single injection of a particular gene therapy. Now, this disease is not macular degeneration, but it really serves as a paradigm to show that gene therapy can work. I think that gene therapy will be useful for macular degeneration in the future and it may require only a single injection to get a very long term effect for several years, or perhaps even a whole lifetime.

GUY EAKIN: That’s incredible. These are the brave new worlds of research that we think will be coming on line.
One of the things we have been hearing about for the last 20 years is stem cell therapy, and macular degeneration is a place where stem cell therapy is really being hotly tested. Do you have any opinions on what you are seeing out in the research world around stem cell therapy? Where is it relative to some of the other drugs and technologies you have been talking about?

JOSHUA DUNAIEF: Stem cell therapy is very exciting. It has a lot of potential. Stem cells are cells that have the potential to develop into any cell type. They are like cells that we have very early on in the process of embryonic development, but it is now possible to get stem cells from an adult where we can take a little piece of skin or blood cells, introduce a few genes that set the clock back, and turn them back into something like stem cells that can then be coaxed to turn into eye cells—into retinal cells. It can turn the clock back and then move it forward again and turn them into retinal cells.

The potential to take cells like these and put them into the retina of somebody with macular degeneration is really very exciting, but it is not really something that has been proven to be effective at this point. There are a number of challenges. One is getting these cells to take up residence in the correct position in the retina and then do all of the things that these cells are supposed to do, including integrating into the circuit that already exists in the retina. There are already millions of cells in the retina and they have already developed their relationships with each other. Trying to get stem cells to form the correct connections to those preexisting cells is really quite a challenge.

There is one particular cell type that is effected in macular degeneration, which is called the retinal pigment epithelial cell. Those may be the first that are going to be successful with the cell transplantation therapy approach. Those cells don’t need to make nerve connections to other cells. They just need to sit under the retina and support the retina. If those cells can be transplanted and coaxed to form an appropriately supportive layer, then they may well be useful for people with macular degeneration.
There have been some initial human clinical trials indicating in very small numbers of cases that this type of transplantation looks like it is safe, but there is really no significant evidence of efficacy yet. I think things are looking promising, but not as far along as gene therapy at this point because, as I mentioned, in gene therapy clinical trials there is really strong evidence of efficacy. The gene therapy gives sight to children who are born nearly blind.

**GUY EAKIN:** We have talked about new drugs and you have told us about gene therapy. We have talked about stem cells, which may come from an adult or they could even come from circulating blood—not even from your eye. One of the things we haven’t talked about, but is out there and captures the imagination like some of these other technologies, is the artificial retina or retinal prosthesis. I am curious, could you say a word about that? You seemed to indicate that gene therapy is further along. Where does this artificial retina stand in relationship to the other therapeutic methods that we have been talking about?

**JOSHUA DUNAIEF:** Sure. The retina consists of multiple layers of different cell types, and there is one layer in particular that gets effected by macular degeneration. These are called the photoreceptors, the cells that sense light. There are other cells that the photoreceptors would normally signal to. Those cell are not effected very much, if at all, in macular degeneration. Even after the photoreceptors are gone, these kind of secondary cells in the retina are still there.

The goal of a prosthesis or an electronic chip that sits on the surface of the retina is to bypass those dead photoreceptors and stimulate the secondary cells directly with an electrical impulse. This has been successful. This has been FDA approved and it worked for people who really can’t see anything at all. It allows them to see a little bit of light, about 60 or 100 pixels of spots that enable them to see maybe a letter at a time, which makes a huge difference to somebody who can’t see at all.

For a lot of people with macular degeneration, even the current state of resolution that they can get with these electronic chips, it would not
improve their vision beyond what they have if they got one of these chips. What I am hoping is that these chips will get bigger and they will have more and more pixels, and they will really get to a stage where they can improve the resolution beyond what somebody with very advanced macular degeneration already has. People with very advanced macular degeneration usually retain their side vision, their peripheral vision, they can see enough to get around carefully and maybe read with a closed circuit television or magnifiers. The kind of resolution that we are getting with these electronic chips currently does not improve vision beyond what these people already have.

**GUY EAKIN:** I’m sure that many of the callers have questions. I want to remind people that if you press *3, that will take you to one of our operators, who can take down your question and you can ask on the line. Before I move into the question and answer session, maybe while people are pressing *3 and submitting their questions, I want to ask one more question of Dr. Dunaief myself.

We have talked about research into new therapies but, AMD has a strong history of drugs that are being repurposed: and that is to say that they were approved for one condition---like cancer, in the case of Avastin---but are now being explored for AMD. As a physician, what does a drug manufacturer have to prove to you to make the medical community willing to begin off-label use? I would be curious if you have any repurposed or repositioned drugs that you are watching.

**JOSHUA DUNAIEF:** Yeah, off-label use categories are very interesting. What it allows us to do is take drugs that are FDA approved for one thing, perhaps for a treatment of a skin disease, and then use them for macular degeneration. These drugs have already gone through rigorous testing, so that lowers the barrier for testing them for macular degeneration. They have already been shown to be safe, at least when given in certain ways.

One example of such a situation, or a similar situation, is a nutraceutical that we would like to test soon in a small clinical trial, called glycolic acid. This an antioxidant that is already available over the counter, and we
would like to start a small clinical trial to see if this will arrest the rate of progression of the geographic atrophy form of advanced macular degeneration. The advantage of this type of small trial is that this compound has already been given to people for over 50 years and it is known that it is really quite safe. That is very different from a brand new compound that is developed and needs to be tested in multiple different ways to make sure that it’s not going to cause any harm. This type of thing has the potential to bring new treatments on the market faster than it would take for a brand new substance. These things could be quite effective.

GUY EAKIN: Wouldn’t that be amazing if the next treatment for macular degeneration has been under our noses for the last 50 years? I find that incredible.

I would like to move on to some of the other questions that are coming in. We have quite a few. Sue from Michigan asking very simply, “Is macular degeneration hereditary?” What do we know, what does research tell us about the genetics of macular degeneration?

JOSHUA DUNAIEF: Macular degeneration is both hereditary and environmental. We know that people who have affected family members have about a twofold increase in risk of developing macular degeneration themselves.

Some of the new genetic techniques have allowed us to determine that some of the genes responsible for this hereditary part of the disease are in this complement cascade. Again, complement is a part of the immune system, and it seems to become overactive in macular degeneration. People who inherit complement mutations that make their complement cascade more active are the ones who seem to be at a higher risk. It makes sense to target the complement cascade with drugs to try to prevent some of that inflammation that these mutations or DNA sequence changes can cause. There are some other genes that also confer some risk, but we don’t understand how those work as well as we do the complement genes, at this point.
Environmental factors are also very important. Smoking is a very strong risk factor. I emphasize to all of my patients that they should try their hardest to stop smoking if they currently smoke. I know it is very difficult to stop, but it is something that significantly increases the risk of losing vision. For those of you who have stopped, congratulations! I know it is extremely difficult.

Another environmental factor is diet. Again, something that is very difficult to change, but a number of studies have shown that people who eat more fruits and vegetables and fatty fish---like salmon, sardines, mackerel, or tuna---twice a week have a reduction in their risk of macular degeneration. Emphasizing a Mediterranean type diet with more fruits and vegetables, and some fish, and a little bit of nuts, and less red meat really seems to make a difference.

Other things that are possible contributors are sunlight---so, people with macular degeneration, we think should wear sunglasses when out in bright light, especially in the snow. A lot of us have a lot of snow exposure recently. On the day after the snowstorm, if it is really sunny, there is a lot of light that reflects off of that snow. It is good to wear sunglasses under those circumstances. When driving, there is a lot of sunlight reflecting off of the road, if you are still able to drive. It is a good idea to wear sunglasses when you are out on a bright sunny day.

GUY EAKIN: I would like to move into a question that is similar. We have two people calling in and asking about the health of their fellow eye or their good eye. They have macular degeneration in one eye and Ruth from California and Charlene from California are asking, “When you have one eye effected by macular degeneration what do we know from the research about how to protect the fellow eye?” You have talked about some of the general behavioral things but is there anything specific to someone who already has macular degeneration that they can do?

JOSHUA DUNAIEF: Yes. Several NIH-sponsored clinical trials over the past decade have taught us a lot about the risk to the second eye. In general, it is about a 10 percent risk per year of the second eye developing advanced macular degeneration and being at significant risk
for losing some vision. That 10 percent can be modified, depending on whether the patient has high blood pressure—high blood pressure also increases the risk; whether they have many drusen—drusen are little white spots that the ophthalmologist can see in the retina, so more drusen increases the risk; and whether they smoke. As I mentioned, smoking also increases the risk. For somebody that has advanced macular degeneration in one eye but not the other, there is a risk that the second eye will be effected.

On the bright side, there is a 90 percent chance in any given year, that the good eye will maintain its good vision. If it starts to develop wet macular degeneration, we do have these anti-VEGF drugs, like Lucentis, that can be injected into the eye to help protect the vision and hopefully minimize the amount of vision loss that occurs going forward. We don’t currently have any drugs for the geographic atrophy form of advanced macular degeneration, but, as I mentioned, Lampalizumab is very far along in clinical trials and it could be that within a few years that one will be available to slow the progression of geographic atrophy. As I mentioned also, in the clinical trial that I would like to do, hopefully glycolic acid would be shown to slow the progression of geographic atrophy.

GUY EAKIN: Marcel from Missouri is asking a question that we have many people come to our Foundation and ask. Marcel has had wet macular degeneration for 10 years and feels that he is losing is sight every day and asks, “How long before I go completely blind?” If you had Marcel in your clinic and he asked that question, what kind of response would you give to Marcel?

JOSHUA DUNAIEF: Marcel, one thing that I would tell you is that it is very unlikely that you could go completely blind from macular degeneration. Macular degeneration typically only affects the macula, which is the very central part of the retina, leaving the edges of the retina, the peripheral retina, intact. You would very likely be able to use your peripheral retina to still see, to get around, and to read very large letters that are very well lit, especially if you look off to the side. If you look off to your side and view things, as we say, centrically, then you can
have the object you are interest in fall on your peripheral retina and it will be visible to your peripheral retina.

**GUY EAKIN:** We have had a number of questions coming in that hint around the idea of how to get enrolled in clinical trials and what do we need to be concerned about. How do I find out about a clinical trial? Once I am in, how do I learn about what the dangers might be?

**JOSHUA DUNAIEF:** The best source of information is going to be your ophthalmologist, your retina specialist. They will have a list of clinical trials and know which ones you might be eligible to enroll in. Each clinical trial will have inclusion and exclusion criteria. They will need people to have a certain range of visual acuity, they will need them to have either wet or dry macular degeneration, there are many factors that would be difficult for you the patient to sort out on your own. Really, the first line is your ophthalmologist.

There is a site that the government has on the internet called ClinicalTrials.gov. You can search for macular degeneration, and you will see that there are hundreds of clinical trials listed on that site under macular degeneration. Specifically, you can look under wet macular degeneration or geographic atrophy, and it will tell you whether a particular study is enrolling patients. You can look at that, but again, I think it would be difficult for you to sort out whether you might be a candidate for any particular trial and what are the potential risks and benefits. These are things that your ophthalmologist can help you sort out.

If you do get referred to the person who is running the clinical trial, they will still screen you and see if you qualify and explain all of the potential risks and benefits of the trial in a process called “informed consent.” You would really need to think about whether you want to enroll in the trial, and someone will explain it to you in great detail. You would need to sign an informed consent form indicating that you understand all of the potential risks and benefits.
Guy Eakin: We have a question here from Ms. Ekta from California, who is saying that there are a number of products out there that you can find in various places—online and other places—that test for AMD risk based on the heredity of the patient. What is your view of these tests that will take a sample from your cheek or blood, maybe, and would compute your risk for macular degeneration?

Joshua Dunaiief: These tests do exist, and I think they will become useful once they have some impact on what you would do given a particular test result. I think they are really only useful if they would enable you to reduce your risk by modifying some behavior or taking some treatment. Currently, there is no strong evidence that these genetic tests would allow you to reduce your risk by taking a medication or by changing your behavior. What we talked about before as ways to reduce risk, eating fruits and vegetables, wearing sunglasses, stopping smoking, and maybe we didn’t mention yet, taking vitamins based on the Age Related Eye Disease Study (AREDS) II.

People who have a certain number of spots in their retina, or drusen, have a significantly reduced risk of developing advanced macular degeneration if they take these AREDS II vitamins every day. Knowing that you have this or that mutation isn’t currently going to influence whether you take the vitamins, or whether you eat that diet, or whether you receive injections of anti-VEGF medications if you have wet macular degeneration. Again, there is really nothing that you are going to change if you get those test results. However, I think that may change in the not-too-distant future. In the Lampalizumab trial for geographic atrophy, a certain subset of patients with a certain mutation in the complement cascade benefited more as compared to other patients.

Guy Eakin: I wanted to point out that we had a question saying that we are talking a lot about wet macular degeneration, but that some of these things apply to dry macular degeneration. Dennis from New York asked if we can explain what geographical atrophy is.

Joshua Dunaiief: Sure. These are kind of confusing terms. Early on in the disease, for people with early macular degenerations, all have dry
macular degeneration. They have these little white spots in the retina called drusen, which represent little deposits of---I like to think of it as garbage underneath the retina. Garbage that accumulated over the years and wasn’t efficiently taken out or removed.

From that stage, people can have early macular degeneration for their whole life and really never lose much vision, which is hopefully what would happen.

In some patients, they progress to advanced macular degeneration or late macular degeneration. With late macular degeneration, the retina can still remain dry, meaning that no new blood vessels have grown and there is no leakage from blood vessels. Instead, there is atrophy, which means that a certain number of the vision-sensitive cells, the photoreceptors, have died in a region of the macula. This region can expand over time, so that all of the photoreceptors in the center of the retina, the macula, die.

People who develop wet macular degeneration have new blood vessels grow into the retina and leak and bleed. This leakage makes the retina kind of soggy and that is why we call it wet.

**GUY EAKIN:** I want to point out that our next Chat the topic of it is “What You Need to Know about Dry Macular Degeneration,” and that will be on Wednesday, March 25, at 1:00 p.m. Eastern and 10:00 a.m. Pacific.

I think we probably have time for about one more question. There is a question from Jackie from New York, who is asking about the bravest of new worlds. She says that her father has macular degeneration and wants to know what we know about eye transplants. That has been in the news in the last year---people trying to get that started. That is a long ways off, but what can you tell us about a whole eye transplant, Dr. Dunaiief?

**JOSHUA DUNAIEF:** I wish we could transplant a whole eye currently, but we can’t do it, because the eye has a nerve attached to the back of it called the optic nerve that contains a million little axons---or little wires, if
you will. Those wires need to be connected to the brain properly for a patient to be able to see. In an embryo or a fetus, those connections can be made. In an adult, we don’t know how to entice those axons to make the appropriate connections.

We have some research going on around the country where people are trying to learn how to entice those axons to reconnect. Some clues come from goldfish, which can reconnect, and other clues come from axons that are grown in a dish and given fertilizer, if you will, or signals that tell them that they should grow and reconnect.

We don’t have eye transplantation as a therapeutic option on the table, I think, for a number of years. We can transplant part of the eye. We can take a cloudy cornea in the front of the eye and remove it and replace it with the cadaver donor cornea. We can remove a cloudy lens in a cataract surgery and replace that with a clear plastic lens, but we can’t, unfortunately, remove or replace a whole eye with a healthy new eye at this point.

GUY EAKIN: Well that sounds like a topic for another Chat. Unfortunately, we are running out of time.

At BrightFocus, we are committed to providing the information that you need most. If you have a second, take a moment and let us know how this Chat worked for you. If you found this topic very helpful, we would love to hear from you: please press 1 if you found it very helpful; press 2 if you found it somewhat helpful; and press 3 if you did not find this helpful at all.

While you are doing that, I want to take a moment and thank everyone for taking the time to speak with us today and thank everyone who joined the call. Thank you, Dr. Dunaief, for taking time out of your week to speak with us.

If you give us about a week, we will be posting a recording and a transcript of the call on our website. You can also listen to and download the past chats through iTunes and SoundCloud, or just call 1-800-437-
2423 to order a print transcript. We also have quite a few publications about macular degeneration and about driving that are available through the Foundation through that telephone number or through the website at www.BrightFocus.org.

Our next chat, as I said, will be on, “What You Need to Know about Dry Macular Degeneration.” That will be on Wednesday, March 25, at 1:00 p.m. Eastern.

We certainly encourage you to register and submit questions in advance, and we’ll be sending you a reminder email. In fact, you can actually register for the March chat right now and request those free materials from BrightFocus, like our “Macular Degeneration Essential Facts” brochure, by visiting our website or calling the number. That’s 1-800-437-2423.

Thank you again to everyone for joining us today, and again to Josh for providing your expertise. If you would like to leave a comment after the call, just stay on the line. Thanks and from all of us at BrightFocus.

Useful Resources and Key Terms

- BrightFocus Foundation website, www.brightfocus.org, or call us at 1-800-437-2423.

- U.S. government website listing clinical trials, clinicaltrials.gov.

Pharmaceuticals Discussed

- Lucentis: currently available, inhibits VEGF.

- Avastin: currently available, inhibits VEGF.

- Eylea: currently available, inhibits VEGF.
• Lampalizumab: in clinical trials, can be used to treat either wet macular degeneration or geographic atrophy.

• Fovista: in clinical trials, can be used to treat wet macular degeneration in combination with anti-VEGF drugs

Treatments Being Researched

• Gene therapy: researchers have found a way to use gene therapy to treat other eye conditions than macular degeneration, with enough success that therapies used in children born nearly blind have helped those children see.

• Stem cells/cell transplantation therapy: stem cells can be grown into retinal cells, and research is being conducted to find a way to transplant these retinal stem cells into the retina of someone with macular degeneration. At this point, research has not yet produced effective results.

• Glycolic acid: a nutraceutical available over the counter that the community would like to test in a small clinical trial for macular degeneration.

• Eye transplantation: it is not yet feasible to transplant an entire eye, because researchers have not yet discovered a way to connect the optic nerve’s axons between the transplanted eye and the brain.