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Issue: January 3, 2022

MCT (Macular Therapeutics)

Macular Therapeutics Inc is an early-stage company with multiple patents covering a unique and potentially safer method to treat the most common blinding disease in the elderly.

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"Patents issued on a new application for botulinum which may treat and retard blindness due to macular degeneration without using intra ocular needles." Gary Borodic, MD

Gary Borodic – Pubmed.gov Search
https://pubmed.ncbi.nlm.nih.gov/?term=borodic

USTPO - Patent Search (type Borodic)
https://patft.uspto.gov/netahtml/PTO/search-bool.html

Interview conducted by:
Lynn Fosse, Senior Editor, CEOCFO Magazine

CEOCFO: ***Dr. Borodic, what is the concept behind Macular Therapeutics, Inc?***
Dr. Borodic: Macular Therapeutics is a early stage company that has embodied critical intellectual property on discoveries made on intraocular effects of botulinum neuromodulators. Botulinum is the active ingredient in many pharmaceuticals, including BOTOX and several other commercially available Type A botulinum neuromodulators. The pivotal discovery fueling the company's efforts revolves around internal macular/retinal effect achieved when the injection is given on the outside of the eye and eyelids in locations often used to achieve the cosmetic effect. Beneficial effect occurred inside the eye that could be detected in patients who had forms of macular degeneration, inclusive of wet macular degeneration, as well as other forms of leaking maculopathy, such as occurs in diabetes and vein occlusions.

The discovery was detected with contemporary high resolution imaging technology known as ocular coherence tomography (OCT). Because both enhanced comfort and reduced risk in using injection from shots outside the eye to get a macular effect, the observation was remarkable. As the convention and available products such as Eylea (Regeneron), Avastin (Genentech), Lucentis (Genentech) and Beovu (Novartis) require injections directly into the eye, the applications are not only

uncomfortable, but run serious risks of retinal detachment, serious internal eye infections and inflammation, cataract, glaucoma and hemorrhage. Patient acceptance can be superior to conventional therapy.

CEOCFO: ***Why did you think it would work? What led you to try this?***
Dr. Borodic: That is a good question. The first observation was a coincidence when the drug was used for other conditions treated with botulinum. When botulinum was used for a patient with hemifacial spasm who suffered from wet age-related macular degeneration, improvement occurred in macular leaking (wet AMD). The benefit was reproduced in multiple patients and multiple injections. Although I could conceive of it happening, the use of the highly accurate OCT technology conventionally used was able to reveal a change in the leakage pattern in the macular. Vision did improve. This is actually human observation; this is not a laboratory experiment.

The exciting improvement can involve safety and comfort to the patients. The approach has the potential to be used with conventional therapy or independently. On independent patients, the method worked on its own. With conventional anti-VEGF therapy, which is the convention did not seem to interfere with expected outcomes. Application did not only involve forms of macular degeneration, but also diabetic macular edema. At first, I thought it could have been a coincidence, maybe a variation disease natural history, but the observation was reproducible experience in individual patients and multiple patients for many patients, the vision improved.

The other feature is the long duration of action of neuromodulators. A conventional anti VEGF therapy, when it is injected into the eye, only lasts for three to four days, and then has a wear off effect of over a month or so. Botulinum has a long duration of action (3-5 months). When a surgeon penetrates the eye with a needle in the eye for the conventional Anti VEGF therapy, loss of vision can occur from infection, hemorrhage, retinal detachment, cataract or glaucoma. It is also painful. The neuromodulator injection location is approximately in the same region as a cosmetic shot. It should be noted that this is not FDA approved and controlled studies need to be conducted to verify observations and utility for licensure. The unique property of botulinum seems to involves intracellular movement of the materials through long nerve cable axons which enter the back of the eye from remoted locations far from the eye and eye socket.

The comfort factor is a major advantage and the method may counteract blood flow compromise can occur with conventional therapy.

CEOCFO: ***I would imagine that patients are much happier or a lot less scared! Just the thought of being able to avoid a needle in the eye makes it worth considering!***
Dr. Borodic: Yes, patients like the idea of avoiding or potential mitigating the number of intra ocular injections needed. It is important also in the long-term management as number of injections into the eye with anti VEGF agents have been associated with possible worsening of

geographic atrophy which is often the irreversible end stage of macular degeneration.

It actually has another effect. Botulinum is used for migraine, neuralgias, facial pain syndromes and post op pain. When it is used with conventional intra-ocular therapy, it makes the intra ocular shots less painful, with an analgesic affect. That is also a very exciting and useful effect.

The potency may not be as great as using a frequent anti -VEGF injections in the eye, but still, any affect for this disease would be a contribution, because the disease is so prevalent and is the largest cause of irreversible blindness in the United States.

Older patients lose their ability to read, they lose their ability to see straight in front of them, and with time, this condition really depreciates the quality of life. The ease in which it is given is so convenient, the side effect profile is has been well studied with conventional dosing in this region for other conditions such as blepharospasm, cosmetics, and dystonia. It may be useful in preventing progression of disease, even in earlier stages.

One of the problems with conventional therapy with Eylea (Aflibercept) tend to constrict macular blood vessels. Over time, although it helps with the wet/leaking degeneration, it may aggravate the progression of the dry degeneration, which can irreversibly blind. Botulinum toxin have an opposite effect. It can work against the loss of blood flow into the macular, and we can actually see that in many of the cases we treat with the new OCT and OCT-A technology. Therefore, it is kind of exciting in that respect. Blood flow voids in capillaries almost always occur in macular degeneration, particularly directly in capillaries underneath the macular. If we can mitigate or stop the progression of those voids, we may be able to slow the disease down, so people can live their life longer with clear vision. This could be so helpful for the elderly population.

The patents are issued but controlled trials are needed. Multiple botulinum sources are available and being evaluated.

CEOCFO: ***What have you patented and where does the FDA come in?***

Dr. Borodic: This is an observation that was made in my clinics. We have actually done some work in the laboratory, as well, that corroborated early observations. However, this has to be put through controlled trials to be a commercial indication. I am highly aware of its side effects. I have many articles, publications on this and I have found that I have not hurt anybody with it over the years. There are some annoying side effects that can occur, but if you keep your doses in the conventional range as used in FDA studies for other indications, the safety factor is can be high. That is where we start. However, studies are needed under FDA and IRB approved protocols.

At this point, what we have to do is a controlled, double blind, placebo-controlled study, using patients at certain stages of macular disease, to assess the reproducibility of the affects, and the degree of affect. There is nothing in this technology that would even contraindicate using it

conventional anti VEGF therapying conjunction. The one thing about it that is very unique in botulinum is how it gets in the eye. I think, as sited in the patents, that the toxin picks up on the nerve, like it is known to do, and it travels inside the nerves which precisely targets undersurface delivery to the macula, and the blood vessels underneath the macular. It goes in the nerve and then it goes inside the eye, and it releases inside the eye. Therefore, you do not get any paralysis. That is really unique. There is no drug that we have ever known that works that way.

CEOCFO: ***Ultimately, when you engage with the FDA, does it matter that you do not know why it works, as long as you can show it does work well?***
Dr. Borodic: There are many reasons why it might work. Although mechanisms are helpful the safety profile and evidence of beneficial effect are most important. Botulinum toxin is an anti-inflammatory agent. It can block a number of inflammatory mediators, and in fact, botulinum toxin can block some of the mediators that release from mast cells, which are known to be involved as part of the pathogenesis. It could also up-regulate proteins that cause cells to stick together better. The loss of the cell adhesion is a problem in macular degeneration, particularly the pigment epithelial cells, that occur as early, and even later in the disease. The drug can interact with VEGF chemistry.

The drug has been known to stabilize blood vessels, and increase blood flow, so that may be a way it could work. It has been used on plastic surgical flaps to increase blood flow. It has been used in Raynaud's disease, which increases blood flow to the fingers, people with cold hands, and particularly people with scleroderma induced difficulty with blood flow in the fingertips. The drug has been shown to increase blood flow in a number of studies in those conditions. That is a potential mechanism. However, the actual mechanism does not really matter, as long as it works in reality.

Additional investment in macular degeneration treatment is needed to advance the trials with botulinum. Availability of product possible from several GMP producers.

CEOCFO: ***What are the next steps for Macular Therapeutics?***
Dr. Borodic: This is essentially a late-stage project, so it is going to be expensive to do the studies. We are looking for investment with appropriate funding to organize a clinical research group to do controlled trials under an IND and/ or internal review board review, to demonstrate efficacy. The purpose of the patents is to provide the incentive for work via a proprietary incentive. If a company puts the effort and money into this, that their proprietary position could be protected by patents.

CEOCFO: ***What is the feeling about macular degeneration among investors? Are investors looking at it? Is there some real push?***
Dr. Borodic: There is a lot of investment. Big companies such as Regeneron, Abbvie-Allergan, Genentech, and Novartis are all in the realm. It is a high need area, as it is the number one cause of irreversible blindness. The quality of life of elderly people are affected. Some of the largest selling biologics in the world are Eylea, which is a

major product for Regeneron. It is a very, very competitive field, and the value of these drugs are enormous. Multiple laboratories are producing GMP product for other purposes.

CEOCFO: ***How do you gain attention?***
Dr. Borodic: Speaking to professional associates. This is a project that goes beyond the usual, because of the need for studies. The studies are going to involve multiple clinical sites. It is going to involve a toxin source that would basically be very similar to what we are using, or at least very similar to what we are using on a day-to-day basis. It is going to be a lot of work to do that and do it well, but it is doable, and it can produce a very important finding in terms of the treatment of some of the most serious eye diseases. These are blinding diseases. Every week I see numerous patients with this problem, today, yesterday, and it is sad, because as one gets older, it is definitely related to age with macular degeneration, or diabetes. People come in and it is the one thing that people do not want to lose as they age in their lifetime; the ability to see well. Yes, it is an exciting thing.

Botulism has now been used for cosmetics, migraine, movement diseases of the face, there is a lot of safety data on this. Therefore, I think that this is not like producing something out of the lab. It has been used for a long time. The patents are written to really protect not only macular but basically much of interocular disease pathology associated with visual loss. Although case studies can be helpful standard of proof needs to be at a higher bar. This is going involve a major effort, involving FDA IND, multi-site studies and the patents. If we can get invest in this and prove utility it will be very valuable to give exclusivity to the person who took the risk of making the investment.

CEOCFO: ***Why should Macular Therapeutics, Inc standout with so many companies with so many new ideas, especially in health?***
Dr. Borodic: We can implement immediately. There are sources that manufacture botulinum only for this purpose and have the personnel for that. The conventional injections into the eye currently used, is a high contrast to a more comfortable easy injection, well accepted non ocular botulinum injection, used every day for other purposes. It would be exciting to use such a familiar drug, with little side and low side effect profile, to enhance the treatment of macular degeneration or slow its progression. The drug can be used with other methods currently used. That is a unique opportunity to serve a need that is there.

The current therapy requires many uncomfortable injections, with potential blinding side effects. Some people need 50 or 60 needles punctures over a number of years. This is a simple injection, placed just a little bit deeper than you would place when you had a cosmetic injection for your wrinkles, with a potential effect that could be monumental. Studies are needed reproduce a benefit against the controls.

In the laboratories we have seen improvement in blood flow. We have seen improvement in blood flow in the clinics as well, using OCTA technology. We have seen fluid go away as part of the wet macular

degeneration and diabetic retinopathy paradigm of disease, as well as several other cousin diseases. The patients accepted as being easy and comfortable treatment format.

What needs to be done is further careful controlled studies at multiple sites to produce the data that would convince the FDA to make this a licensed indication.

About CEOCFO Magazine:
CEOCFO Magazine, is an independent business news and investment publication that highlights important technology, products, services, medical, clean-tech and financial companies. Publishing since September 1999, CEOCFO brings interviews with CEOs and other top executives in their own words and thoughts to our worldwide readership. In a CEOCFO interview you will find salient insights into product discovery, development, go to market strategy, customer and partnership acquisition and retention.

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