

Improving the Delivery and Safety of Drugs, Vaccines and Biologics through Cochleate Technology

Healthcare
Biotech

Aquarius Biotechnologies Inc.
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J Carl Craft, MD
CEO

BIO: Carl is the New Chief Executive Officer of Aquarius Biotechnologies Inc. making drugs, biologics and vaccine orally bioavailable. Formerly Chief Medical Officer Aquarius he moved to the CEO position replacing Raphael Mannino. Prior to joining Aquarius he was a member of the Cempra Inc. Scientific Advisory Board. Cempra is developing solithromycin a new fluoroketolide now in Phase III for the treatment of moderate to-severe community-acquired bacterial pneumonia. Retired as Chief Scientific Officer from Medicines for Malaria Venture, Geneva Switzerland in 2007 after 5 years and

pushing the development of 3 new ACT's now available to treat malaria. Retired as Senior Head Anti-Infective Venture, Pharmaceutical Products Research and Development, Abbott Laboratories. He was responsible for clarithromycin and temafloxacin. Spent 8 year as a Professor of Pediatric Infectious Diseases at Tulane University prior to joining Abbott. He has a history of over 15 successful NDA filings from 1970 to present.

About

Aquarius Biotechnologies Inc.:

The mission of Aquarius Biotechnologies Inc. is to improve the delivery and safety of existing drugs, new drugs, vaccines, and biologics. Aquarius accomplishes this goal by reformulating drugs, vaccines, and biologics using a proprietary delivery method called "cochleate" technology.

Cochleates have been shown to improve existing drugs by providing 1) targeted delivery, thus reducing toxicity and 2) oral delivery of drugs now only available intravenously. Cochleates work by encapsulating molecules of drugs in a solid, crystalline structure, protecting them as they pass through the gastrointestinal (GI) tract where they are transported across the mucous membrane by the M cells of the gastrointestinal tract. The M cells are specialized cells which pick up large molecules and antigens from the GI tract. Once the cochleates have crossed the mucosal barrier they are picked up by macrophages. The macrophages in the intestinal wall migrate into the intestinal lymphatics where they are transported through the lymphatic system make their way to the blood stream. Once inside the

blood stream, the cochleae's inside macrophages - with the drug inside - migrate to the site of infection or to the target organ.

The cochleae's are stable in the presence of calcium but intracellular calcium concentration are very low and the cochleae's open and slowly release the drug. In this way, cochleae's are able to deliver the drug from the patient's gut to the target cell before releasing the drug. Cochleate formulations of multiple types of therapeutics have been created, including drugs, proteins, peptides, and oligonucleotides. Aquarius presently has 2 drugs in development cochleated Amphotericin B in Phase I and cochleated Amikacin in preclinical development.

Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine

CEOCFO: Dr. Craft, you have recently taken on the CEO role at Aquarius Biotechnologies. Why was this the right time?

Dr. Craft: It was necessary for the company to continue to make progress. The company is relatively new and I have only been with the company approximately a year. However, Raph Mannino, who was the CEO, is the son of the inventor, Raphael Mannino and he is just finishing his MBA at the University of Chicago and has lots of debt associated with school and needed to have a job where it paid. It was probably going to be a while before Aquarius Biotechnologies starts making enough money to pay Raph. Since I have retired three times and do not really need to be paid and I am

one of the investors in the company it seems like an obvious thing to do.

CEOCFO: What attracted you? What is the concept at Aquarius Biotechnologies?

Dr. Craft: A little over a year ago Aquarius contacted me, because they wanted a Phase II protocols for Visceral Leishmaniasis. I am on the scientific advisory board for DNDi and work with Visceral Leishmaniasis and neglected tropical diseases, I said, "Sure, not a problem." However, I realized that they were going to need more help than they had asked of me. It was such an important new way of delivering drugs and vaccines and other products that I did not want it to fall by the wayside. I thought this was too important to set on the sidelines. Therefore, I came out of retirement again and took up this project originally as the Chief Medical Officer.

CEOCFO: What have you figured out at Aquarius Biotechnologies Inc. that people were not able to do before?

Dr. Craft: Everyone who works at Aquarius Biotechnologies are PhDs or MBAs and they lacked anyone with clinical experience. I have a lot of experience in developing drugs. I was the head of the Anti-infective Venture at Abbott Laboratories and developed clarithromycin and temafloxacin. Having been the Chief Scientific Officer at Medicines for Malaria Venture (MMV), and during my stay at MMV we got three new anti malarial drugs approved; I have the clinical and regulatory experience that they did not have and was able to add that experience to the company.

CEOCFO: What is it that has been developed at Aquarius Biotechnologies Inc.?

Dr. Craft: The technology that has been developed has actually been around for a fair amount of time. It was licensed to BDI, Bio Delivery International. However, at the time that they were working with it then, the product cochleate formulation required a phospholipid that was sixty dollars a gram, which made it economically unfeasible for the products they were considering. It

showed very good promise for an oral influenza vaccine. However, all vaccines have to be dirt cheap, because they need to be able to be administered to a millions of people for the least amount of money, although, the fact that it does not require a cold chain makes this technology very useful. It was also being developed for an oral form of Amphotericin B. Ampherticin B is the most potent antifungal available but unfortunately it is also one of the most toxic antifungals available. However, in the development, which has already gotten into phase I in humans, it appears to be less toxic because of the way it is delivered to the infection site avoiding the blood stream, which is where the toxicity occurs. That is because Amphotericin B in the blood goes through the kidneys and it damages the kidneys, which is the main problem for many drugs.

CEOCFO: What were the main challenges in developing the

**"The cochleates are the future of medicine in the 21st century."
- J Carl Craft, MD**

technology?

Dr. Craft: The technology is actually pretty simple. Anyone, if you explain it to them and they have any science background says, "Oh, that is obvious once you done it." Companies have spent a lot of money trying to make lipid formulations for drugs which were effective but toxic or difficult to give intravenously. Amphotericin B was one of those drugs and AmBisome[®] was developed but very expensive and very difficult to make the formulation. Aquarius technology actually makes it simpler, cheaper and can be given intravenous or orally, but it does require a good deal of art of the chemistry, rather than the science, as with AmBisome[®] which is very difficult to make. Therefore, everyone who has tried to make generic AmBisome[®] or another liposome formulations of other drugs, have never quite matched the AmBisome[®] in its ability to be safer. However, our technology allows you to give it orally and for it to be safer. It should be useful in several areas; one for Visceral Leishmaniasis, which is third

world diseases, but also for fungal infections in immunocompromised hosts, like children with leukemia or people who are immunosuppressed for other reasons. Patients with AIDS develop serious fungal infections. Therefore, in that respect it would be a great advance for delivering these drugs as well as other drugs.

CEOCFO: There are so many potential candidates for the platform technology; how have you decided what to work on first and how you will go through the pipeline?

Dr. Craft: Since the cochleate Amphotericin B is so far advanced that is where we are pushing the most to get a proof of concept. However, we are also working with companies that have new drugs that have problems of being absorbed. Therefore, we are formulating new drugs for other companies new products and trying to use the platform as broadly as possible. That makes for some difficulties, but if you have partners that are willing to support the development of formulations for them, it makes that easier. However, as far as developing drugs ourselves, I think

that although we do have two potentials; the cochleate Amphotericin B and the cochleate Amikacin, that the best use of the product line was to partner with other drug companies to improve their products. Also, in the future vaccines given this way would not require the injections or a cold chain, which limits the availability of many vaccines. Therefore, I think the future for the platform is really in the delivery of vaccines. No one likes to have a child given a shot every few months to prevent childhood disease. However, if it can all be given by oral forms like the old oral polio vaccine, which is not used in the US anymore, it would make a the hesitation of parent over children immunized go away.

CEOCFO: Is the medical and the investment community interested? Where does your concept fit in?

Dr. Craft: Probably one of our biggest problems is that if you talk to physicians they say, "This would be great! We should have drugs or

vaccines in your cochleate formulation.” The problem is getting investors. Investors like to back a drug, so getting them to back in a cochleate is more likely than having them support a platform which will do many other things. That is because it is harder to tell them where the end point is. You have investors and they invest in a drug and you get it through Phase III and you get it on the market. At that point the investors can recoup their investment. A platform is not at easy. Therefore, I think that we will need to get investors to invest in each individual product like cochleate Amphotericin B. There are some companies that are talking to us about investing in the platform, so it will probably be easier to convince them than it is to convince investors who want to see the a quick endpoint.

CEOCFO: Are you funded right now to get through the next steps or are you somewhat on hold?

Dr. Craft: We are partially funded at the present burn rate for 12 months. We have enough money to keep everything going and pay for the labs and pay for the formulation work that we are doing. To get to the next steps, the Phase II clinical studies for cochleate Amphotericin B; those clinical studies are expensive. Therefore, we are looking to get investor funding. Instead of having one million dollars on hand we need to have five to ten million dollars on hand before starting those studies. Much of it would be taken care of by funding from organizations like DNDi for Visceral Leishmaniasis, and Cutaneous Leishmaniasis from the US Army and the Gates Foundation and NIH for the antifungals. Therefore, much of the work can start with not having to have a large amount of money that would normally be needed, because of the potential investment from these groups.

CEOCFO: Why is this the time to pay attention to Aquarius Biotechnologies Inc?

Dr. Craft: It is because it is the future. It is hard to make new drugs. However, there are many drugs that are not being used, simply because of the way they have to be given or the toxicity. This technology can reduce some of these concerns make old drugs new again. For vaccines, the Gates Foundation is very interested in breaking the cold chain problem for vaccines. This technology may be one way for them to break the problem of the high cost having a refrigerator in every village in Africa where you need to give vaccines.



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