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Q&A with Dr. Robert Ward, President and CEO of ExThera Medical Corporation developing a revolutionary Broad-Spectrum 'Sorbent Hemoperfusion Device' capable of Removing Bacteria, Viruses, Toxins and Cytokines from the Blood Stream reducing Infections and Morbidity

Dr. Robert Ward
President & Chief Executive Officer

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Interview conducted by:
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CEOCFO Magazine

CEOCFO: ***Dr. Ward, what is the vision behind ExThera Medical Corporation?***
Dr. Ward: To satisfy an unmet clinical need for the removal of drug-resistant pathogens from blood, thereby reducing morbidity and mortality in patients who contract bloodstream infections. Our technology can remove bacteria, viruses and toxins from blood in a therapy that is much like dialysis. Blood flows out of the body, through a novel filter we call Seraph®. Disease-causing microbes and toxins are left behind on the filter's surface. Seraph works as well on drug-resistant pathogens as it does against drug-susceptible pathogens.

CEOCFO: ***When would it be used? At the first sign of infection? Might it be done in a preventative manner?***
Dr. Ward: Early effective treatment of bloodstream infections is needed to avoid their progression to a dysregulated immune response that leads to sepsis and organ failure. Seraph is very broad-spectrum in its action. It therefore has a high probability of being effective when used at the first sign of a bloodstream infection, even before the pathogen is identified. Because the list of pathogens Seraph can remove from blood is very long, the chance of *successful* empirical or prophylactic use of Seraph, is higher than with any single anti-infective drug.

CEOCFO: ***What is Seraph and how does it work?***
Dr. Ward: Seraph uses a 'biomimetic absorption media' that mimics the binding sites that pathogens and toxins use to when they invade the body. These sites are chemically bonded to the surface of small polymer beads within the Seraph filter. We start with the anticoagulant drug heparin because of its similarity to heparan sulfate, which is present on the surface of cells in the body, and which is a common target for bacteria, viruses and their toxins. Seraph is stealthy in the sense that it tricks the pathogen into binding inside the filter instead of on the endothelial surface of blood vessels in the body.

CEOCFO: ***Where are you today with Seraph?***
Dr. Ward: We are about ¾ of the way through a CE-Mark EU clinical trial using Seraph concurrent with dialysis in the treatment of dialysis patients with bloodstream infections. The filter goes 'in series' upstream of the dialyzer, and we run for four hours, which is the typical length of a hemodialysis treatment. We have recently added two additional clinical trial centers in northern Germany which are interested in Seraph therapy for patients with bloodstream infections.

CEOCFO: ***What have you learned that surprised you so far from the concept to where you are right now?***
Dr. Ward: Definitely the ease of use and how well it is tolerated by patients. We know from our work with other heparinized devices that our heparin surface is the "gold standard" for blood-contacting surfaces. Together with our device design, it appears that the patients can't tell they are being treated with Seraph, in terms of any sensible differences relative to dialysis alone. Another very preliminary result appears to be possible improvement in some vital signs relative to dialysis alone, which can negatively affect patients during treatment. I would say too that we were happy that our initial design was so compatible with existing dialysis machines, that Seraph can quickly be added to the circuit, primed and

deaired the way a dialysis circuit is normally prime without Seraph. Then you are off and running. We have not had a single device-related adverse event in the trial so far, so that has been very encouraging, too.

CEOCFO: ***What has been the reception from the medical community or people who have looked at what you are doing? How has it compared to what other new treatments or potential treatments are available?***
Dr. Ward: In our independent market research surveys, it is reported that even on a blinded basis, the product is of great interest not only to clinicians, but also hospital administrators and payers**.** Seraph is the only broad-spectrum 'sorbent hemoperfusion device' capable of removing bacteria, viruses, toxins and even cytokines. It is very unique in that sense. I doubt there will be a comparable device available for many years, based on insight we gained as part of a DOD program we were involved in.

CEOCFO: ***Did you know in the beginning? Did you have a real strong gut feeling it would work and why?***
Dr. Ward: Yes! We have been developing and manufacturing medical devices since 1971, including the biomaterials used in critical blood-contacting devices and implanted devices. This often required the chemical modification of polymer surfaces to achieve specific biological interactions. Seraph is a very exciting application of that experience to create a new therapy. In the future we hope to use Seraph to help septic patients recover. We think Seraph has a very good chance of being useful in that indication, after we demonstrate effectiveness in larger clinical trials.

"We definitely have an 'out-of-the-box' approach to bacteremia and viremia… Sepsis, which can result when the body over responds to an infection with a runaway immune response, kills about half of the people who die in hospital. The idea that we could intervene early in the bloodstream infection to *prevent* the progression to sepsis could save many, many lives every year at a reasonable cost, with what I think will be proven to be a very safe therapy. In addition, as a *device* Seraph does not add to the growing problem of drug-resistant infections."- Dr. Robert Ward

CEOCFO: ***Would you tell us about the physical components? Are there individual pieces of equipment for different patients? What physically is needed or will be the end product that people will use?***
Dr. Ward: Our device has an optically transparent housing, two and a half inches in diameter and about eight inches long. It is filled with small polymer (plastic) beads about the size of coarse table salt. There are thick retaining plates on each end of the cartridge, and tubing fittings that are the same type used in dialysis circuits. The clinician takes the sterile Seraph filter out of the package and connects it with simple luer lock connections, and then de-airs it as you would normally to start up a dialysis session.

CEOCFO: ***Is there a shelf life?***
Dr. Ward: The shelf life is very long. The immobilized heparin that is responsible for binding the pathogens and toxins and has already been tested for a three-year shelf life. When a similar surface has been used in implantable medical devices like vascular grafts, the surface has been still active years after implantation. Seraph is stored dry, it does not have to be packed wet, and it does not have to be refrigerated. It is pretty rugged stuff.

CEOCFO: ***Where does cost come into play?***
Dr. Ward: It is comparable to other anti-infective treatments in initial cost, but we expect to show economic benefit by reducing length of hospital stay, and fewer ICU days and ventilator days, and by avoiding the progression of the bacteremia to sepsis and organ failure. Therefore, Seraph can have a substantial economic *and* patient benefit which we hope to show conclusively in our clinical trials. We expect Seraph will be very cost effective. Heparin is a USP-grade pharmaceutical that is widely available, we are happy to say. If we were doing this with antibodies, for instance, or other biotech approaches, it could be prohibitively expensive.

CEOCFO: ***Would you tell us about funding? Where are you today?***
Dr. Ward: We are in funding mode now, kicking off our C round of funding. We are looking for $20 to $25 million to bring us to break even, we hope. We have a large plant in Martinez, California and we have built a pilot capability for absorption media, and a production-scale clean room for device assembly. We've ordered all the process equipment we need for manufacturing scale up. We have recently been granted Expedited Access Pathway designation by FDA and we are working with the FDA on our clinical protocol right now. We hope to start a US clinical trial later this year. Sometime in 2019 we expect to be on the market in Europe under the CE Mark and, depending upon how the US trial goes, and how big the trial has to be for FDA clearance, maybe another year after that in the US, but this is just an estimate.

CEOCFO: ***How do you deal with some of the frustration and the time it takes to get things moving?***
Dr. Ward: It wakes me up in the middle of the night! Not because I don't think we're going to be successful. It is just pure frustration. We have done what I think many startups do, and that is write our inclusion and exclusion criteria for our clinical trials too tightly in an attempt to have a good clinical trial on the first try. I think that this slowed the initial recruitment of patients. However, every patient that we have treated has responded well, and the safety appears to be excellent so far. So, we are very happy with that outcome. Because the rate of patient enrollment was slow at first we added some additional clinical centers. This has resulted in an increase rate of enrollment over the past few months. We expect to complete the European trial around the middle of this 2018. However, the US regulatory clearance process has also started recently. We are very happy to get the EAP designation. FDA responds very quickly to submissions and supplements under EAP, which is very helpful.

CEOCFO: ***There are certainly so many new ideas to look at and consider. Why does ExThera Medical and Seraph stand out? Why should they stand out?***
Dr. Ward: We definitely have an 'out-of-the-box' approach to bacteremia and viremia. It's a therapy that's easy to get nephrologists excited about, because they treat chronic kidney disease, and the second leading cause of death in that patient population is bloodstream infection. Sepsis, which can result when the body over responds to an infection with a runaway immune response, kills about half of the people who die in hospital. The idea that we could intervene early in the bloodstream infection to *prevent* the progression to sepsis could save many, many lives every year at a reasonable cost, with what I think will be proven to be a very safe therapy. In addition, as a *device* Seraph does not add to the growing problem of drug-resistant infections. Empirical prescription of anti-infective drugs and other misuse and over use of anti-infective drugs is one of the reasons we have the problem we do with drug-resistant pathogens. There is no way that we can imagine that bacteria or viruses can evolve *not* to bind to our absorption media in our filter. That's because if they will not bind there then they will not bind and proliferate in the body! With the Seraph *device* we can deal with drug-resistant pathogens and not contribute to the problem with yet another antibiotic that works for a while until the bugs evolve and become resistant to it.

CEOCFO: ***So, you have got a real answer to the problem here!***
Dr. Ward: I think so! In recently-completed DARPA Dialysis-Like Therapeutics (DLT) program, we made it to the fourth and final phase of GLP testing. In that phase the agency tested Seraph against four different drug-resistant pathogens in a pre-clinical model. Seraph was able to remove them all during this testing. We are very happy with those results which we are confident will translate to human patients.