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USING BLOOD PURIFICATION TO SAVE SOLDIERS' LIVES

Trauma, burn, and smoke inhalation injuries are among the most common life-threatening injuries to the armed forces, as well as the general public. These injuries trigger a massive inflammatory response that affects the entire body and risks the development of dangerous complications, such as lung injury, kidney failure, other organ dysfunction, infection and death. Current therapies are predominantly focused on supportive care and not on preventing or treating these complications.

To address this need, the US Army Medical Research and Materiel Command has awarded Phase II Small Business Innovation Research (SBIR) funding to CytoSorbents Corporation of Monmouth Junction, New Jersey, to help fund using the company's CytoSorb blood purification platform technology to treat trauma, burn and smoke inhalation injuries in large animal models. CytoSorbents is a critical care focused therapeutic device company that utilizes blood purification to modulate the immune system and fight multi-organ failure in life-threatening illnesses. Company researchers base their purification technology on biocompatible, highly porous polymer beads that can actively remove toxic substances from blood and other bodily fluids by pore capture and surface adsorption.

The New Jersey company's flagship product is CytoSorb®, based on highly biocompatible porous polymer beads, roughly the size of a grain of salt, that act like tiny sponges to extract substances from blood and other bodily fluids based on pore capture and surface adsorption. It is protected by 32 issued US patents with multiple applications pending. The technology was originally developed to treat kidney failure patients and remove mid-molecular weight toxins from blood that standard high flux dialysis could not. These toxins, such as b2-microglobulin can accumulate in the body and cause major problems such as disability and death.

"However, through collaborations with John Kellum, at the University of Pittsburgh Medical Center, we have been focused on the use of

CytoSorb to prevent or treat organ failure in the intensive care unit (ICU)--one of the largest and most pressing unmet medical needs in modern medicine," said Phillip Chan, MD, PhD, chief executive officer of CytoSorbents Corp. CytoSorb is approved in the European Union as an extracorporeal cytokine filter that can be used in any situation where cytokines are elevated.

Cytokines are very potent small proteins that normally stimulate and regulate the immune system in low quantities. The immune system is at the root cause of organ failure in many cases. Common conditions seen in the Intensive Care Unit (ICU) such as sepsis and infection, trauma, burns, lung injury, pancreatitis, and surgical complications often trigger the massive production of cytokines, or 'cytokine storm', which leads to widespread inflammation. But cytokine storm can trigger a deadly systemic inflammatory response syndrome (SIRS) that, in turn, can cause the failure of many organs, such as the lungs, heart, kidneys, and liver.

Despite the best medical treatment, multiple organ failure accounts for nearly half of all deaths in the ICU, with few to no therapies capable of treating it, according to Chan. "Physicians have good supportive care therapies (for example, mechanical ventilation, dialysis, vasopressors) to help keep a patient alive on `life support,' when organs fail, but they have no good `active' therapies that can help prevent or treat organ failure. Because of this, the mortality is often greater than 30% and patients frequently linger in the ICU, running the risk of additional hospital acquired infections, and other complications. This comes at a staggering cost of $2,000 to $3,000 per day in the ICU, frequently leading to large losses for the hospital," added the CytoSorbents CEO. Chan reported that CytoSorb is proven to safely reduce cytokine storm in critically ill patients in a multi-center randomized controlled trial in Germany. By reducing cytokine storm, the goal of CytoSorb is to control SIRS and actively prevent or treat organ failure, thereby reducing illness severity and helping patients to heal and recover faster. "If successful, this would represent one of the most significant developments in modern medicine, potentially saving millions of lives and billions of dollars in hospital losses by finally giving physicians the ability to proactively treat these major unmet medical needs," he declared. From the trial in Germany, early data already suggests that CytoSorb can improve survival in high-risk patients, such as those older than age 65 and patients with very high cytokine levels. This needs to be proven, however, in large-scale randomized controlled trials.

Among the challenges facing the CytoSorbent team was developing a biocompatible polymer technology that could remove a broad range of cytokines and other inflammatory mediators. "CytoSorb is one of the highest purity medical sorbents in the medical device market today in the US or Europe, and meets numerous standards, including ISO 10993 biocompatibility and USP particulate standards," said Chan.

Another hurdle he and his team faced was manufacturing a high-purity, blood compatible polymer with good yields. "Our manufacturing facility is now ISO 13485 Full Quality Systems certified, which confirms that our manufacturing and quality systems meet the same high standards required of other major US medical device companies selling into Europe," he explained. Of the possible options, Full Quality Systems certification is the most stringent and efficient route to CE Mark approval for CytoSorb and other future CytoSorbents products.

Advancing the technology to animal treatment and then to human clinical trials was another major effort for the CytoSorbents researchers, who completed a 43-patient randomized controlled trial confirming the primary endpoints of safety and cytokine efficacy. These efforts won CytoSorb approval for use in Europe as one of the only extracorporeal cytokine filters in the European Union. CytoSorb is a hemoperfusion cartridge filled with beads that remove cytokines. This cartridge is placed into a standard hospital hemodialysis machine, and blood is pumped out of the body through a temporary dialysis catheter in a major vein, and then through this cartridge. Cytokines get trapped in the pores of the beads and are removed from blood, while the 'purified' blood is then re-circulated back to the patient. Over a 6-hour treatment period, CytoSorb can treat a patient's blood 20 to 30 times. For critical illnesses, treatment was carried out for 6 hours a day for 7 consecutive days. Chan reported physicians have safely treated patients with continuous CytoSorb treatment for 24 hours.

CytoSorbents has been awarded $1.1 million in Phase I & II SBIR grants from the US Army to develop its technology to help treat burn injury and trauma patients with rhabdomyolysis. The original Phase I was focused on trauma, but the Phase II has now been expanded to include large animal studies in both burn injury and trauma. "We are finalizing our contract negotiations with them on the Phase II program and expect to start work in the next few months. We will be collaborating with some of the top researchers in the US military on these studies," explained Chan.

The New Jersey company was also awarded a $3.8 million contract over five years by the US Defense Advanced Research Projects Agency (DARPA) to optimize their technology for the treatment of sepsis and to remove both toxins and cytokines. DARPA strongly believes in blood purification to treat sepsis and is funding the development of an easy-to-use blood purification machine that can detect the substances in blood that are leading to sepsis (for example, pathogens, cytokines, toxins, and activated cells) and remove them in an intelligent fashion. Chan pointed out that three of the major reasons warfighters die or suffer debilitating injury are polytrauma, burn injury, and sepsis. If they survive the initial injury, they often develop multiple organ failure, which, just as with the civilian population, cannot be dealt with effectively in the ICU. The CytoSorbent technology is easy to use, and easily stockpiled, with a shelf life of 3 years at room temperature. Using a simple blood pump and an extracorporeal blood circuit, and a source of electricity (even battery or solar power) the therapy could be applied in forward hospital installations relatively easily.

Trends that Chan has observed in critical care solutions for the military is improving the safety and quality, storage, and ease-of-administration of blood products, as can potentially be addressed by his company's HemoDefend blood purification technology, faster evacuation to definitive care, better hemostatic control at the point of injury, implementation of more effective therapies to improve the blood supply, blood substitutes, and freeze-dried plasma.

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