FORM 10-K

Cytosorbents Corp - CTSO

Filed: March 09, 2016 (period: December 31, 2015)

Annual report with a comprehensive overview of the company

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)
☒ **ANNUAL REPORT PURSUANT TO SECTION 13 or 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2015

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 or 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission file number 000-51038

CYTOSORBENTS CORPORATION
(Exact name of registrant as specified in its charter)

Delaware	**98-0373793**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

7 Deer Park Drive, Suite K
Monmouth Junction, New Jersey 08852
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code **(732) 329-8885**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class:	Name of each exchange on which registered:
Common Stock, $0.001 par value	**NASDAQ Stock Market LLC**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. ☐ Yes ☑ No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. ☐ Yes ☑ No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.
☑ Yes ☐ No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).
Yes ☐ No ☑

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer ☐ Accelerated Filer ☑

Non-accelerated Filer ☐ (do not check if a smaller reporting company) Smaller reporting company ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act.)
☐ Yes ☑ No

The aggregate market value of the common stock of the registrant held by non-affiliates as of June 30, 2015 was approximately $104,000,000. As of March 4, 2016 there were outstanding 25,406,056 shares of common stock.

Documents incorporated by reference:

Portions of the CytoSorbents Corporation definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year are incorporated by reference into Part III of this Form 10-K and certain documents are incorporated by reference into Part IV of this Form 10-K.

CYTOSORBENTS CORPORATION
ANNUAL REPORT ON FORM 10-K
TABLE OF CONTENTS

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Report, contains "forward-looking statements" within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. Forward-looking statements discuss matters that are not historical facts. Because they discuss future events or conditions, forward-looking statements may include words such as "anticipate," "believe," "estimate," "intend," "could," "should," "would," "may," "seek," "plan," "might," "will," "expect," "predict," "project," "forecast," "potential," "continue" negatives thereof or similar expressions. These forward-looking statements are found at various places throughout this Report and include information concerning possible or assumed future results of our operations; business strategies; future cash flows; financing plans; plans and objectives of management; any other statements regarding future operations, future cash needs, business plans and future financial results, and any other statements that are not historical facts. Unless otherwise indicated, the terms "CytoSorbents," "Company," "we," "us" and "our" refer to CytoSorbents Corporation.

From time to time, forward-looking statements also are included in our other periodic reports on Forms 10-Q and 8-K, in our press releases, in our presentations, on our website and in other materials released to the public. Any or all of the forward-looking statements included in this Report and in any other reports or public statements made by us are not guarantees of future performance and may turn out to be inaccurate. These forward-looking statements represent our intentions, plans, expectations, assumptions and beliefs about future events and are subject to risks, uncertainties and other factors. Many of those factors are outside of our control and could cause actual results to differ materially from the results expressed or implied by those forward-looking statements. In light of these risks, uncertainties and assumptions, the events described in the forward-looking statements might not occur or might occur to a different extent or at a different time than we have described. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this Report. All subsequent written and oral forward-looking statements concerning other matters addressed in this Report and attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this Report.

Except to the extent required by law, we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, future events, a change in events, conditions, circumstances or assumptions underlying such statements, or otherwise. For discussion of factors that we believe could cause our actual results to differ materially from expected and historical results see "Item 1A — Risk Factors" below.

TRADEMARKS

This Report includes our trademarks and trade names, such as CytoSorb®, BetaSorb™ and HemoDefend™, which are protected under applicable intellectual property laws and are the property of CytoSorbents Corporation and its subsidiaries. This Report also contains the trademarks, trade names and service marks of other companies, which are the property of their respective owners. Solely for convenience, trademarks, trade names and service marks referred to in this Report may appear without the ™, ®, or ^{SM} symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, trade names and service marks. We do not intend tour use or display of other parties' trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties.

PART I

Item 1. Business.

Overview

We are a leader in critical care immunotherapy commercializing our CytoSorb blood purification technology to reduce deadly uncontrolled inflammation in hospitalized patients around the world, with the goal of preventing or treating multiple organ failure in life-threatening illnesses. Organ failure is the cause of nearly half of all deaths in the intensive care unit, with little to improve clinical outcome. CytoSorb, our flagship product, is approved in the European Union as a safe and effective extracorporeal cytokine filter and is designed to reduce the "cytokine storm" that could otherwise cause massive inflammation, organ failure and death in common critical illnesses such as sepsis, burn injury, trauma, lung injury, and pancreatitis. These are conditions where the mortality is extremely high, yet no effective treatments exist. In addition, CytoSorb can be used in other inflammatory conditions such as cardiac surgery, autoimmune disease flares, and potentially for cancer, cytokine release syndrome in cancer immunotherapy, and cancer cachexia, a common syndrome that affects cancer patients, where cytokines play a major role in the cause of inflammation. CytoSorb has been used in more than 10,000 human treatments. Our purification technologies are based on biocompatible, highly porous polymer beads that can actively remove toxic substances from blood and other bodily fluids by pore capture and surface adsorption. We have numerous products under development based upon this unique blood purification technology, protected by 32 issued U.S. patents and multiple applications pending, including HemoDefend, ContrastSorb, DrugSorb, and others.

In March 2011, our flagship product, CytoSorb, an extracorporeal cytokine filter indicated for use in clinical situations where cytokines are elevated was CE marked. The CE Mark demonstrates that a conformity assessment has been carried out and the product complies with Medical Devices Directive 93/42/EEC in the European Union (EU). The goal of CytoSorb is to prevent or treat organ failure by reducing cytokine storm and the potentially deadly systemic inflammatory response syndrome (SIRS) in diseases such as sepsis, trauma, burn injury, acute respiratory distress syndrome, pancreatitis, liver failure, and many others. Organ failure is the leading cause of death in the intensive care unit, and remains a major unmet medical need, with little more than supportive care therapy (e.g., mechanical ventilation, dialysis, vasopressors, fluid support, etc.) as treatment options. By potentially preventing or treating organ failure, CytoSorb may improve clinical outcome, including survival, while reducing the need for costly intensive care unit treatment, thereby potentially saving significant healthcare costs.

Our CE Mark enables CytoSorb to be sold throughout all 28 countries of the EU and member states of the European Economic Area. In addition, many countries outside the EU accept CE Mark approval for medical devices, but may also require registration with or without additional clinical studies. The broad approved indication enables CytoSorb to be used in a variety of diseases where cytokines are elevated including, but not limited to, critical illnesses such as those mentioned above, autoimmune disease flares, cancer cachexia, and many other conditions where cytokine-induced inflammation plays a detrimental role.

Cytokines are small proteins that normally stimulate and regulate the immune response. However, in certain diseases, particularly life-threatening conditions commonly seen in the ICU, such as sepsis and infection, trauma, acute respiratory distress syndrome (ARDS), severe burn injury, liver failure, and acute pancreatitis, cytokines are often produced in vast excess – a condition often called cytokine storm. Left unchecked, this cytokine storm can lead to a severe maladaptive SIRS that can then cause cell death, multiple organ dysfunction syndrome, and multiple organ failure. Failure of vital organs such as the heart, lungs, and kidneys, accounts for nearly half of all deaths in the intensive care unit, despite the wide availability of supportive care therapies, or "life support", such as dialysis, mechanical ventilation, extracorporeal membrane oxygenation, and vasopressors. By replacing the function of failed organs, these supportive care therapies can initially help to keep patients alive, but do not help patients recover faster, and in many cases can increase the risk of dangerous complications. Unlike these supportive care therapies, the goal of the CytoSorb cytokine filter is to proactively prevent or treat organ failure by reducing cytokine storm and reducing the maladaptive SIRS response. In doing so, CytoSorb targets the reduction in the severity of patient illness and the need for intensive care, while potentially improving clinical outcome and saving healthcare costs.

As part of the CE Mark approval process, we completed our randomized, controlled, European Sepsis Trial amongst 14 trial sites in Germany in 2011, with enrollment of 100 patients with sepsis and respiratory failure. The trial established that CytoSorb was sufficiently safe in this critically-ill population to support the CE Mark. Taking into account all 100 patients, the treatment was well tolerated with no serious device related adverse events reported in more than 300 human treatments in the trial. Although the trial was not powered to demonstrate significant reduction in other clinical endpoints such as mortality, these were also included as secondary and exploratory endpoints in the trial.

The first 22 patients in the study represented a sepsis pilot study. In the next 31 patients, a compromise of the manual randomization schedule at two trial sites led to an imbalance in the severity of illness between the control and treatment patient groups of the study. After a thorough review, the Scientific Advisory Board and the independent Data Safety Monitoring Board both recommended that due to this enrollment bias, these 31 patients should only be used for safety evaluation purposes and that new patients should be enrolled into the trial using electronic web-based randomization to randomly assign patients into either the control or treatment arms.

Excluding four patients that withdrew, the remaining 43 patients enrolled under electronic randomization were relatively balanced in terms of the severity of illness in treatment and control patients, confirming the findings of the Scientific Advisory Board and the Data Safety Monitoring Board. An independent Contract Research Organization, RCRI, Inc., (Minneapolis, MN), analyzed cytokine data from these 43 patients in the European Sepsis Trial and showed, based upon their analysis methodology, on a statistically significant basis ($p<0.05$), the ability of CytoSorb to reduce circulating levels of key cytokines from whole blood in treated patients on the average of 30% to 50% over the seven day treatment period. Additionally, post-hoc subgroup analyses of the clinical outcome data from patients enrolled under electronic randomization demonstrated statistically significant reduction in mortality in patients at high risk of death in sepsis, specifically in patients with:

- Very high cytokine levels (IL-6 ≥ 1,000 pg/mL and/or IL-1ra ≥ 16,000 pg/mL) where 28-day mortality was 0% treated as compared to 63% control, p=0.03, n=14; and
- Age ≥ 65 (14-day mortality: 0% treated as compared to 36% control, p=0.04, n=21).

We plan to conduct larger, prospective studies in septic patients in the future to confirm these findings. According to a recent study by the U.S. Centers for Disease Control and Prevention (CDC), those older than age 65 account for approximately two-thirds of patients hospitalized in the U.S. for sepsis, and were responsible for the doubling in the incidence of sepsis over the past decade. Without effective therapies to treat sepsis, the incidence of sepsis and sepsis-related deaths are expected to continue to increase significantly over the course of the next decade, particularly as the baby boomer generation, which began turning 65 in 2011, continues to get older.

In addition to CE Mark approval, we also achieved ISO 13485:2003 Full Quality Systems certification, an internationally recognized quality standard designed to ensure that medical device manufacturers have the necessary comprehensive management systems in place to safely design, develop, manufacture and distribute medical devices in the European Union. We manufacture CytoSorb at our manufacturing facilities in New Jersey for commercial sales abroad and for additional clinical studies. In September 2013, we were granted a two-year renewal for the CytoSorb CE Mark. In June 2015, we successfully completed an ISO 13485:2003 surveillance audit maintaining our good standing with our Notified Body. We also established a reimbursement path for CytoSorb in Germany and Austria.

From September 2011 through June 2012, we began a controlled market release of CytoSorb in select geographic territories in Germany. The purpose of this program was to prepare for commercialization of CytoSorb in Germany in terms of manufacturing, reimbursement, logistics, infrastructure, marketing, contacts, and other key issues.

In late June 2012, following the establishment of our European subsidiary, CytoSorbents Europe GmbH, a wholly-owned operating subsidiary of CytoSorbents Corporation, we began the commercial launch of CytoSorb in Germany with the hiring of Dr. Christian Steiner as Vice President of Sales and Marketing and three additional sales representatives who joined us and completed their sales training during the third quarter of 2012. The fourth quarter of 2012 represented the first quarter of direct sales with the full sales team in place. During this period, we expanded our direct sales efforts to include both Austria and Switzerland.

Fiscal 2013 represented the first full year of CytoSorb commercialization. We focused our direct sales efforts in Germany, Austria and Switzerland with four sales representatives. The focus of the team was to encourage acceptance and usage by key opinion leaders (KOLs) throughout these countries. By the end of 2015, we had hundreds of KOLs in critical care, cardiac surgery, and blood purification who are either using CytoSorb or planning to use CytoSorb in the near future. We believe these KOL relationships will be essential to drive adoption and recurrent usage of CytoSorb by the department, facilitate purchases by the hospital administration, arrange reimbursement, and generate data for papers and presentations. In addition, we now currently have more than 50 investigator initiated studies being planned around the world in multiple applications including sepsis, cardiac surgery, lung injury, trauma, pancreatitis, liver failure, kidney failure, and others, with 17 enrolling patients and 4 completed. These studies are being supported by our European Director of Scientific Affairs. As of March 1, 2016, we have increased our sales force to include eight direct sales people, one contract sales person, and nine sales and distributor support staff.

We have complemented our direct sales efforts with sales to distributors and/or corporate partners. In 2013, we reached agreement with distributors in the United Kingdom, Ireland, the Netherlands, Russia and Turkey. In April 2014, we announced distribution of CytoSorb in the Middle East, including Saudi Arabia, the United Arab Emirates, Kuwait, Qatar, Bahrain, and Oman (the Gulf Cooperative Council (GCC)) and Yemen, Iraq, and Jordan through an exclusive agreement with TechnoOrbits. In December 2014, we entered into an exclusive agreement with Smart Medical Solutions S.R.L., to distribute CytoSorb for critical care applications in Romania and the neighboring Republic of Moldova. In 2015, we announced exclusive distribution agreements with Aferetica SRL to distribute CytoSorb in Italy, AlphaMedix Ltd. to distribute CytoSorb in Israel, TekMed Pty Ltd. to distribute CytoSorb in Australia and New Zealand, and Hoang Long Pharma to distribute CytoSorb in Vietnam.

We have been expanding our strategic partnerships by number and scope. In September 2013, we entered into a strategic partnership with Biocon Ltd., India's largest biotech company, with an initial distribution agreement for India and select emerging markets, under which Biocon has the exclusive commercialization rights for CytoSorb initially focused on sepsis. In September 2014, the Biocon partnership was expanded to include all critical care applications and cardiac surgery. In addition, Biocon committed to higher annual minimum purchases of CytoSorb to maintain distribution exclusivity and committed to conduct and publish results from multiple investigator initiated studies and patient case studies.

In addition, in November 2014, we entered into an initial partnership agreement with a leading global medical device company in cardiac surgery and other cardiovascular diseases, to use CytoSorb intra-operatively during cardiac surgery in France. Following a positive evaluation of the device during the term of the agreement, we are now in discussions with multiple potential cardiac surgery partners for distribution rights to CytoSorb in the field of cardiac surgery.

In December 2014, we entered into a multi-country strategic partnership with Fresenius Medical Care AG & Co KGaA (Fresenius) to commercialize the CytoSorb therapy. Under the terms of this agreement, Fresenius has exclusive rights to distribute CytoSorb for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership will allow Fresenius to offer an innovative and easy way to use blood purification therapy for removing cytokines in patients that are treated in the intensive care unit. To promote the success of CytoSorb, Fresenius will also engage in the ongoing clinical development of the product. This includes the support and publication of a number of small case series and patient case reports as well as the potential for future larger, clinical collaborations.

Overall, we have established either direct sales (as above) or distribution (via distributors or strategic partners) of CytoSorb in 32 countries worldwide. Registration of CytoSorb is typically required in each of these countries prior to active commercialization. With CE Mark approval, this can be typically achieved within several months in EU countries. Outside of the EU, the process is more variable and can take months to more than a year due to different requirements for documentation and clinical data. Variability in the timing of registration affects the initiation of active commercialization in these countries, which affects the timing of expected CytoSorb sales. We actively support all of our distributors and strategic partners in the product registration process. Outside of the EU, CytoSorb is actively being commercialized in Turkey, India Australia, New Zealand, and Saudi Arabia, having achieved Saudi FDA approval in 2015. We and our distribution partner in Russia have submitted all requested documentation for registration, and await a response from the Russian authorities. We cannot generally predict the timing of these registrations, and there can be no guarantee that we will ultimately achieve registration in countries where we have established distribution. For example, in August 2014 we announced exclusive distribution of CytoSorb in Taiwan with Hemoscien Corporation. However, in March 2015, due to the complexity we encountered with Taiwanese product registration, we elected to terminate our agreement with Hemoscien. We also cannot guarantee that we will generate meaningful sales in the countries where we have established registration, due to other factors such as market adoption and reimbursement. We are currently actively evaluating other potential distributor and strategic partner networks in other major countries that accept CE Mark approval.

The market focus for CytoSorb is the prevention or treatment of organ failure in life-threatening conditions, including commonly seen illnesses in the intensive care unit such as infection and sepsis, trauma, burn injury, ARDS, and others. Severe sepsis and septic shock, a potentially life-threatening systemic inflammatory response to a serious infection, accounts for approximately 10% to 20% of all ICU admissions and is one of the largest target markets for CytoSorb. Sepsis is a major unmet medical need with, to our knowledge, no approved products in the U.S. or Europe to treat it. As with other critical care illnesses, multiple organ failure is the primary cause of death in sepsis. When used with standard of care therapy, that includes antibiotics, the goal of CytoSorb in sepsis is to reduce excessive levels of cytokines and other inflammatory toxins, to help reduce the SIRS response and either prevent or treat organ failure.

In addition to the sepsis indication, we intend to conduct or support additional clinical studies in sepsis, cardiac surgery, and other critical care diseases where CytoSorb could be used, such as ARDS, trauma, severe burn injury, acute pancreatitis, and in other acute conditions that may benefit by the reduction of cytokines in the bloodstream. Some examples include the prevention of post-operative complications of cardiac surgery (cardiopulmonary bypass surgery) and damage to organs donated for transplant prior to organ harvest. We intend to generate additional clinical data to expand the scope of clinical experience for marketing purposes, to increase the number of treated patients, and to support potential future publications.

We have completed a single arm, dose ranging trial in Germany amongst several clinical trial sites to evaluate the safety and efficacy of CytoSorb when used 24 hours per day for seven days, each day with a new device and are conducting final statistical analysis of the data. Patients are being stratified for age, cytokine levels, and co-morbid illnesses in this matched pairs analysis. These additional dosing data are intended to help clinicians with additional treatment options for CytoSorb, help support the positive clinical data from our first European Sepsis Trial, and help shape the trial protocol for a pivotal sepsis study.

In addition to the dosing study, we plan to use data generated and published in the more than 50 investigator initiated studies and trials sponsored by us currently planned, enrolling or completed in certain countries around the world. Approximately 17 of these studies are currently enrolling patients with four such studies completed. These trials, which are funded and supported by well-known university hospitals and KOLs, are the equivalent of Phase 1 and/or Phase 2 clinical studies. We anticipate that these studies and data that may be available in the public realm will provide invaluable information regarding the potential success of the device in the treatment of sepsis, cardio-pulmonary bypass surgery, trauma, and many other indications, and, depending on the results, may be integral in helping to drive additional usage and adoption of CytoSorb.

In addition to sepsis and other critical care applications, cardiac surgery is emerging as an important potential application for CytoSorb in the European market. There are approximately one million cardiac surgery procedures performed annually in the U.S. and EU including, for example, coronary artery bypass graft surgery, valve replacement surgery, heart and lung transplant, congenital heart defect repair, aortic reconstruction, and left ventricular assist device (LVAD) implantation. Cardiac surgery can result in inflammation and the production of high levels of inflammatory cytokines, as well as hemolysis, leading to the release of free hemoglobin. These can lead to post-operative complications such as respiratory failure and acute kidney injury. CytoSorb has a unique competitive advantage as the only cytokine and free hemoglobin removal technology that can be used during the operative procedure and can be easily installed in a bypass circuit in a heart-lung machine without the need for an additional pump. Direct cytokine and hemoglobin removal with CytoSorb enables it to replace the existing market for leukoreduction filters in cardiac surgery that attempt to indirectly reduce cytokines by capturing cytokine-producing leukocytes – an inefficient and suboptimal approach.

In February 2015, the U.S. Food and Drug Administration (FDA) approved our Investigational Device Exemption (IDE) application to commence a planned U.S. cardiac surgery feasibility study called REFRESH I (REduction of FREe plaSma Hemoglobin) amongst 20 patients and three U.S. clinical sites. The FDA subsequently approved an amendment to the protocol, expanding the trial to be a 40 patient randomized controlled study (20 treatment, 20 control) in eight clinical centers. REFRESH I represents the first part of a larger clinical trial strategy intended to support the approval of CytoSorb in the U.S. for intra-operative use during cardiac surgery. The study is designed to evaluate the safety of CytoSorb when used intra-operatively in a heart-lung machine to reduce plasma free hemoglobin and cytokines in patients undergoing complex cardiac surgery. The length, complexity and invasiveness of these procedures cause hemolysis and inflammation, leading to high levels of plasma free hemoglobin, cytokines, activated complement, and other substances. These inflammatory mediators directly correlate with the incidence of serious post-operative complications such as kidney injury and failure. The goal of CytoSorb is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications. As of March 4, 2016, the trial is approximately 35% enrolled and is expected to be completed by mid-2016.

Even though we have obtained CE Mark approval, no guarantee or assurance can be given that our CytoSorb product will work as intended or that we will be able to obtain FDA approval to sell CytoSorb in the U.S. or approval in any other country or jurisdiction. Because of the limited studies we have conducted, we are subject to substantial risk that our technology will have little or no effect on the treatment of any indications that we have targeted.

We have been successful in obtaining technology development contracts from agencies in the U.S. Department of Defense, including the Defense Advanced Research Projects Agency (DARPA), the U.S. Army, and the U.S. Air Force, as well as the National Institutes of Health.

In June 2013, we announced that the U.S. Air Force will fund a 30 patient, single site, randomized controlled human pilot study in the U.S. amongst trauma patients with rhabdomyolysis. The primary endpoint is myoglobin removal. The FDA approved our IDE application for this study and we also received ethics committee approval, allowing the study to commence. However, because of the stringency of our inclusion criteria, and because of the patient mix seen at our single center, we have experienced difficulty in enrolling patients. We have subsequently modified one of the key inclusion criteria and have expanded the number of clinical trial sites to three in a revised protocol which has been submitted to and approved by the FDA. Though we do not expect to receive material direct funding from this $3 million budgeted program, the study may generate valuable data that can be used commercially or in future trauma studies.

In September 2012, we were awarded a Phase II Small Business Innovation Research (SBIR) contract by the U.S. Army Medical Research and Materiel Command to evaluate our technology for the treatment of trauma and burn injury in large animal models. In 2013, we finalized the Phase II SBIR contract which provided for a maximum funding of approximately $753,000 with the granting agency. This work is supported by the U.S. Army Medical Research and Material Command under an amendment to Contract W81XWH-12-C-0038. As of December 31, 2015, we received approximately $649,000 in funding under this contract and no further amounts are expected from this contract.

In August 2012, we were awarded a $3.8 million, five-year contract by DARPA for our “Dialysis-Like Therapeutics” (DLT) program to treat sepsis. DARPA has been instrumental in funding many of the major technological and medical advances since its inception in 1958, including development of the Internet, development of global positioning system (GPS), and robotic surgery. The DLT program in sepsis seeks to develop a therapeutic blood purification device that is capable of identifying the cause of sepsis (e.g., cytokines, toxins, pathogens, activated cells) and remove these substances in an intelligent, automated, and efficient manner. Our contract is for advanced technology development of our hemocompatible porous polymer technologies to remove cytokines and a number of pathogen and biowarfare toxins from blood. We are in Year 4 of the program and are currently working with the systems integrator, Battelle Laboratories, and its subcontractor NxStage Medical, who are responsible for integrating the technology developed by us and others into a final medical device design prototype, and evaluating this device in septic animals and eventually in human clinical trials in sepsis. Our work is supported by DARPA and SSC Pacific under Contract No. N66001-12-C-4199. As of December 31, 2015, we have received approximately $3,499,000 to date and has approximately $301,000 not yet billed under this contract.

In September 2013, the National Heart, Lung, and Blood Institute (NHLBI) a division of the National Institutes of Health (NIH), awarded us a Phase I SBIR contract valued at $203,351 to further advance our HemoDefend blood purification technology for packed red blood cell (pRBC) transfusions. The University of Dartmouth collaborated with us as a subcontractor on the project, entitled “Elimination of blood contaminants from pRBCs using HemoDefend hemocompatible porous polymer beads”. The overall goal of this program is to reduce the risk of potential side effects of blood transfusions, and help to extend the useful life of pRBCs.

In October 2015, we were awarded a Phase II SBIR contract by the NHLBI to help advance our HemoDefend blood purification technology towards commercialization for the purification of pRBC transfusions. The contract, entitled “pRBCs Contaminant Removal with Porous Polymer Beads”, provides for maximum funding of approximately $1,520,000 over a two year period, with funding to begin in 2016.

We are also exploring potential eligibility in several other government sponsored grant programs which could, if approved, represent a substantial future source of non-dilutive funds for our research programs.

In addition to CytoSorb, we are developing other products utilizing our adsorbent polymer technology that have not yet received regulatory approval including HemoDefend, ContrastSorb, DrugSorb, BetaSorb, and others. The HemoDefend technology platform is a development-stage blood purification system that can remove contaminants in transfused blood products, with the goal of reducing potentially fatal transfusion reactions and improving the quality of blood. ContrastSorb is designed to remove intravenous radiocontrast (IV contrast), that is administered during interventional radiology procedures, for example, coronary angiograms for heart disease, and computed tomography (CT scans) or computer axial tomography imaging (CAT scans) that can cause kidney failure in high risk patients, for example, those with pre-existing kidney disease, diabetes, hypertension, congestive heart failure, and who are of old age. DrugSorb is designed to remove toxic drugs from blood, such as in drug overdose. The BetaSorb filter was designed for use with renal replacement therapy in end-stage renal disease patients, to remove mid-molecular weight toxins that are not adequately removed by hemodialysis or hemofiltration. BetaSorb is not the current focus of our near-term commercialization plans. With the exception of HemoDefend, all of these products are known medically as hemoperfusion devices. During hemoperfusion, blood is removed from the body via a catheter or other blood access device, perfused through a filter medium where toxic compounds are removed, and returned to the body. Hemoperfusion, along with hemodialysis and hemofiltration, are the three major forms of blood purification.

HemoDefend is a development-stage blood purification technology platform designed to safeguard and protect the blood supply. We seek to license the HemoDefend platform and have not yet received regulatory approval in any markets. HemoDefend consists of a mixture of proprietary porous polymer beads that target the removal of contaminants that can cause transfusion reactions or cause disease in patients receiving the tens of millions of transfused blood products administered worldwide each year. These contaminants include, for example, foreign antibodies, antigens, cytokines, free hemoglobin, bioactive lipids, toxins, drugs, and other inflammatory mediators that either were from the donor or accumulated during blood storage. The goal of the HemoDefend technology is to reduce these contaminants in transfused blood products to reduce transfusion reactions, to keep new blood fresh, and to improve the quality and safety of blood.

The HemoDefend beads are intended to be used in multiple configurations, including as a common in-line filter between the blood bag and the patient as well as a patent-pending “Beads in a Bag” treatment configuration, where the beads are placed directly into a blood storage bag. Once blood is put into this bag, the beads begin to automatically remove contaminants from the blood, and are designed to continue purifying blood throughout the entire blood storage period. The use of neutrally buoyant beads eliminates the need for mixing and is compatible with current blood storage conditions. Integrated filters in the bag prevent beads from leaving the bag during the transfusion process. The base polymer meets ISO 10993 standards for biocompatibility, hemocompatibility, genotoxicity, cytotoxicity, acute sensitivity and complement activation and can therefore directly contact blood for extended periods of time. In addition, the beads are inert and stable at a wide range of temperatures, and do not contain any antibodies, biologics, ligands, or drugs. Because of this, the beads have a very long shelf life that is consistent with blood storage bag manufacturing standards. No special equipment or handling is required, making it well-suited for mainstream and military applications, as well as for use in less developed countries that are not well-equipped to test and process blood products.

ContrastSorb is a development-stage blood purification technology that is being optimized for the removal of IV contrast from blood in order to prevent contrast-induced nephropathy (CIN). CIN is the acute loss of renal function within the first 48 hours following IV contrast administration. An estimated 65 million CT scans are performed worldwide with IV contrast each year to enhance the images and make it easier to identify anatomic structures. IV contrast is also administered during vascular interventional radiology procedures and angiography of blood vessels in the brain, heart, limbs, and other parts of the body to diagnose and treat atherosclerosis (narrowing of blood vessels due to cholesterol deposits), vascular injury, aneurysms, etc. For example, an estimated 10 million coronary angiograms are performed worldwide each year to diagnose and treat coronary artery disease by placing coronary stents, performing balloon angioplasty, or atherectomy (removal of plaque in arteries). The reported risk of CIN in patients undergoing contrast enhanced CT scans has been reported to be 2% to 13%. For coronary intervention, the risk has been estimated to be as high as 20% to 30% in high risk patients with pre-existing renal insufficiency, long-term diabetes, hypertension, congestive heart failure, and older age. The use of low osmolar IV contrast, hydration of patients pre-procedure, orally administration of N-acetylcysteine, and other agents to prevent CIN have demonstrated modest benefit in some clinical studies, but in many cases, the results across studies have been equivocal and inconsistent. In high risk patients, the direct removal of IV contrast from the blood with ContrastSorb to prevent CIN represents a potentially more effective alternative.

DrugSorb is a development-stage blood purification technology that is capable of removing a wide variety of drugs and chemicals from blood, as a potential treatment for drug overdose, drug toxicity, toxic chemical exposure, use in high-dose regional chemotherapy, and other applications. It has demonstrated extremely high single pass removal efficiency of a number of different drugs that exceeds the extraction capability of hemodialysis or other filtration technologies. It is similar in action to activated charcoal hemoperfusion cartridges that have been available for many years, but has the advantage of having inherent biocompatibility and hemocompatibility without coatings, and can be easily customized for specific agents.

Our BetaSorb device is intended to remove beta$_2$-microglobulin and other mid-molecular weight toxins from the blood of patients suffering from chronic kidney failure who rely on long term dialysis therapy to sustain their life. Standard high-flux hemodialysis is very effective in removing small uremic toxins, but much less effective in removing these mid-molecular weight toxins that functional kidneys normally remove. BetaSorb utilizes an adsorbent polymer packed into a similarly shaped and constructed cartridge as utilized for our CytoSorb product, although the polymers used in the two devices are physically different, with one optimized for short-term critical care use and the other specifically designed for the needs of long-term chronic usage. The BetaSorb device also incorporates industry standard connectors at either end of the device, which connect directly into the extra-corporeal circuit (bloodlines) in series with a dialyzer. To date, we have manufactured the BetaSorb device on a limited basis for testing purposes, including for use in clinical studies.

We initially identified end stage renal disease as the target market for our polymer-based adsorbent technology. However, during the development of BetaSorb, we identified several applications for our adsorbent technology in the treatment of critical care patients. As a result, we shifted our priorities to pursue critical care applications (such as for the treatment of sepsis) for our technology given that the potential for usage of BetaSorb in chronic conditions such as end stage renal disease is anticipated to have a longer and more complex regulatory pathway. We may pursue our BetaSorb product in the future after the commercialization of the CytoSorb device. At such time as we determine to proceed with our proposed BetaSorb product, if ever, we will need to conduct additional clinical studies using the BetaSorb device and obtain separate regulatory approval in Europe and/or the U.S.

We have conducted clinical studies using our BetaSorb device in patients with chronic kidney failure, which have provided valuable data that underpin the development of the critical care applications for our technology. The BetaSorb device has been used in a total of four human pilot studies, involving 20 patients, in the U.S. and Europe. The studies included approximately 345 treatments, with some patients using the device for up to 24 weeks (in multiple treatment sessions lasting up to four hours, three times per week) in connection with the application of our products to patients suffering from chronic kidney failure.

Corporate History

We were originally organized as a Delaware limited liability company in August 1997 as Advanced Renal Technologies, LLC. We changed our name to RenalTech International, LLC in November 1998, and to MedaSorb Technologies, LLC in October 2003. In December 2005, MedaSorb Technologies, LLC converted from a limited liability company to a corporation. CytoSorbents Corporation was incorporated in Nevada on April 25, 2002 as Gilder Enterprises, Inc., and was originally engaged in the business of installing and operating computer networks that provided high-speed access to the Internet. On June 30, 2006, we disposed of our original business, and pursuant to an Agreement and Plan of Merger, acquired all of the stock of MedaSorb Technologies, Inc., a Delaware corporation, in a merger, and the business of MedaSorb Technologies, Inc. became our business. Following the merger, in July 2006, we changed our name to MedaSorb Technologies Corporation. In November 2008, we changed the name of our operating subsidiary from MedaSorb Technologies, Inc. to CytoSorbents, Inc. In May 2010, we finalized the name change of MedaSorb Technologies Corporation to CytoSorbents Corporation. On October 28, 2014, we changed the name of our operating subsidiary from CytoSorbents, Inc. to CytoSorbents Medical, Inc.

On December 3, 2014, we effected a twenty-five-for-one (25:1) reverse split of our common stock. As a result of this reverse stock split, shares of our common stock outstanding were reduced by approximately 96%. Based on the 582,097,092 shares of common stock outstanding as of December 3, 2014, the total number of shares of common stock outstanding after the reverse stock split, including accounting for fractional shares which were rounded up to the next whole number, were 23,284,040 shares. Accordingly, all share, option and warrant information included in this Annual Report has been retroactively adjusted to reflect the reduced number of shares resulting from this action. Immediately after the reverse stock split, pursuant to an Agreement and Plan of Merger dated December 3, 2014 (i) on December 3, 2014, we changed our state of incorporation from the State of Nevada to the State of Delaware, whereby we merged with and into our recently formed, wholly-owned Delaware subsidiary. At the effective time of the merger, (i) we merged with and into our Delaware subsidiary, (ii) our separate corporate existence in Nevada ceased to exist, (iii) the Delaware subsidiary became the surviving corporation, (iv) the certificate of incorporation, as amended and restated, and the bylaws of the Delaware subsidiary became our certificate of incorporation and bylaws, and (v) each share of our common stock outstanding immediately prior to the effective time was converted into one fully-paid and non-assessable share of our common stock as a Delaware corporation. The reverse stock split, the merger and the Agreement and Plan of Merger were approved by our Board of Directors and stockholders representing a majority of our then-outstanding common stock. All references to "us", "we", or the Company, on or after December 3, 2014, refer to CytoSorbents Corporation, a Delaware corporation.

Our executive offices are located at 7 Deer Park Drive, Suite K, Monmouth Junction, New Jersey 08852, and our telephone number is (732) 329-8885.

We have been engaged in research and development since our inception and have raised approximately $98 million from investors. These proceeds have been used to fund the development of multiple product applications and to conduct clinical studies, to establish in-house manufacturing capacity to meet commercial and clinical testing needs, expand our intellectual property through additional patents, and to develop extensive proprietary know-how with regard to our products. For the years ended December 31, 2015 and 2014, our research and development expenses amounted to approximately $3,871,000 and $2,432,000, respectively.

We have raised funds through various means including convertible note offerings and equity transactions. Our most significant financing transactions are discussed below.

Shelf Registration

On July 29, 2015, our registration statement on Form S-3 (Registration No. 333-205806), as filed with the SEC on July 23, 2015 (Shelf Registration Statement), was declared effective using a "shelf" registration process. Under this shelf registration statement, we may issue, in one or more offerings, any combination of common stock, preferred stock, senior or subordinated debt securities, warrants, or units, up to a total dollar amount of $100 million.

Principal Terms of the November 4, 2015 Controlled Equity Offering

On November 4, 2015, we entered into a Controlled Equity Offering℠ Sales Agreement (Sales Agreement) with Cantor Fitzgerald and Co., as agent (Cantor), pursuant to which we may offer to sell, from time to time through Cantor, shares of our common stock, having an aggregate offering price of up to $25,000,000 (Shares). Any Shares offered and sold will be issued pursuant to our Shelf Registration Statement, as supplemented by a prospectus supplement dated November 4, 2015, which we filed with the SEC pursuant to Rule 424(b)(5) under the Securities Act.

Under the Sales Agreement, Cantor may sell Shares by any method permitted by law and deemed to be an "at the market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended (Securities Act), including sales made directly on The NASDAQ Capital Market, on any existing trading market for our common stock or to or through a market maker. In addition, under the Sales Agreement, Cantor may sell the Shares by any other method permitted by law, including in privately negotiated transactions. We may instruct Cantor not to sell Shares if the sales cannot be effected at or above the price designated by us from time to time.

We are not obligated to make any sales of Shares under the Sales Agreement, and if we elects to make any sales, we can set a minimum sales price for the Shares. The offering of Shares pursuant to the Sales Agreement will terminate upon the earlier of (i) the sale of all the shares subject to the Sales Agreement, or (ii) the termination of the Sales Agreement by Cantor or by us, as permitted therein. In the fourth quarter of 2015, we sold 28,880 shares at an average selling price of $8.02 per share, generating net proceeds of approximately $225,000 under the Sales Agreement.

We pay a commission rate of 3.0% of the aggregate gross proceeds from each sale of shares under the Sales Agreement, and have agreed to provide Cantor with customary indemnification and contribution rights. We have also reimbursed Cantor $50,000 for certain specified expenses in connection with entering into the Sales Agreement.

We intend to use the net proceeds raised through "at the market" sales for research and development activities, which include the funding of additional clinical studies and costs of obtaining regulatory approvals in countries not covered by the CE Mark, capital expenditures and other costs necessary to expand production capacity, support of various sales and marketing efforts, product development and general working capital purposes.

Principal Terms of the January 2015 $10,312,500 Equity Offering

On January 14, 2015, we closed on an underwritten public offering (the January 2015 Offering), consisting of 1,250,000 shares of our common stock at a price of $8.25 per share for an aggregate price of $10,312,500.

We received net proceeds from the January 2015 Offering of approximately $9,409,000, which are being used to fund clinical studies, expansion of production capacity, support various sales and marketing efforts, product development and general working capital purposes.

We conducted the January 2015 Offering pursuant to a registration statement on Form S-1 (File No. 333-199762) which was declared effective by the Securities and Exchange Commission on January 8, 2015. We filed a final prospectus on January 9, 2015, disclosing the final terms of the January 2015 Offering.

In connection with the January 2015 Offering, on January 8, 2015, we entered into underwriting agreements with Brean Capital, LLC and H.C. Wainwright & Co., LLC, (the Representatives), who acted as book-running managers and as representatives of the underwriters in the January 2015 Offering.

In connection with the successful completion of the January 2015 Offering, the underwriters received aggregate discounts and commissions of 6% of the gross proceeds of the sale of the shares in the January 2015 Offering. In addition, we agreed to issue warrants (Representatives' warrants) to the Representatives that allow for the purchase of shares of our common stock equal to 3% of the aggregate number of shares sold in the January 2015 Offering. The Representatives' warrants are exercisable at any time for a period of five years, commencing on January 8, 2015, at a price per share equal to 120% of the public offering price per share of the common stock in the January 2015 Offering. We also agreed to reimburse the underwriters for actual out-of-pocket expenses related to the January 2015 Offering, which amounted to approximately $85,000. We further granted the Representatives a right of first refusal to participate in any subsequent offering or placement of our securities that would have taken place within nine months of January 8, 2015.

Principal Terms of the March 2014 $10,200,000 Equity Offering

On March 7, 2014, we entered into subscription agreements with certain investors providing for our issuance and sale (the March 2014 Offering), of 1,632,000 units (the Units), for an aggregate purchase price of $10,200,000. Each Unit is comprised of one share of our common stock, priced at $6.25 per share, and a warrant to purchase 0.50 shares of our common stock at an exercise price of $7.8125 per share. The warrants are convertible into a total of 816,000 shares of our common stock. Each warrant is exercisable for a period of five years beginning on March 11, 2014, the date of the closing of the sale of these securities, and is only exercisable for cash if at the time of exercise there is an effective registration statement registering the warrants and shares underlying the warrants.

We received net proceeds from the March 2014 Offering of approximately $9,451,000, which are being used for building additional sales and marketing infrastructure, clinical studies, working capital and general corporate purposes.

We conducted the March 2014 Offering pursuant to a registration statement on Form S-1 (File No. 333-193053) which was declared effective by the Securities and Exchange Commission on February 14, 2014 and an additional registration statement on Form S-1 (File No. 333-194394) to register an additional amount of securities having a proposed maximum aggregate offering price of $2,762,500, which increased the total registered amount to $16,575,000 assuming the full cash exercise of the warrants for cash. We filed a final prospectus on March 7, 2014, disclosing the final terms of the March 2014 Offering.

In connection with the March 2014 Offering, on March 7, 2014, we entered into a placement agency agreement with Brean Capital, LLC pursuant to which the placement agent agreed to act as our exclusive placement agent for the March 2014 Offering and sale of the Units.

In connection with the successful completion of the March 2014 Offering, the placement agent received an aggregate cash placement agent fee equal to 6% of the gross proceeds of the sale of the Units in the Offering and a warrant to purchase 48,960 shares of our common stock at an exercise price of $7.50 per share exercisable for five years from the effective date of the placement agency agreement. The placement agent warrant contains piggy-back registration rights which expire on the fifth anniversary of the effective date of the registration statement. We have also agreed to reimburse the placement agent for actual out-of-pocket expenses up to a maximum of 2% of gross proceeds from the transaction. We also granted the placement agent a right of first refusal to participate in any subsequent offering or placement of our securities that takes place within twelve months following the effective date of the registration statement.

Conversion of Preferred Stock to Common Stock

On October 9, 2014, we filed with the Nevada Secretary of State an Amendment (the Series A Amendment), to the Certificate of Designation, as amended (the Series A Certificate of Designation), of the Series A Preferred Stock. The Series A Amendment, which became effective on October 9, 2014, (i) amended the Series A Certificate of Designation to allow the stockholders representing eighty percent (80%) of the issued and outstanding shares of Series A Preferred Stock to elect to convert all issued and outstanding shares of Series A Preferred Stock into our common stock, at the then-effective "Conversion Price," as defined in the Series A Certificate of Designation, and (ii) as consideration for approving such amendment, amended the conversion price of our Series A Preferred Stock from $31.25 per share to $19.25 per share, except with respect to the shares of Series A Preferred Stock covered by that certain Agreement and Consent dated as of June 25, 2008 by and among us and certain holders of Series A Preferred Stock. The fair value of the reduction in the conversion price was determined based on the five day volume weighted average price of our common stock at the date of the conversion. Immediately following effectiveness of the Series A Amendment, the stockholders representing over 88 percent (88%) of the then-issued and outstanding Series A Preferred Stock elected to convert all issued and outstanding Series A Preferred Stock into shares of our common stock at the amended conversion price. As a result of this election by the holders of Series A Preferred Stock, 1,894,969 shares of Series A Preferred Stock were converted into 103,332 post-split shares of our common stock.

After giving effect to the conversion of the Series A Preferred Stock described above, there are no shares of Series A Preferred Stock issued and outstanding as of December 31, 2014.

In addition, on October 9, 2014, we also filed with the Nevada Secretary of State an Amendment (the Series B Amendment) to the Certificate of Designation (the Series B Certificate of Designation) of the Series B Preferred Stock. The Series B Amendment, which became effective on October 9, 2014, amended the Series B Certificate of Designation to allow the holders of a majority of the Series B Preferred Stock, including NJTC Investment Fund, LP, to elect to convert all issued and outstanding shares of Series B Preferred Stock into common stock. Immediately following effectiveness of the Series B Amendment, the stockholders representing over 93 percent (93%) of the then-issued and outstanding Series B Preferred Stock elected to convert all issued and outstanding Series B Preferred Stock into common stock. Each share of Series B Preferred Stock had a stated value of $100.00 (the Series B Stated Value), and was convertible into that number of shares of common stock equal to the Series B Stated Value at a conversion price of $0.90. As consideration for approving the Series B Amendment, the holders of Series B Preferred Stock received a one-time dividend equal to ten percent (10%) of the shares of Series B Preferred Stock then held. As a result of this election by the holders of Series B Preferred Stock, 84,283.99 shares of Series B Preferred Stock were issued a dividend of 10% and then the 92,712.27 shares were converted into 10,244,450 post-split shares of common stock. As a result of the conversion, the carrying value of the Series B stock was reclassified to permanent equity.

After giving effect to the conversion of the Series B Preferred Stock described above, there are no shares of Series B Preferred Stock issued and outstanding as of December 31, 2014.

Research and Development

We have been engaged in research and development since inception. Our research and development costs were approximately $3,871,000 and $2,432,000 for the years ended December 31, 2015 and 2014, respectively. Since 2012, we have been awarded approximately $6.75 million in grants and contracts from DARPA ($3.8M over 5 years), the U.S. Army ($100,000 Phase I SBIR; $50,000 Phase I extension, $1 million Phase II SBIR), and the National Heart, Lung and Blood Institute ($203,000 Phase I SBIR; $1.5 million Phase 2 SBIR) to further develop our technologies for sepsis, trauma and burn injury, and blood transfusions, respectively. Payments are based on achieving certain technology milestones. In addition, the U.S. Air Force is funding a 30-patient, randomized controlled human pilot study evaluating CytoSorb in patients with severe trauma and rhabdomyolysis, for which we are the sponsor. In response to slower than expected enrollment, a protocol amendment was submitted to the FDA to increase the number of trial sites to three and to modify the study's inclusion criteria. The FDA approved this trial under an IDE application in 2013 and approved the amended protocol in 2015.

Technology, Products and Applications

For approximately the past half-century, the field of blood purification has been focused on hemodialysis, a mature, well accepted medical technique primarily used to sustain the lives of patients with permanent or temporary loss of kidney function. It is widely understood by the medical community that dialysis has inherent limitations in that its ability to remove toxic substances from blood drops precipitously as the size of toxins increases. Our hemocompatible adsorbent technology is expected to address this shortcoming by removing toxins and toxic compounds largely untouched by dialysis technology.

Our polymer adsorbent technology can remove drugs, bioactive lipids, inflammatory mediators such as cytokines, free hemoglobin, toxins, and immunoglobulin from blood and physiologic fluids depending on the polymer construct. It is believed that the technology may have many applications in the treatment of common, chronic and acute healthcare conditions including, but not limited to, the adjunctive treatment and/or prevention of sepsis; the treatment of other critical care illnesses such as severe burn injury, trauma, acute respiratory distress syndrome and pancreatitis; the prevention of post-operative complications of cardiopulmonary bypass surgery; the treatment of cancer cachexia; the treatment of cytokine release syndrome in cancer immunotherapy, the prevention of damage to organs donated by brain-dead donors prior to organ harvest; the prevention of transfusion reactions caused by contaminants in transfused blood products; the prevention of contrast induced nephropathy, the treatment of drug overdose, and the treatment of chronic kidney failure. These applications vary by cause and complexity as well as by severity but share a common characteristic i.e. high concentrations of inflammatory mediators and toxins in the circulating blood.

Our flagship product, CytoSorb, and other products under development, including BetaSorb, ContrastSorb, and DrugSorb, consist of a cartridge containing adsorbent, porous polymer beads, although the polymers used in these devices are physically different. The cartridges incorporate industry standard connectors at either end of the device, which connect directly to the extracorporeal circuit (bloodlines) in series with a dialyzer as a standalone device. The extra-corporeal circuit consists of plastic blood tubing, our blood filtration cartridges containing adsorbent polymer beads, pressure monitoring gauges, and a blood pump to maintain blood flow. The patient's blood is accessed through a catheter inserted into his or her veins. The catheter is connected to the extra-corporeal circuit and the blood pump draws blood from the patient, pumps it through the cartridge and returns it back to the patient in a closed loop system. All of these devices are expected to be compatible with standard blood pumps or hemodialysis machines used commonly in hospitals and will therefore not require hospitals to purchase additional expensive equipment, and will require minimal training.

The polymer beads designed for the HemoDefend platform are intended to be used in multiple configurations, including a point-of-transfusion in-line filter between the blood bag and the patient, as well as a patent-pending "Beads in a Bag" configuration, where the beads are placed directly into a blood storage bag.

Markets

We are a critical care focused immunotherapy company. Immunotherapy is the ability to control the immune response to fight disease. Critical care medicine includes the treatment of patients with serious or life-threatening conditions who require comprehensive care in the ICU, with highly-skilled physicians and nurses and advanced technologies to support critical organ function to keep patients alive. Examples of such conditions include severe sepsis and septic shock, severe burn injury, trauma, acute respiratory distress syndrome and severe acute pancreatitis. In the U.S., an estimated $82 billion or 0.7% of the U.S. gross domestic product is spent annually on critical care medicine. In most larger hospitals, critical care treatment accounts for up to 20% of a hospital's overall budget and often results in financial losses for the hospital.

In many critical care illnesses, the mortality is often higher than 30%. A major cause of death is multiple organ failure, where vital organs such as the lungs, kidneys, heart and liver are damaged and no longer function properly. Such patients are kept alive with supportive care therapy, or "life support", such as mechanical ventilation, dialysis and vasopressor treatment, that is designed to keep the patient from dying while using careful patient management to tip the balance towards gradual recovery over time. Unfortunately, most supportive care therapies only help to keep patients alive by supporting organ function but do not help reverse the underlying causes of organ failure and do not help patients recover more quickly. Because of this, the treatment course is often poorly defined and highly variable, leading to lengthy ICU stays, a higher risk of adverse outcomes from hospital acquired infections, medical errors, and other factors, as well as exorbitant costs. There is an urgent need for more effective "active" therapies that can help to reverse or prevent organ failure. Our main product, CytoSorb, is a unique cytokine filter designed to try to address this void, by reducing "cytokine storm" and working to reduce the subsequent deadly inflammation that can lead to organ failure and death. Together the total addressable market to address these numerous critical care applications in the U.S. and EU with CytoSorb is estimated at $10 billion to $15 billion.

Sepsis

Sepsis is characterized by a systemic inflammatory response triggered by a severe infection. It is commonly seen in the intensive care unit, accounting for approximately 10% to 20% of all ICU admissions. However, there are currently no approved products that are available to treat sepsis in the U.S. or EU Each year, there are more than one million and 1.5 million new cases of severe sepsis or septic shock in the U.S. and Europe, respectively. Based on the reported incidence of sepsis in a number of developed countries, the worldwide incidence is estimated to be 18 million cases per year. The Global Sepsis Alliance estimates more than 27 million cases per year. According to the U.S. Centers of Disease Control and Prevention (CDC), the incidence of serious infection and sepsis has doubled in the U.S. in the past 10 years. The main driver of sepsis incidence is the aging demographic, specifically patients who are older than age 65 who are more prone to infection and now account for two-thirds of patients hospitalized for sepsis and the majority of sepsis deaths. Other factors contributing to the increase in sepsis incidence include the spread of antibiotic resistant bacteria like methicillin-resistant Staphylococcus aureus (MRSA), an increase in co-morbid conditions like HIV, cancer and diabetes that increases the risk of infection, an increasing use of implantable devices like artificial hips and knees that are prone to colonization by bacteria, and the appearance of new highly virulent or contagious strains of common pathogens such as H1N1 influenza.

There are generally three categories of sepsis, including mild to moderate sepsis, severe sepsis and septic shock. Mild to moderate sepsis typically occurs with an infection that is responsive to antibiotics or antiviral medication. An example is a patient with self-limiting influenza or a treatable community acquired pneumonia. Mortality is generally very low. Severe sepsis is sepsis with evidence of organ dysfunction. An example is a patient who develops respiratory failure due to a severe pneumonia and requires mechanical ventilation in the intensive care unit. Severe sepsis has a mortality rate of approximately 25% to 35%. Septic shock, or severe sepsis with low blood pressure that is not responsive to fluid resuscitation, is the most serious form of sepsis with an expected mortality in excess of 40% to 50%.

In sepsis, there are two major problems: the infection and the body's immune response to the infection. Antibiotics are main therapy used to treat the triggering infection, and although antibiotic resistance is growing, the infection is often eventually controlled. However, it is the body's immune response to this infection that frequently leads to the most devastating damage. The body's immune system normally produces large amounts of inflammatory mediators called cytokines to help stimulate and regulate the immune response during an infection. In severe infection, however, many people suffer from a massive, unregulated overproduction of cytokines, often termed "cytokine storm" that can kill cells and damage organs, leading to multiple organ dysfunction syndrome and multiple organ failure, and in many cases death. Until recently, there have been no available therapies in the U.S. or EU that can control the aberrant immune response and cytokine storm. Our CytoSorb device is a first-in-class, clinically-proven broad-spectrum extracorporeal cytokine filter currently approved for sale in the EU The goal of CytoSorb is to prevent or treat organ failure by reducing cytokine storm and controlling a "run-away" immune response, while antibiotics work to control the actual infection. CytoSorb has been evaluated in the randomized, controlled European Sepsis Trial in 100 patients in Germany with predominantly septic shock and acute respiratory distress syndrome or acute lung injury. The therapy was safe in more than 300 human treatments and generally well tolerated. CytoSorb demonstrated the ability to reduce a broad range of cytokines from the blood of critically ill patients. In a post-hoc analysis, this was associated with improvements in clinical outcome in two high-risk patient populations – those with very high cytokine levels and patients 65 years of age and older. We have completed a follow-up Dosing study at several clinical trial sites in Germany, supporting the safety of continuous treatment, exchanging a new device daily for up to7 days.

The only treatment that had been approved to treat sepsis in the U.S. or EU was Xigris (Eli Lilly). Because of concerns of cost, limited efficacy, and potentially dangerous side effects including the increased risk of fatal bleeding events such as intracranial bleeding for those at risk, and also because of problems with reimbursement, worldwide sales of Xigris decreased from $160M in 2009 to $104M in 2010. In October 2011, following its PROWESS SHOCK trial that demonstrated no benefit in mortality in septic shock patients, Lilly voluntarily withdrew Xigris from all markets worldwide, and is no longer available as a treatment.

Development of most other experimental therapies has been discontinued, including Eritoran from Eisai, CytoFab from BTG/Astra Zeneca, Talactoferrin from Agennix, and others. Currently, there are three late stage trials ongoing. In November 2012, an 800 patient Phase III randomized controlled SCARLET study began for Recomodulin (ART 123, Artisan/Asahi Kasei), a recombinant human thrombomodulin, for the treatment of septic patients with coagulopathy. In mid-2013, following an interim analysis of safety data, the Data Safety Monitoring Board (DSMB) recommended that the trial continue. The primary completion date of the trial is expected to be March 2015, however based on a January 2016 update to www.clinicaltrials.gov, the trial is still enrolling patients. Recomodulin has been approved in Japan since 2009 for the treatment of disseminated intravascular coagulation, a late complication of sepsis, at a cost of $5,800 per treatment. Although it has other activity, it works primarily by a similar anticoagulant mechanism to Xigris. Because of this, it has only demonstrated a limited mortality benefit (~9%: 34.6% control as compared to 26% treatment), similar to that seen in Xigris' initial PROWESS Trial (~6%: 31% control as compared to 25% treatment) and is unlikely to have greater benefit in larger scale studies.

Atox Bio is a development stage company in clinical studies with peptide therapeutics that are designed to prevent superactivation of the immune response by certain toxins such as toxic shock syndrome toxin. It is currently focused on necrotizing soft tissue infections. The investigational peptide, AB103, is being evaluated in the ACCUTE Trial; a Phase 3 randomized controlled trial in 40 investigative sites in the U.S in 290 patients with necrotizing soft tissue infections. Primary outcomes include 28-day survival, amputation, and reduction in the modified sequential organ failure assessment score. The estimated study completion date is January 2018.

Spectral Medical, Inc. is collaborating with Toray on the EUPHRATES trial, combining an endotoxin assay with extracorporeal endotoxin removal by Toraymyxin, a polymyxin-B immobilized polystyrene fiber cartridge. The study began in June 2010 and is still enrolling patients. Endotoxemia is a result of Gram negative sepsis, which only accounts for 45% of cases of sepsis. It is a potent stimulator of cytokine storm. However, all anti-endotoxin strategies have failed pivotal studies to date, believed to be the result of intervening too late in the sepsis cascade. The original trial was designed as a randomized control trial in 360 patients with septic shock and high endotoxin levels (≥ 0.60 EAA units) as confirmed by Spectral's Endotoxin Activity Assay (EAA). In a second interim analysis finalized in April 2014, following the enrollment of 184 patients with 28-day follow-up, the DSMB recommended that the trial continue. However, the expected trial size was increased to 650 patients and the exclusion criteria was modified to only accept sicker patients with a multiple organ dysfunction syndrome score greater than 9. In September 2015, Spectral reported that the composite mortality in the new subgroup had risen to ~50%, from ~30% previously. New statistical analysis on patients in the new subgroup, and comparable patients in a European treatment registry, led to a sample size recalculation of 446 evaluable patients. As of January 11, 2016, Spectral reported that trial enrollment had reached 400 patients (90% complete) and was recruiting the last 46 patients in the trial. Spectral stated that it expects to complete the trial in 2016. Because of the lack of available therapies, there remains a significant medical need for improved treatments for sepsis.

Severe sepsis and septic shock patients are amongst the most expensive patients to treat in a hospital. Because of this, we believe that cost savings to hospitals and/or clinical efficacy, rather than the cost of treatment itself, will be the determining factor in the adoption of CytoSorb in the treatment of sepsis. CytoSorb is approved in the EU and is being sold directly in Germany, Austria, and Switzerland with reimbursement in Germany and Austria at more than $500 per unit. We have established strategic partnerships with Fresenius Medical Care, the world's largest dialysis company, for exclusive distribution of CytoSorb in France, Poland, Denmark, Sweden, Norway, and Finland, and Biocon Ltd, India's largest biotechnology company, for exclusive distribution of CytoSorb in India and other select emerging markets. We have ongoing discussions with potential corporate partners and independent distributors to market CytoSorb in other select EU countries and in other countries outside the EU that accept CE Mark approval. We have established direct sales or distribution of CytoSorb in 32 countries worldwide.

We estimate that the market potential in Europe for our products is larger than that in the U.S. For example, in the U.S. and Europe, there are an estimated one million and 1.5 million new cases, respectively, of severe sepsis and septic shock annually. In Germany alone, according to the German Sepsis Society (GSS), there are approximately 154,000 cases of severe sepsis each year. Germany is the largest medical device market in Europe and the third largest in the world.

Sepsis patients are treated in the intensive care unit for 12 to 18 days on average and for a total of 20 to 25 days in the hospital. A typical severe sepsis or septic shock patient in the U.S. costs approximately $45,000 to $60,000 to treat without using CytoSorb. CytoSorb therapy for sepsis typically costs in the range of $1,000 to $5,000, depending on the number of treatments. The goal of therapy is to not only improve clinical outcomes, but to also reduce the severity of illness and reduce the need for costly ICU care (estimated at approximately$2,000 to $3,000 per day in the ICU). The cost of CytoSorb therapy represents a fraction of what is currently spent on the treatment of patients with sepsis and would be cost-effective if it decreased ICU stay by one to two days. Based upon this price point, the total addressable market for CytoSorb for the treatment of sepsis in the U.S. and EU is approximately $6billion to $8 billion.

Cardiac Surgery

There are approximately 500,000 cardiopulmonary bypass and cardiac surgery procedures performed annually in the U.S., 500,000 in the EU, and approximately 1.5 million procedures worldwide. These include relatively common procedures including coronary artery bypass graft surgery, valve replacement surgery, heart and lung transplant, aortic reconstruction, congenital heart defect repair, and left ventricular assist device implantation for the treatment of heart failure. Cardiac surgery can result in inflammation and the production of high levels of inflammatory cytokines, activation of complement, as well as hemolysis, causing the release of free hemoglobin. These can lead to post-operative complications including infection, pulmonary, renal, and neurological dysfunction. Complications lead to longer ICU recovery times and hospital stays, increased morbidity and mortality, and higher costs. An average coronary artery bypass graft procedure already costs approximately $36,000 in the U.S. without complications. According to the National Foundation for Transplants, a heart and lung transplant and first year expenses costs $1.2 million in the U.S. The use of CytoSorb to reduce cytokines and other inflammatory mediators during and after the surgical procedure may prevent or mitigate these post-operative complications. During the procedure, the CytoSorb filter can be incorporated in a bypass circuit in the heart-lung machine without the need for a separate pump, a unique competitive advantage over other technologies. After the surgery, CytoSorb can be used similarly to dialysis on patients that develop a severe post-operative inflammatory response. Direct cytokine and hemoglobin removal with CytoSorb enables it to replace the existing market for leukoreduction filters in cardiac surgery that attempt to indirectly reduce cytokines by capturing cytokine-producing leukocytes – an inefficient and suboptimal approach. Modified ultrafiltration is sometimes used after termination of cardiopulmonary bypass in cardiac surgery to remove excess fluid and inflammatory substances, but has had mixed benefit. The peri-procedural total addressable market for CytoSorb in the U.S. and EU in cardiothoracic surgery procedures is estimated to be $500 million to $1 billion.

Acute Respiratory Distress Syndrome

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are two of the most serious conditions on the continuum of respiratory failure when both lungs are compromised by inflammation and fluid infiltration, severely compromising the lung's ability to both oxygenate the blood and rid the blood of carbon dioxide produced by the body. There are an estimated 165,000 cases of acute respiratory distress syndrome in the U.S. each year, with more cases in the EU. Patients with ALI and ARDS typically require mechanical ventilation, and sometimes extracorporeal membrane oxygenation therapy, to help achieve adequate oxygenation of the blood. Patients on mechanical ventilation are at high risk of ongoing ventilator-induced lung injury, oxygen toxicity, ventilator-acquired pneumonias, and other hospital acquired infections, and outcome is significantly dependent on the presence of other organ dysfunction as well as co-morbid conditions such as pre-existing lung disease (e.g., emphysema or chronic obstructive pulmonary disease) and age. Because of this, mortality is typically greater than 30%, even with modern medicine and ventilation techniques. ALI and ARDS can be precipitated by a number of conditions including pneumonia and other infections, burn and smoke inhalation injury, aspiration, reperfusion injury and shock. Cytokine injury plays a major role in the vascular compromise and cell-mediated damage to the lung. Reduction of cytokine levels may either prevent or mitigate lung injury, enabling patients to wean from mechanical ventilation faster, potentially reducing numerous sequelae such as infection, pneumothoraces, and respiratory muscle deconditioning, and allow faster intensive care unit discharge, thereby potentially saving costs. CytoSorb treatment of patients with either ALI or ARDS in the setting of sepsis was the subject of our European Sepsis Trial where in a post-hoc analysis in patients with very high cytokine levels, we observed faster ventilator weaning in CytoSorb treated patients that showed a statistical trend to benefit. Future, prospectively defined, larger studies are required to confirm these findings. Although a number of therapies have been tried such as corticosteroids, nitric oxide, surfactant therapy, and others, there are currently no approved treatments for ARDS. Only low tidal volume ventilation has been demonstrated to improve mortality (31.0 as compared to 39.8% control) in this patient population. However, even with this intervention, mortality is still unacceptably high. The total addressable market for CytoSorb to treat ARDS and ALI in the EU is estimated to be between $500 million to $1.25 billion, and between $1 billion to $2 billion in the U.S. and EU.

Severe Burn Injury

In the U.S., there are approximately 2.4 million burn injuries per year, with 650,000 treated by medical professionals and approximately 75,000 requiring hospitalization. Aggressive modern management of burn injury, including debridement, skin grafts, anti-microbial dressings and mechanical ventilation for smoke and chemical inhalation injury has led to significant improvements in survival of burn injury to approximately 95% on average in leading burns centers. However, there remains a need for better therapies to reduce the mortality in those patients with large burns and inhalation injury as well as to reduce complications of burn injury and hospital length of stay for all patients. According to National Burn Repository Data, the average hospital stay for burn patients is directly correlated with the percent total body surface area (TBSA) burned. Every 1% increase of TBSA burned equates to approximately 1 additional day in the hospital. A single patient with more than 30% TBSA burned who survives, is hospitalized for an average of 30 days and costs approximately $200,000 to treat. Major causes of death following severe burn and smoke inhalation injury are multiple organ failure (hemodynamic shock, respiratory failure, acute renal failure) and sepsis, particularly in patients with greater than 30% TBSA burns. Specifically, burns and inhalation injury lead to severe systemic and localized lung inflammation, loss of fluid, and cytokine overproduction. This "cytokine storm" causes numerous problems, including: hypovolemic shock and inadequate oxygen and blood flow to critical organs, acute respiratory distress syndrome preventing adequate oxygenation of blood, capillary leakage resulting in tissue edema and intravascular depletion, hypermetabolism leading to massive protein degradation and catabolism and yielding increased risk of infection, impaired healing, severe weakness and delayed recovery, immune dysfunction causing a higher risk of secondary infections (wound infections, pneumonia) and sepsis, and direct apoptosis and cell-mediated killing of cells, leading to organ damage. Up to a third of severe hospitalized burn patients develop multiple organ failure and sepsis that can often lead to complicated, extended hospital courses, or death. Broad reduction of cytokine storm has not been previously feasible and represents a novel approach to limiting or reversing organ failure, potentially enabling more rapid mechanical ventilation weaning, prevention of shock, reversal of the hypermetabolic state encouraging faster healing and patient recovery, reducing hospital costs, and potentially improving survival. The total addressable market in the EU for CytoSorb to address burn and smoke inhalation injury is estimated at $150 million to $350 million and $300 million to $600 million in the U.S and EU.

Trauma

According to the National Center for Health Statistics, in the U.S., there are more than 31 million visits to hospital emergency rooms, with 1.9 million hospitalizations, and 167,000 deaths every year due to injury. The leading causes of injury are trauma from motor vehicle accidents, being struck by an object or other person, and falls. Trauma is a well-known trigger of the immune response and a surge of cytokine production or cytokine storm. In trauma, cytokine storm contributes to a systemic inflammatory response syndrome and a cascade of events that cause cell death, organ damage, organ failure and often death. Cytokine storm exacerbates physical trauma in many ways. For instance, trauma can cause hypovolemic shock due to blood loss, while cytokine storm causes capillary leak and intravascular volume loss, and triggers nitric oxide production that causes cardiac depression and peripheral dilation. Shock can lead to a lack of oxygenated blood flow to vital organs, causing organ injury. Severe systemic inflammation and cytokine storm can lead to acute lung injury and acute respiratory distress syndrome as is often seen in ischemia and reperfusion injury following severe bleeding injuries. Penetrating wound injury from bullets, shrapnel and knives, can lead to infection and sepsis, another significant cause of organ failure in trauma. Complicating matters is the breakdown of damaged skeletal muscle, or rhabdomyolysis, from blunt trauma that can lead to a massive release of myoglobin into the blood that can crystallize in the kidneys, leading to acute kidney injury and renal failure. Renal failure in trauma is associated with a significant increase in expected mortality. Cytokine and myoglobin reduction by CytoSorb and related technologies may have benefit in trauma, potentially improving clinical outcome. In December 2011 and September 2012, we were awarded a Phase I and a Phase II SBIR award, respectively, from the U.S. Army Medical Research and Materiel Command to develop our technology for the treatment of trauma and burn injury. The US Air Force is also currently funding a 30 patient human pilot study to treat trauma and rhabdomyolysis patients with CytoSorb. The total addressable market for CytoSorb for the treatment of trauma is estimated to be $1.5 billion to $2.0 billion in the U.S. and the EU.

Severe Acute Pancreatitis

Acute pancreatitis is the inflammation of the pancreas that results in the local release of digestive enzymes and chemicals that cause severe inflammation, necrosis and hemorrhage of the pancreas and local tissues. Approximately 210,000 people in the U.S. are hospitalized each year with acute pancreatitis with roughly 20% requiring ICU care. It is caused most frequently by a blockage of the pancreatic duct or biliary duct with gallstones, cancer, or from excessive alcohol use. Severe acute pancreatitis is characterized by severe pain, inflammation, and edema in the abdominal cavity, as well as progressive systemic inflammation, generalized edema, and multiple organ failure that is correlated with high levels of cytokines and digestive enzymes in the blood. Little can be done to treat severe acute pancreatitis today, except for pancreatic duct decompression with endoscopic techniques, supportive care therapy, pain control, enternal tube feeding, and fluid support. ICU stay is frequently measured in weeks and although overall ICU mortality is approximately 10%, patients with multiple organ failure have a much higher risk of death. CytoSorb may potentially benefit overall outcomes in episodes of acute pancreatitis by removing a diverse set of toxins from blood. The total addressable market for CytoSorb for the treatment of severe acute pancreatitis in the U.S. and EU is estimated to be between $400 million to $600 million.

Cancer Cachexia and Cancer Immunotherapy

Cancer cachexia is a progressive wasting syndrome characterized by rapid weight loss, anorexia, and physical debilitation that significantly contributes to death in the majority of cancer patients. Cancer cachexia is a systemic inflammatory condition, driven by excessive pro-inflammatory cytokines and other factors, that cripples the patient's physical and immunologic reserve to fight cancer. Despite afflicting millions of patients worldwide each year, there are no effective approved treatments for cancer cachexia, with only symptomatic treatments available. CytoSorb blood purification may stop or reverse cancer cachexia through broad reduction of cytokines and other inflammatory mediators, when treated over time. For example, CytoSorb efficiently removes TNF-alpha (originally called "cachectin" or "cachexin" when first isolated in cancer cachexia patients) and other major pro-inflammatory cytokines including IL-1, IL-6, and gamma interferon that can cause cachexia. This broad immunotherapy approach may lead to improved clinical outcomes while reducing patient suffering.

In February 2014, we announced a research collaboration with researchers at the University of Pennsylvania School of Veterinary Medicine to evaluate the use of CytoSorb as a treatment for cancer cachexia in animals. Demonstrating the potential benefit of CytoSorb therapy in animals may provide the data to begin evaluating the therapy in human cancer patients in the U.S. and Europe. CytoSorb is approved in the EU with a broad indication for use, allowing it to be used in any clinical situation where cytokines are elevated, including the potential treatment today of cancer related issues such as cancer cachexia. Because of this, any positive data from this collaboration could potentially be translated to human studies relatively quickly.

The collaboration will also explore the use of CytoSorb as a primary immunotherapy to treat cancer, or in synergy with more traditional chemotherapy or immunotherapy agents. Cancer cells have evolved ways to proliferate while confusing and evading the immune response. Many of these mechanisms rely on immunologic messages relayed by cytokines and other soluble factors that CytoSorb has the potential to remove. In doing so, CytoSorb may help to restore the ability of the immune system to attack cancer cells.

CytoSorb may also represent a rescue or salvage therapy in activated T-cell cancer immunotherapy, where cytokine release syndrome (i.e. cytokine storm) is common, and can lead to organ failure and death in certain patients. .

The total addressable market for CytoSorb for the treatment of cancer cachexia and cancer in the U.S. and EU is estimated to be in excess of $4 billion.

Brain-Dead Organ Donors

There are in excess of 6,000 brain dead organ donors each year in the United States; worldwide, the number of these organ donors is estimated to be at least double the U.S. brain dead organ donor population. There is a severe shortage of donor organs. Currently, there are more than 100,000 individuals on transplant waiting lists in the United States. Cytokine storm is common in these organ donors, resulting in reduced viability of potential donor organs. The potential use of CytoSorb hemoperfusion to control cytokine storm in brain dead organ donors could increase the number of viable organs harvested from the donor pool and improve the survival of transplanted organs. A proof-of-concept pilot study using our technology in human brain dead donors has been published. In addition, CytoSorb treatment in a porcine animal model of brain death demonstrated a reduction in cytokines as well as a preservation of cardiac function compared to untreated controls.

Blood Transfusions

The HemoDefend platform is a development-stage technology designed to be a practical, low cost, and effective way to safeguard the quality and safety of the blood supply. In the U.S. alone, 15 million packed red blood cell (pRBC) transfusions and another 15 million transfusions of other blood products (e.g., platelet, plasma, and cryoprecipitate) are administered each year with an average of 10% of all U.S. hospital admissions requiring a blood transfusion. The sheer volume of transfusions, not just in the U.S., but worldwide, complicates an already difficult task of maintaining a safe and reliable blood supply. Trauma, invasive operative procedures, critical care illnesses, supportive care in cancer, military usage, and inherited blood disorders are just some of the drivers of the use of transfused blood. In war, hemorrhage from trauma is a leading cause of preventable death, accounting for an estimated 30% to40% of all fatalities. For example, in Operation Iraqi Freedom, due to a high rate of penetrating wound injuries, up to 8% of admissions required massive transfusions, defined as 10 units of blood or more in the first 24 hours. There is a clear need for a stable and safe source of blood products. However, blood shortages are common and exacerbated by the finite lifespan of blood. According to the Red Cross, pRBC units have a refrigerated life span of 42 days. However, many medical experts believe there is an increased risk of infection and transfusion reactions once stored blood ages beyond two weeks. Transfusion-related acute lung injury is the leading cause of non-hemolytic transfusion-related morbidity and mortality, with an incidence of 1 in 2,000-5,000 transfusions and a mortality rate of up to 10%. Fatal cases of transfusion-related acute lung injury have been most closely related to anti-HLA or anti-granulocyte antibodies found in a donor's transfused blood. Other early transfusion reactions such as transfusion-associated dyspnea, fever and allergic reactions occur in 3% to 5% of all transfusions and can vary in severity depending on the patient's condition. These are caused by cytokines, bioactive lipids, free hemoglobin, toxins, foreign antigens, certain drugs, and a number of other inflammatory mediators that accumulate in transfused blood products during storage. Leukoreduction can remove the majority of white cells that can produce new cytokines but cannot eliminate those cytokines already in blood, and cannot otherwise remove other causative agents such as free hemoglobin and antibodies. Automated washing of pRBC is effective but is impractical due to the time, cost, and logistics of washing each unit of blood. The HemoDefend platform is a potentially superior alternative to purify blood transfusion products to these methods. The total addressable market for HemoDefend is more than $500 million for pRBCs alone.

Radiocontrast Removal

ContrastSorb is a development-stage blood purification technology that is being optimized for the removal of IV contrast from blood in order to prevent contrast-induced nephropathy (CIN). Contrast-induced nephropathy is the acute loss of renal function within the first 48 hours following IV contrast administration. IV contrast is widely administered to patients undergoing CT scans, to enhance the images and make it easier to identify anatomic structures. IV contrast is also administered during vascular interventional radiology procedures and angiography of blood vessels in the brain, heart, limbs, and other parts of the body to diagnose and treat atherosclerosis (narrowing of blood vessels due to cholesterol deposits), vascular injury, aneurysms, etc. For example, an estimated 10 million coronary angiograms are performed worldwide each year to diagnose and treat coronary artery disease by placing coronary stents, performing balloon angioplasty, or atherectomy (removal of plaque in arteries). Overall, there are an estimated 80 million doses of IV contrast administered worldwide each year, split between approximately 65 million contrast-enhanced CT scans, 10 million coronary angiograms, and 5 million conventional angiograms. There are an estimated 30 million doses administered each year in the U.S. alone. The reported risk of CIN in patients undergoing contrast enhanced CT scans has been reported to be 2% to 13%. For coronary intervention, the risk has been estimated to be as high as 20% to 30% in high risk patients with pre-existing renal insufficiency, long-term diabetes, hypertension, congestive heart failure, and older age. The use of low osmolar IV contrast, hydration of patients pre-procedure, orally administration of N-acetylcysteine, and other agents to prevent CIN have demonstrated modest benefit in some clinical studies, but in many cases, the results across studies have been equivocal and inconsistent. In high risk patients, the direct removal of IV contrast from the blood with ContrastSorb to prevent CIN represents a potentially more effective alternative. The worldwide market opportunity for ContrastSorb in this high risk group is approximately $1 billion to $2 billion.

Drug Removal

DrugSorb is a development-stage blood purification technology that is capable of removing a wide variety of drugs and chemicals from blood, as a potential treatment for drug overdose, drug toxicity, toxic chemical exposure, use in high-dose regional chemotherapy, and other applications. It has demonstrated extremely high single pass removal efficiency of a number of different drugs that exceeds the extraction capability of hemodialysis or other filtration technologies. It is similar in action to activated charcoal hemoperfusion cartridges that have been available for many years, but has the advantage of having inherent biocompatibility and hemocompatibility without coatings, and can be easily customized for specific agents.

Chronic Kidney Failure

The National Kidney Foundation estimates that more than 20 million Americans have chronic kidney disease. Left untreated, chronic kidney disease can ultimately lead to chronic kidney failure, which requires a kidney transplant or chronic dialysis (generally three times per week) to sustain life. There are approximately 400,000 patients in the U.S. currently receiving chronic dialysis and more than 3.0 million worldwide. Approximately 66% of patients with chronic kidney disease are treated with hemodialysis. One of the problems with standard high-flux dialysis is the limited ability to remove certain mid-molecular weight toxins such as β_2-microglobulin. Over time, β_2-microglobulin can accumulate and cause amyloidosis in joints and elsewhere in the musculoskeletal system, leading to pain and disability. Our BetaSorb device has been designed to remove these mid-molecular weight toxins when used in conjunction with standard dialysis. Standard dialysis care typically involves three sessions per week, averaging approximately 150 sessions per year.

Products

The polymer adsorbent technology used in our products can remove middle molecular weight toxins, such as cytokines, from blood and physiologic fluids. All of the potential applications described below (i.e., the adjunctive treatment and/or prevention of sepsis; the adjunctive treatment and/or prevention of other critical care conditions such as acute respiratory distress syndrome, burn injury, trauma and pancreatitis; the prevention of damage to organs donated by brain-dead donors prior to organ harvest; the prevention of post-operative complications of cardiopulmonary bypass surgery; the prevention of kidney injury from IV contrast; and the treatment of chronic kidney failure) share in common high concentrations of toxins in the circulating blood. However, because of the limited studies we have conducted to date, we are subject to substantial risk that our technology will have little or no effect on the treatment of any of these indications. In 2011, we completed our European Sepsis Trial of our CytoSorb device. The study was a randomized, open label, controlled clinical study in fourteen (14) sites in Germany of one hundred (100) critically ill patients with predominantly septic shock and respiratory failure. The trial successfully demonstrated the ability of CytoSorb to reduce levels of key cytokines from whole blood in treated patients, and that treatment was safe in these critically-ill patients with multiple organ failure. We completed the CytoSorb technical file review with our Notified Body and CytoSorb subsequently received EU regulatory approval under the CE Mark as an extracorporeal cytokine filter indicated for use in any clinical situation where cytokines are elevated. Given sufficient and timely financial resources, we intend to continue to commercialize in Europe and conduct additional clinical studies of our products. However, there can be no assurance that we will ever obtain regulatory approval for any other device, or that the CytoSorb device will be able to generate significant sales.

The CytoSorb Device (Critical Care)

APPLICATION: Adjunctive Therapy in the Treatment of Sepsis

Sepsis is a potentially life threatening disease defined as a systemic inflammatory response in the presence of a known or suspected infection. Sepsis is mediated by high levels of inflammatory mediators such as cytokines, which are released into the blood stream as part of the body's immune response to severe infection or injury. Excessive concentrations of these mediators cause severe inflammation and damage healthy tissues, which can lead to organ dysfunction and failure. Organ failure is the leading cause of death in the ICU. Sepsis is very expensive to treat and has a high mortality rate.

Potential Benefits: To the extent our adsorbent blood purification technology is able to prevent or reduce the accumulation of cytokines, toxins, or other inflammatory mediators in the circulating blood, we believe our products may be able to prevent or mitigate severe inflammation, organ dysfunction and failure in sepsis patients. Therapeutic goals as an adjunctive therapy include improved clinical outcome, reduced ICU and total hospitalization time, and reduced hospital costs.

Background and Rationale: We believe that the effective treatment of sepsis is the most valuable potential application for our technology. Severe sepsis (sepsis with organ dysfunction) and septic shock (severe sepsis with persistent hypotension despite fluid resuscitation) carries mortality rates of between 20% and 80%. Death can occur within hours or days, depending on many variables, including cause, severity, patient age and co-morbidities. There are approximately 1.6 million new cases of sepsis in the U.S. each year; and based on estimates by the Sepsis Alliance, the worldwide incidence is estimated to be 26 million cases annually. The incidence of sepsis is also rising due to:

1) an aging population;
2) increased incidence of antibiotic resistance;
3) increase in co-morbid conditions like cancer and diabetes; and
4) increased use of indwelling medical devices that are susceptible to infection.

In the U.S. alone, treatment of sepsis costs nearly $20 billion annually. According to the CDC, sepsis is a top ten cause of death in the U.S. The incidence of sepsis is believed to be under-reported as the primary infection (i.e., pneumonia, pyelonephritis, etc.) is often cited as the cause of death.

An effective treatment for sepsis has been elusive. Pharmaceutical companies have been trying to develop drug therapies to treat the condition. With the exception of Xigris® from Eli Lilly, no other products have been approved in either the U.S. or Europe for the treatment of sepsis. In 2011 after completing a follow up study required by the FDA, it was subsequently determined that Xigris® does not have a statistically significant mortality benefit, and Eli Lilly has withdrawn Xigris® from all markets worldwide.

Many medical professionals believe that blood purification for the treatment of sepsis holds tremendous promise. Studies using dialysis and hemofiltration technology have been encouraging, but have only had limited benefit to sepsis patients. The reason for this appears to be rooted in a primary limitation of dialysis technology itself: the inability of standard dialysis to effectively and efficiently remove significant quantities of larger toxins such as cytokines from circulating blood. CytoSorb has demonstrated the ability to safely reduce key cytokines in the blood of septic patients with multiple organ failure in our European Sepsis Trial.

The ability of CytoSorb to interact safely with blood (hemocompatibility) has been demonstrated through ISO 10993 testing, which includes testing for hemocompatibility, biocompatibility, cytotoxicity, genotoxicity, acute sensitivity and complement activation. CytoSorb use has been considered safe and well-tolerated in more than 10,000 human treatments to date.

CytoSorb has been designed to achieve broad-spectrum removal of both pro- and anti-inflammatory cytokines, preventing or reducing the accumulation of high concentrations in the bloodstream. It also removes a wide range of inflammatory mediators such as activated complement, bacterial toxins, bilirubin, and many others. This approach is intended to modulate the immune response without causing damage to the immune system. For this reason, researchers have referred to the approach reflected in our technology as immunomodulatory" therapy.

Projected Timeline: In 2011, the CytoSorb filter received EU regulatory approval under the CE Mark as an extracorporeal cytokine filter to be used in clinical situations where cytokines are elevated. Our manufacturing facility has also achieved ISO 13485:2003 Full Quality Systems certification, an internationally recognized quality standard designed to ensure that medical device manufacturers have the necessary comprehensive management systems in place to safely design, develop, manufacture and distribute medical devices in the EU. We are currently manufacturing our CytoSorb device for commercial sale in the EU. We are currently selling CytoSorb in Germany, Austria, and Switzerland with a direct sales force. Based on its CE Mark approval, CytoSorb can also be sold throughout all 28 countries of the EU and the European Economic Area and countries outside the EU that will accept European regulatory approval with registration. Overall, we have established either direct sales (as above) or distribution (via distributors or strategic partners) of CytoSorb in 32 countries worldwide. Registration of CytoSorb is typically required in each of these countries prior to active commercialization. With CE Mark approval, this can be typically achieved within several months in EU countries. Outside of the EU, the process is more variable and can take months to more than a year due to different requirements for documentation and clinical data. Variability in the timing of registration affects the initiation of active commercialization in these countries, which affects the timing of expected CytoSorb sales. We actively support all of our distributors and strategic partners in the product registration process. Outside of the EU, CytoSorb is actively being commercialized in Turkey, India, Australia, New Zealand, and Saudi Arabia, having achieved Saudi FDA approval in 2015. CytoSorb and our distribution partner in Russia have submitted all requested documentation for registration, and await a response from the Russian authorities. We cannot generally predict the timing of these registrations, and there can be no guarantee that we will ultimately achieve registration in countries where we have established distribution. We also cannot guarantee that we will generate meaningful sales in the countries where we have established registration, due to other factors such as market adoption and reimbursement. We are currently actively evaluating other potential distributor and strategic partner networks in other major countries that accept CE Mark approval. With sufficient resources and continued positive clinical data, assuming availability of adequate and timely funding, and continued positive results from our clinical studies, we intend to continue our commercialization plans for our product worldwide as well as to pursue U.S. clinical trials to seek FDA regulatory approval for CytoSorb in the U.S., the timing of which has not yet been determined.

APPLICATION: Adjunctive Therapy in Other Critical Care Applications

Potential Benefits: Cytokine-mediated organ damage and immune suppression can increase the risk of death and infection in patients with commonly seen critical care illnesses such as acute respiratory distress syndrome, severe burn injury, trauma and pancreatitis. By reducing both pro- and anti-inflammatory cytokines, CytoSorb has the potential to reduce the systemic inflammatory response and:

- prevent or mitigate multiple organ dysfunction syndrome (MODS) and/or multiple organ failure (MOF);

- prevent or reduce secondary infections;
- reduce the need for expensive life-sparing supportive care therapies such as mechanical Ventilation; and
- reduce the need for ICU care, freeing expensive critical care resources, and reducing hospital costs and costs to the healthcare system.

Background and Rationale: A shared feature of many life-threatening conditions seen in the ICU is severe inflammation (either sepsis or systemic inflammatory response syndrome) due to an over-reactive immune system and high levels of cytokines that can cause or contribute to organ dysfunction, organ failure and patient death. Examples of such conditions include severe burn injury, trauma, acute respiratory distress syndrome and severe acute pancreatitis. MODS and MOF are common causes of death in these illnesses and mortality is directly correlated with the number of organs involved. There are currently few active therapies to prevent or treat MODS or MOF. If CytoSorb can reduce direct or indirect cytokine injury of organs, it may mitigate MODS or MOF, improve overall patient outcome and reduce costs of treatment. In addition, secondary infection, such as ventilator-acquired pneumonia, urinary tract infections, or catheter-related line infections, are another major cause of morbidity and mortality in all patients treated in the ICU that increase with longer ICU stay. Prolonged illness, malnutrition, age, multiple interventional procedures, and exposure to antibiotic resistant pathogens are just some of the many risk factors for functional immune suppression and infection. In sepsis and systematic inflammatory response syndrome (SIRS), the overexpression of pro-inflammatory cytokines can also cause a depletion of immune effector cells through apoptosis and other means, and anti-inflammatory cytokines can cause profound immune suppression, both major risk factors for infection.

Projected Timeline: The EU CE Mark approval for CytoSorb as an extracorporeal cytokine filter and its broad approved indication to be used in any clinical situation where cytokines are elevated, allows it to be used "on label" in critical care applications such as acute respiratory distress syndrome, severe burn injury, trauma, liver failure, and pancreatitis, and in other conditions where cytokine storm, sepsis and/or SIRS plays a prominent role in disease pathology. Our goal is to stimulate investigator-initiated clinical studies with our device for these applications. Currently, we have or are aware of more than 50 investigator initiated, third party or company-sponsored studies being planned, with 17 enrolling, and 4 completed. We have been moving forward in parallel with a program to further understand the potential benefit of CytoSorb hemoperfusion in these conditions through additional investigational animal studies and potential human pilot studies in the U.S. funded either directly by us, through grants, or through third-parties. Commencement of these and other formal studies is contingent upon adequate funding and, in the case of U.S. human studies, FDA Investigational Device Exemption (IDE) approval of the respective human trial protocols.

APPLICATION: Prevention and treatment of post-operative complications of cardiopulmonary bypass surgery

Potential Benefits: If CytoSorb is able to prevent or reduce high levels of cytokines, free hemoglobins, and other inflammatory mediators from accumulating in the blood system during and following cardiac surgery, we anticipate that post-operative complications of cardiopulmonary bypass surgery may be able to be prevented or mitigated. The primary goals for this application are to:

- reduce ventilator and oxygen therapy requirements;
- reduce post-operative complications such as ARDS, acute kidney injury, post-perfusion syndrome, and the SIRS;
- reduce length of stay in hospital intensive care units; and
- reduce the total cost of patient care.

Background and Rationale: Due to the highly invasive nature of cardiopulmonary bypass surgery, high levels of cytokines are produced by the body, triggering severe inflammation. In addition, hemolysis of red blood cells frequently occurs, resulting in the release of free hemoglobin into the bloodstream. These inflammatory mediators can lead to post-operative complications. CytoSorb is the only cytokine reduction technology approved in the EU that can be used intraoperatively in a bypass circuit in a heart-lung machine during cardiopulmonary bypass without the need for another machine. If our products are able to prevent or reduce the accumulation of cytokines or free hemoglobin in a patient's blood stream, we may be able to prevent or mitigate post-operative complications caused by an excessive or protracted inflammatory response to the surgery. Intra-operative use of CytoSorb on high risk cardiac surgery patients, where the risk of post-operative complications is the highest, is expected to be the main initial target market. The use of CytoSorb in the post-operative period to treat post-operative SIRS is another application of the technology.

Projected Timeline: We commissioned the University of Pittsburgh to conduct a study to characterize the production of cytokines as a function of the surgical timeline for cardiopulmonary bypass surgery. An observational study of 32 patients was completed, and information was obtained with respect to the onset and duration of cytokine release. Cardiac surgeons and cardiac perfusionists in Germany and Austria have now used CytoSorb successfully intra-operatively and post-operatively on more than 1,000 cardiac surgery patients. This application is also the subject of many planned and enrolling investigator-initiated studies in Germany and Austria.

In February 2015, the FDA approved our IDE application to commence a planned U.S. cardiac surgery feasibility study called REFRESH I (REduction of FREe plaSma Hemoglobin) amongst 20 patients and three U.S. clinical sites. The FDA subsequently approved an amendment to the protocol, expanding the trial to be a 40 patient randomized controlled study (20 treatment, 20 control) in eight clinical centers. REFRESH I represents the first part of a larger clinical trial strategy intended to support the approval of CytoSorb in the U.S. for intra-operative use during cardiac surgery. The study is designed to evaluate the safety of CytoSorb when used intra-operatively in a heart-lung machine to reduce plasma free hemoglobin and cytokines in patients undergoing complex cardiac surgery. The length, complexity and invasiveness of these procedures cause hemolysis and inflammation, leading to high levels of plasma free hemoglobin, cytokines, activated complement, and other substances. These inflammatory mediators directly correlate with the incidence of serious post-operative complications such as kidney injury and failure. The goal of CytoSorb is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications. As of March 4, 2016, the trial is approximately 35% enrolled and is expected to be completed by mid-2016. If successful, we plan to file an IDE application with the FDA to begin a pivotal, registration trial called REFRESH II in the fourth quarter of 2016 or in the first quarter of 2017.

APPLICATION: *Prevention and treatment of organ dysfunction in brain-dead organ donors to increase the number and quality of viable organs harvested from donors*

Potential Benefits: If CytoSorb is able to prevent or reduce high-levels of cytokines from accumulating in the bloodstream of brain-dead organ donors, we believe CytoSorb may be able to mitigate organ dysfunction and failure, which results from severe inflammation following brain-death. The primary goals for this application are:

- improving the viability of organs which can be harvested from brain-dead organ donors, and
- increasing the likelihood of organ survival following transplant.

Background and Rationale: When brain death occurs, the body responds by generating large quantities of inflammatory cytokines. This process is similar to the systemic inflammatory response syndrome and sepsis. A high percentage of donated organs are never transplanted due to this response, which damages healthy organs and prevents transplant. In addition, inflammation in the donor may damage organs that are harvested and reduce the probability of graft survival following transplant. CytoSorb treatment in a porcine animal model of brain death demonstrated a reduction in cytokines as well as a preservation of cardiac function compared to untreated controls.

There is a shortage of donated organs worldwide, with approximately 100,000 people currently on the waiting list for organ transplants in the U.S. alone. Because there are an insufficient number of organs donated to satisfy demand, it is vital to maximize the number of viable organs donated, and optimize the probability of organ survival following transplant.

Projected Timeline: Studies have been conducted under a $1 million grant from the Health Resources and Services Administration (HRSA), an agency of the U.S. Department of Health and Human Services. Researchers at the University of Pittsburgh Medical Center and the University of Texas, Houston Medical Center have completed the observational and dosing phases of the project. The results were published in Critical Care Medicine, January 2008. The next phase of this study, the treatment phase, would involve viable donors treated with the CytoSorb device. In this phase of the project, viable donors will be treated and the survival and function of organs in transplant recipients will be tracked and measured. The treatment phase would be contingent upon further discussion with the FDA and HRSA regarding study design, as well as obtaining additional funding.

The HemoDefend Blood Purification Technology Platform (Acute and Critical Care)

APPLICATION: Reduction of contaminants in the blood supply that can cause transfusion reactions or disease when administering blood and blood products to patients.

Potential Benefits: The HemoDefend blood purification technology platform is designed to reduce contaminants in the blood supply that can cause transfusion reactions or disease. It is a development stage technology that is not yet approved in any markets, but is comprised of our highly advanced, biocompatible, polymer bead technology. If this technology is successfully developed and then incorporated into a regulatory approved product, it could have a number of important benefits, including:

- reduce the risk of transfusion reactions and improve patient outcome;
- improve the quality, or extend the shelf life of stored blood products;
- improve the availability of blood and reduce blood shortages by reducing the limitations of donors to donate blood; and
- allow easier processing of blood.

Background and Rationale: The HemoDefend technology platform was built upon our successes in designing and manufacturing porous polymer beads that can remove cytokines. We have expanded the technology to be able to remove substances as small as drugs and bioactive lipids, to proteins as large as antibodies from blood that can cause transfusion reactions and disease. Although the frequency of these reactions are relatively low (approximately3% to 5%), the sheer number of blood transfusions is so large, that the number of transfusion reactions, ranging from mild to life-threatening, is substantial, ranging from several hundreds of thousands to millions of reactions each year. In critically-ill patients, the risk of transfusion reactions is significantly higher than in the general population and can increase the risk of death because their underlying illnesses have depleted protective mechanisms and have primed their bodies to respond more vigorously to transfusion-associated insults.

A number of retrospective studies have also suggested that administration of older blood leads to increased adverse events and even increased mortality, compared with blood recently harvested. Biological studies have demonstrated the accumulation of erythrocyte storage lesions that compromise the function and structural integrity of packed red blood cells and have also demonstrated the accumulation of substances during blood storage that can lead to transfusion reactions. Three adult, prospective, randomized, controlled studies, RECESS (completed), ABLE (completed), and TRANSFUSE (ongoing) were designed to evaluate the morbidity and mortality in cardiovascular surgery patients, critically ill patients, and critically-ill patients, respectively, treated with either “new or fresh” or “older” blood. The RECESS Trial was a randomized, controlled trial in a total of 1,098 evaluable patients undergoing complex cardiac surgery given fresh blood (≤10 days old) as compared to older blood (≥21 days old). The overall conclusion was that the age of blood had no statistically significant impact on the progression to organ dysfunction (as measured by the multiple organ dysfunction syndrome score) or death. However, a statistically significant increase in hepatobiliary-related serious adverse events (5% fresh vs 9% older, p=0.02) was related to hyperbilirubinemia, possibly caused by hemolysis and release of free hemoglobin in old blood. The serious adverse event rate in both new and old blood groups was approximately 50%, which is considered high for this group of patients. There are many details and subgroup analyses that were not discussed, particularly an analysis of those patients receiving more units of blood than average, as the risk of adverse events is cumulative. The ABLE Trial was a randomized, controlled trial in 2,430 critically-ill patients receiving either fresh (≤ 7 days) or standard issue blood. There was no difference in 90-day mortality between the two groups. The outcomes of the RECESS and ABLE trials do not alter the current pressing need for better solutions to purify transfused blood products in order to reduce transfusion-related adverse events and improve clinical outcome, but suggest that age of blood is not the critical factor

Projected Timeline: The HemoDefend platform is a development stage product based on our advanced polymer technology. The base polymer is ISO 10993 biocompatible, meeting standards for biocompatibility, hemocompatibility, cytotoxicity, genotoxicity, acute sensitivity and complement activation. HemoDefend has demonstrated the *in vitro* removal of many different substances from blood such as antibodies, free hemoglobin, cytokines and bioactive lipids. We have also prototyped a number of different implementations of the HemoDefend technology, including the “Beads in a Bag” blood treatment blood storage bag, and standard in-line blood filters. The technology has been supported by the National Heart, Lung and Blood Institute (NHLBI), under a Phase I and more recently, an awarded $1.5M Phase II SBIR contract. Under the Phase II program, we expect to advance the in-line filter to human testing. We seek to out-license this technology to a strategic partner in the transfusion medicine space, but may elect to continue our development in parallel with out-licensing efforts.

ContrastSorb (Radiology and Interventional Radiology)

APPLICATION: Removal of IV contrast in blood administered during CT imaging, an angiogram, or during a vascular interventional radiology procedure, in order to reduce the risk of contrast-induced nephropathy.

Potential Benefits: IV contrast can lead to contrast-induced nephropathy (CIN), in susceptible patients. Risk factors include chronic kidney disease and renal insufficiency caused by age, diabetes, congestive heart failure, long-standing hypertension, and others co-morbid illnesses. CIN can lead to increased risk of patient morbidity and mortality. Removal of IV contrast by ContrastSorb may:

- reduce the risk of acute kidney injury
- improve the safety of these procedures and reduce the risk of morbidity and mortality

Background and Rationale: Contrast-induced nephropathy is the acute loss of renal function within the first 48 hours following IV contrast administration. IV contrast is widely administered to patients undergoing CT scans, to enhance the images and make it easier to identify anatomic structures. IV contrast is also administered during vascular interventional radiology procedures and angiography of blood vessels in the brain, heart, limbs, and other parts of the body to diagnose and treat atherosclerosis (narrowing of blood vessels due to cholesterol deposits), vascular injury, aneurysms, etc. The reported risk of CIN undergoing contrast enhanced CT scans has been reported to be 2% to 13%. For coronary intervention, the risk has been estimated to be as high as 20% to 30% in high risk patients with pre-existing renal insufficiency, and other risk factors. The use of low osmolar IV contrast, hydration of patients pre-procedure, orally administration of N-acetylcysteine, and other agents to prevent CIN have demonstrated modest benefit in some clinical studies, but in many cases, the results across studies have been equivocal and inconsistent. In high risk patients, the direct removal of IV contrast from the blood with ContrastSorb to prevent CIN represents a potentially more effective alternative.

Projected Timeline: ContrastSorb has demonstrated the high efficiency single pass removal of IV contrast and is in the process of optimization. The underlying polymer is made of the same ISO 10993 biocompatible polymer as CytoSorb, but with different structural characteristics. The ContrastSorb device is a hemoperfusion device similar in construction to CytoSorb and BetaSorb. Assuming successful optimization of the ContrastSorb polymer, safety and efficacy of IV contrast removal will need to be established in human clinical studies. We seek to out-license this technology to a potential strategic partner.

The BetaSorb Device (Chronic Care)

APPLICATION: Prevention and treatment of health complications caused by the accumulation of metabolic toxins in patients with chronic renal failure

Potential Benefits: If BetaSorb is able to prevent or reduce high levels of metabolic waste products from accumulating in the blood and tissues of long-term dialysis patients, we anticipate that certain health complications characteristic to these patients can be prevented or mitigated. The primary goals for this application are to:

- improve and maintain the general health of dialysis patients;
- reduce disability and improve the quality of life of these patients
- reduce the total cost of patient care; and
- increase life expectancy.

Background and Rationale: Our BetaSorb device is intended for use on patients suffering from chronic kidney failure who rely on long-term dialysis therapy to sustain life. Due to the widely recognized inability of dialysis to remove larger proteins from blood, metabolic waste products, such as beta$_2$-microglobulin , accumulate to toxic levels and are deposited in the joints and tissues of patients. Specific toxins known to accumulate in these patients have been linked to their severe health complications, increased healthcare costs, and reduced quality of life.

Researchers also believe that the accumulation of toxins may play an important role in the significantly reduced life expectancy experienced by dialysis patients. In the U.S., the average life expectancy of a dialysis patient is five years. Industry research has identified links between many of these toxins and poor patient outcomes. If our BetaSorb device is able to routinely remove these toxins during dialysis and prevent or reduce their accumulation, we expect our BetaSorb device to maintain or improve patient health in the long-term. We believe that by reducing the incidence of health complications, the annual cost of patient care will be reduced and life expectancy increased.

The poor health experienced by beta$_2$-microglobulin patients is illustrated by the fact that in the U.S. alone, more than $33 billion is spent annually caring for this patient population. According to the United States Renal Data System, at a cost of approximately $88,000 per patient annually.

Projected Timeline: We have collected a significant amount of empirical data for the development of this application. As the developer of this technology, we had to undertake extensive research, as no comparable technology was available for reference purposes. We have completed four human pilot studies, including a clinical pilot of six patients in California for up to 24 weeks in which our BetaSorb device removed the targeted toxin, beta$_2$-microglobulin, as expected. In total, we have sponsored clinical studies utilizing our BetaSorb device on 20 patients involving approximately 345 total treatments. Each study was conducted by a clinic or hospital personnel with us providing technical assistance as requested.

As discussed above, due to practical and economic considerations, we are focusing our efforts and resources on commercializing our CytoSorb device for critical care and cardiac surgery applications. Following commercial introduction of the CytoSorb device, and with sufficient additional resources, we may continue development of the BetaSorb resin and may conduct additional clinical studies using the BetaSorb device in the treatment of end stage renal disease patients.

Commercial and Research Partners

Biocon LTD

In September 2013, we entered into a strategic partnership with Biocon Ltd. (Biocon), India's largest biotech company, with an three-year initial Distribution Agreement, for India and select emerging markets under which Biocon has the exclusive commercialization rights for CytoSorb initially focused on sepsis. Biocon committed to annual minimum purchases to maintain marketing exclusivity. Either party may terminate the Distribution Agreement upon the occurrence of a material breach or default of any contractual obligation by the other party and the failure of the breaching party to cure the default within thirty (30) days written notice of the breach. After the first 12 months of the Distribution Agreement, either party may terminate such agreement for convenience upon 60 days' written notice. The Agreement contains standard representations and warranties of the parties.

On October 30, 2014, we entered into the First Amendment to the Distribution Agreement with Biocon, which, among other things, provided for the extension of the term of the original agreement to September 20, 2017. Pursuant to the First Amendment, the Biocon partnership was expanded to include all critical care applications and cardiac surgery. In addition, Biocon committed to higher annual minimum purchases of CytoSorb to maintain distribution exclusivity and committed to conduct and publish results from multiple investigator-initiated studies and patient case studies. Otherwise, the original terms of the Distribution Agreement remain in full force and effect.

Fresenius Medical Care AG

In December 2014, we entered into a multi-country strategic partnership with Fresenius Medical Care AG & Co KGaA, (Fresenius), to commercialize the CytoSorb therapy. Under the terms of this agreement, Fresenius has exclusive rights to distribute CytoSorb for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership will allow Fresenius to offer an innovative and easy way to use blood purification therapy for removing cytokines in patients that are treated in the intensive care unit. To promote the success of CytoSorb, Fresenius will also engage in the ongoing clinical development of the product. This includes the support and publication of a number of small case series and patient case reports as well as the potential for future larger, clinical collaborations.

Fresenius Medical Care is the one of the world's largest, integrated provider of products and services for individuals with chronic kidney failure. Through its network of more than 2,100 dialysis clinics in North America, Europe, Latin America, Asia-Pacific, and Africa, Fresenius Medical Care provides dialysis treatment to hundreds of thousands of patients around the globe. Fresenius Medical Care is also the world's largest provider of dialysis products, such as hemodialysis machines, dialyzers and related disposable products.

Separately, in 1999, we entered into an exclusive, long-term agreement with Fresenius Medical Care for the global marketing and distribution of our BetaSorb device for the treatment of renal disease, which we cancelled in 2015. We may or may not pursue our BetaSorb product after the commercialization of the CytoSorb product. At such time as we determine to proceed with our proposed BetaSorb product, if ever, we will need to conduct additional clinical studies using the BetaSorb device to obtain European or FDA approval.

Cardiac Surgery Company

In November 2014, we entered into an initial partnership agreement with a leading global medical device company in cardiac surgery and other cardiovascular diseases, to use CytoSorb intra-operatively during cardiac surgery in France. Under the terms of the agreement, the partnership commenced with an initial market evaluation period to determine various market parameters, to obtain clinical data, and to build key opinion leader support in France. Following a positive evaluation of the device during the term of the agreement, we are currently in discussions with multiple leading cardiac surgery companies for potential partnership opportunities.

University of Pittsburgh Medical Center

Two government research grants by the National Institutes of Health (NIH) and the U.S. Department of Health and Human Services have been awarded to investigators at the University of Pittsburgh to explore the use of adsorbent polymers in the treatment of sepsis and organ transplant preservation. Under “Sub Award Agreements” with the University of Pittsburgh, we have been developing polymers for use in these studies.

A grant of $1 million was awarded to the University of Pittsburgh Medical Center in 2003. The project seeks to improve the quantity and viability of organs donated for transplant by using CytoSorb to detoxify the donor’s blood. The observational and dosing phases of the study, involving 30 viable donors and eight non-viable donors, respectively, have been completed. The next phase of this study, the treatment phase, will involve viable donors. We are not currently focusing our efforts on the commercialization of CytoSorb for application in organ donors. The treatment phase would be contingent upon further discussion with the FDA and HRSA regarding study design, as well as obtaining additional funding.

In September 2005, the University of Pittsburgh Medical Center was awarded a grant of approximately $7 million from NIH entitled “Systems Engineering of a Pheresis Intervention for Sepsis (SEPsIS)” to study the use of adsorbent polymer technology in the treatment of severe sepsis. The study, which lasted for a total of five years, commenced in September 2005. Under a SubAward Agreement, we worked with researchers at the University of Pittsburgh - Critical Care Medicine Department. We believe that the only polymers used in this study were polymers we have developed specifically for use in the study, which are similar to the polymers used in our devices. Under the SubAward Agreement, for our efforts in support of the grant during 2006 through 2010, we received approximately $402,000.

These grants represent a substantial research cost savings to us and demonstrate the strong interest of the medical and scientific communities in our technology.

Researchers at UPMC have participated in nearly every major clinical study of potential sepsis intervention during the past twenty years. Drs. Derek Angus and John Kellum were investigators for Eli Lilly's sepsis drug, Xigris®. Dr. Kellum, a member of the UPMC faculty since 1994, is the Chairman of our Severe Sepsis and Inflammatory Disease Advisory Board. Dr. Kellum's research interests span various aspects of Critical Care Medicine, but center on critical care nephrology (including acid-base, and renal replacement therapy), sepsis and multiple organ failure, and clinical epidemiology. He is Professor and Vice Chair for Research in the Critical Care department, and Director of the Center for Critical Care Nephrology(CRISMA) at the University of Pittsburgh Medical Center**,** has authored more than 400 publications and has received numerous research grants from foundations and industry.

DARPA

In August 2012, we were awarded a $3.8 million, five-year contract by the Defense Advanced Research Projects Agency (DARPA), for its "Dialysis-Like Therapeutics" (DLT), program to treat sepsis. DARPA has been instrumental in funding many of the major technological and medical advances since its inception in 1958, including development of the Internet, development of GPS, and robotic surgery. The DLT program in sepsis seeks to develop a therapeutic blood purification device that is capable of identifying the cause of sepsis (e.g., cytokines, toxins, pathogens, activated cells) and remove these substances in an intelligent, automated, and efficient manner. Our contract is for advanced technology development of our hemocompatible porous polymer technologies to remove cytokines and a number of pathogen and biowarfare toxins from blood. We are in Year 3 of the program and are currently working with the systems integrator, Battelle Laboratories, and its subcontractor NxStage Medical, who are responsible for integrating the technology developed by us and others into a final medical device design prototype, and evaluating this device in septic animals and eventually in human clinical trials in sepsis. Our work is supported by DARPA and SSC Pacific under Contract No. N66001-12-C-4199. As of December 31, 2015, we have received approximately $3,499,000 to date and have approximately $301,000 not yet billed under this contract.

United States Army

In September 2012, we were awarded a Phase II Small Business Innovation Research (SBIR) contract by the US Army Medical Research and Materiel Command to evaluate our technology for the treatment of trauma and burn injury in large animal models. In 2013, we finalized the Phase II SBIR contract which provided for a maximum funding of approximately $753,000 with the granting agency. This work is supported by the U.S. Army Medical Research and Material Command under an amendment to Contract W81XWH-12-C-0038. As of December 31, 2015, we received approximately $649,000 in funding under this contract and no further amounts are expected from this contract.

National Heart, Lung, and Blood Institute (NHLBI)

In September 2013, the NHLBI, a division of the National Institutes of Health, awarded us a Phase I SBIR contract valued at $203,351 to further advance our HemoDefend blood purification technology for packed red blood cell (pRBC) transfusions. The University of Dartmouth collaborated with us as a subcontractor on the project, entitled "Elimination of blood contaminants from pRBCs using HemoDefend hemocompatible porous polymer beads. The overall goal of this program is to reduce the risk of potential side effects of blood transfusions, and help to extend the useful life of pRBCs.

In October 2015, we were awarded a Phase II or SBIR contract by the NHLBI to help advance our HemoDefend blood purification technology towards commercialization for the purification of pRBC transfusions. The contract, entitled "pRBCs Contaminant Removal with Porous Polymer Beads", provides for maximum funding of approximately $1,520,000 over a two year period, with funding to begin in 2016.

Advisory Boards

From time to time our management meets with scientific advisors who sit on our Scientific Advisory Board, our Medical Advisory Board – Critical Care Medicine, our Medical Advisory Board – Chronic Kidney Failure / Dialysis and our Scientific Advisory Board – Cardiac Surgery.

Our Scientific Advisory Board consists of three scientists with expertise in the fields of fundamental chemical research, and polymer research and development.

Our Sepsis Advisory Board consists of four medical doctors, one of whom is affiliated with UPMC, with expertise in critical care medicine, sepsis, multiple organ failure and related clinical study design.

Our Trauma Advisory Board consists of four medical doctors with expertise in trauma, burn injury and critical care medicine.

Our Cardiac Surgery Advisory Board consists of seven medical doctors with experience in cardiac surgery and complications caused by inflammation generated by the surgery.

We compensate members of our Advisory Boards at the rate of $2,000 for each full-day meeting they attend in person; $1,200 if attendance is by telephone. When we consult with members of our Advisory Board (whether in person or by telephone) for a period of less than one day, we compensate them at the rate of $200 per hour. We also reimburse members of our Advisory Boards for their travel expenses for attending our meetings.

Royalty Agreements

With Principal Stockholder

In August 2003, in order to induce Guillermina Vega Montiel, a principal stockholder of ours at the time, to make a $4 million investment in the Company, we granted Ms. Montiel a perpetual royalty equal to three percent of all gross revenues received by us from sales of CytoSorb in the applications of sepsis, cardiopulmonary bypass surgery, organ donor, chemotherapy and inflammation control. In addition, for her investment, Ms. Montiel received 1,230,770 membership units of the Company, which at the time was a limited liability company. Those membership units ultimately became 7,420 shares of our common stock following our June 30, 2006 merger. For the year ended December 31, 2015 we have recorded royalty costs of approximately $118,000.

With Purolite

In 2003, Purolite filed a lawsuit against us asserting, among other things, co-ownership and co-inventorship of certain of our patents. On September 1, 2006, the United States District Court for the Eastern District of Pennsylvania approved a Stipulated Order and Settlement Agreement under which we and Purolite agreed to the settlement of the action. The Settlement Agreement provides us with the exclusive right to use our patented technology and proprietary know how relating to adsorbent polymers for a period of 18 years. In particular, the Settlement Agreement relates to several of our issued patents and several of our pending patent applications covering our biocompatible polymeric resins, our methods of producing these polymers, and the methods of using the polymers to remove impurities from physiological fluids, such as blood.

Under the terms of the Settlement Agreement, we have agreed to pay Purolite royalties of 2.5% to 5% on the sale of those of our products, if and when those products are sold commercially, that are used in direct contact with blood. However, if the first product we offer for commercial sale is a biocompatible polymer to be used in direct contact with a physiological fluid other than blood, royalties will be payable with respect to that product as well. The royalty payments provided for under the Settlement Agreement would apply to our currently envisioned CytoSorb and BetaSorb products. For the year ended December 31, 2015 per the terms of the license agreement we have recorded royalty costs of approximately $158,000.

Following the expiration of the eighteen year term of the Settlement Agreement, the patents and patent applications that are the subject of the Settlement Agreement should have expired under current patent laws, and the technology claimed in them will be available to the public. However, following such time, we would continue to exclusively own any confidential and proprietary know how.

Product Payment & Reimbursement

CytoSorb

Europe

Payment for our CytoSorb device for the removal of cytokines in patients with life-threatening illnesses is country dependent in Europe. We are initially marketing the device in Germany where a path for separate CytoSorb reimbursement has been established. Reimbursement can also be covered by the standard "diagnosis related group" (DRG) acute care reimbursement. Under this system, hospitals would purchase CytoSorb and subtract the cost from a pre-determined lump-sum payment made by the payor to the hospital based on the patient's diagnosis. We intend to pursue reimbursement of CytoSorb in other major territories, with our partners, such as France, England, Italy and Spain, representing the other four economic leaders in Europe. Reimbursement is specific to each country. There can be no assurances that reimbursement will be granted or that additional clinical data may not be required to establish reimbursement.

United States

We have not yet sought reimbursement for the CytoSorb device in the U.S., but expect to in the future. As in Germany, payment for our CytoSorb device in the U.S. for the treatment and prevention of sepsis and other related acute care applications is initially anticipated to fall under the Diagnosis Related Group (DRG) in-patient reimbursement system, which is currently the predominant basis of hospital inpatient billing in the U.S. Under this system, predetermined payment amounts are assigned to DRGs, which are based upon diagnosis and severity or complicating conditions. All related inpatient services rendered during the applicable period for that DRG are covered by the global payment. Reimbursement is not determined by the actual procedures used in the treatment of these patients, and a separate reimbursement decision would not be required to be made by Medicare, the HMO or other provider of medical benefits in connection with the actual method used to treat the patient.

Critical care applications such as those targeted by our CytoSorb device involve a high mortality rate and extended hospitalization, coupled with extremely expensive ICU time. In view of these high costs and high mortality rates, we believe acceptance of our proprietary technology by critical care practitioners and hospital administrators will primarily depend on safety and efficacy factors rather than solely based on cost.

Competition

General

We believe that our products represent a unique approach to disease states and health complications associated with the presence of larger toxins (often referred to as middle molecular weight toxins) in the bloodstream, including sepsis, acute respiratory distress syndrome, trauma, severe burn injury, pancreatitis, post-operative complications of cardiac surgery, damage to organs donated for transplant prior to organ harvest, and renal disease. Researchers have explored the potential of using existing membrane-based dialysis technology to treat patients suffering from sepsis. These techniques are unable to effectively remove the middle molecular weight toxins. We have demonstrated the ability of CytoSorb to reduce key cytokines in the blood of human patients with predominantly septic shock and acute respiratory distress syndrome. In a post-hoc subgroup analysis of our European Sepsis Trial, we have also demonstrated statistically significant improvements in mortality in patients at high risk of death, including patients with either very high cytokine levels or patients older than age 65, both of which have a high predicted mortality. Larger studies are needed to confirm these preliminary data.

The CytoSorb, DrugSorb, ContrastSorb, and BetaSorb devices consist of a cartridge containing adsorbent polymer beads. The cartridge incorporates industry standard connectors at either end of the device which connect directly to an extra-corporeal circuit (bloodlines) on a standalone basis. The extra-corporeal circuit consists of plastic tubing through which the blood flows, our cartridge containing our adsorbent polymer beads, pressure monitoring gauges, and a blood pump to maintain blood flow. The patient's blood is accessed through a catheter inserted into his or her veins. The catheter is connected to the extra-corporeal circuit and the blood pump draws blood from the patient, pumps it through the cartridge and returns it back to the patient in a closed loop system. As blood passes over the polymer beads in the cartridge, toxins are adsorbed from the blood, without removing any fluids from the blood or the need for replacement fluid or dialysate.

There are three common forms of blood purification, including hemodialysis, hemofiltration, and hemoperfusion. All modes are generally supported by standard hemodialysis machines. All take blood out of the body to remove toxins and unwanted substances from blood, and utilize extracorporeal circuits and blood pumps. Dialysis and hemofiltration remove substances from blood by diffusion and ultrafiltration, respectively, through a semi-permeable membrane, allowing the passage of certain sized molecules across the membrane, but preventing the passage of other, larger molecules. Hemoperfusion utilizes solid or porous sorbents to remove substances based on pore capture and surface adsorption, not filtration.

CytoSorb is a hemoperfusion cartridge, using an adsorbent of specified pore size, which controls the size of the molecules which can pass into the adsorbent and vastly increases the area available for surface adsorption. As blood flows over our polymer adsorbent, middle molecules such as cytokines flow into the polymer adsorbent and are adsorbed. Our devices do not use semipermeable membranes or dialysate. In addition, our devices do not remove fluids from the blood like hemodialysis or hemofiltration. Accordingly, we believe that our technology has significant advantages as compared to traditional dialysis techniques, including ease of use.

Our HemoDefend platform is a development-stage technology utilizing a mixture of proprietary porous polymer beads that target the removal of contaminants that can cause transfusion reactions or cause disease in patients receiving transfused blood products. The HemoDefend beads can be used in multiple configurations, including the common in-line filter between the blood bag and the patient as well as a unique, patent-pending “Beads in a Bag” treatment configuration, where the beads are placed directly into a blood storage bag.

Sepsis

Researchers have explored the potential of using existing membrane-based dialysis technologies to treat patients suffering from sepsis. These techniques are unable to effectively remove middle molecular weight toxins, which leading researchers have shown to cause and complicate sepsis. The same experts believe that a blood purification technique that efficiently removes, or significantly reduces, the circulating concentrations of such toxins might represent a successful therapeutic option. CytoSorb has demonstrated the ability to remove middle molecular weight toxins, such as cytokines, from circulating blood in a statistically significant manner.

Medical research during the past two decades has focused on drug interventions aimed at chemically blocking or suppressing the function of one or two inflammatory agents. In hindsight, some researchers now believe this approach has little chance of significantly improving patient outcomes because of the complex pathways and multiple chemical factors at play. Clinical studies of these drug therapies have been largely unsuccessful. An Eli Lilly drug, Xigris®, cleared by the FDA in November 2001, is the first and only drug to be approved for the treatment of severe sepsis. Clinical studies demonstrated that use of Xigris® resulted in an average absolute 6% reduction in 28-day mortality, and an absolute 13% reduction in 28-day mortality in the most severe sepsis patients. The drug remains controversial and is considered expensive when compared to the percentage of patients who benefit. In 2011 after completing a follow up study required by the FDA, it was subsequently determined that Xigris® does not have a statistically significant mortality benefit, and in October 2011, Eli Lilly withdrew Xigris® from all markets worldwide.

Development of most other experimental therapies has been discontinued, including Eritoran from Eisai, CytoFab from BTG/Astra Zeneca, Talactoferrin from Agennix, and others. In April 2015, Leading Biosciences began a 260 patient randomized, controlled Phase 2 clinical SSAIL trial in septic shock patients using its investigational orally administered drug, LB1148, also known as tranexemic acid. Tranexemic acid is a serine protease inhibitor, designed to inhibit digestive enzymes and preserve and promote healing of the intestine’s mucosal barrier, with the goal of preventing the escape of potent digestive enzymes into the blood, which could exacerbate sepsis. Leading Biosciences expects completion of the trial in December 2016.

Currently, there are three late stage trials ongoing. In November 2012, an 800 patient Phase III randomized controlled study began for Recomodulin (ART 123, Artisan/Asahi Kasei), a recombinant human thrombomodulin, for the treatment of septic patients with coagulopathy. In mid-2013, following an interim analysis of safety data, the Data Safety Monitoring Board (DSMB) recommended that the trial continue. The primary completion date of the trial was expected to be March 2015; however, based on a January 2016 update to www.clinicaltrials.gov, the trial is still enrolling patients. Recomodulin has been approved in Japan since 2009 for the treatment of disseminated intravascular coagulation, a late complication of sepsis, at a cost of $5,800 per treatment. Although it has other activity, it works primarily by a similar anticoagulant mechanism to Xigris. Because of this, it has only demonstrated a limited mortality benefit (~9%: 34.6% control vs 26% treatment), similar to that seen in Xigris’ initial PROWESS Trial (~6%: 31% control vs 25% treatment) and is unlikely to have greater benefit in larger scale studies.

Atox Bio is a development stage company in clinical studies with peptide therapeutics that are designed to prevent superactivation of the immune response by certain toxins such as toxic shock syndrome toxin. It is currently focused on necrotizing soft tissue infections. The investigational peptide, AB103, is being evaluated in the ACCUTE Trial, a Phase 3 randomized controlled trial in 40 investigative sites in the U.S in 290 patients with necrotizing soft tissue infections. Primary outcomes include 28-day survival, amputation, and reduction in the modified sequential organ failure assessment score. The estimated study completion date is January 2018.

Using a medical device to treat sepsis remains a relatively novel treatment approach. Toray Industries currently markets an endotoxin removal cartridge called Toraymyxin™ for the treatment of sepsis in Europe, Japan, and 16 other countries, but is not yet approved in the United States. To date, it has been used in more than 100,000 treatments since 1994. Toraymyxin does not directly reduce cytokines. Spectral Medical Inc. has obtained exclusive development and commercial rights in the U.S. for Toraymyxin, with plans to combine the use of its endotoxin activity assay to create a theranostic product. Spectral is collaborating with Toray on the EUPHRATES trial, combining an endotoxin assay with extracorporeal endotoxin removal by Toraymyxin, a polymyxin-B immobilized polystyrene fiber cartridge. The study began in June 2010 and is still enrolling patients. Endotoxemia is a result of Gram negative sepsis, which only accounts for 45% of cases of sepsis. It is a potent stimulator of cytokine storm. However, all anti-endotoxin strategies have failed pivotal studies to date, believed to be the result of intervening too late in the sepsis cascade. The original trial was designed as a randomized control trial in 360 patients with septic shock and high endotoxin levels (≥ 0.60 EAA units) as confirmed by Spectral's Endotoxin Activity Assay (EAA). In a second interim analysis finalized in April 2014, following the enrollment of 184 patients with 28-day follow-up, the DSMB recommended that the trial continue. However, the expected trial size was increased to 650 patients and the exclusion criteria was modified to only accept sicker patients with a multiple organ dysfunction syndrome score greater than 9. In September 2015, Spectral reported that the composite mortality in the new subgroup had risen to ~50%, from ~30% previously. New statistical analysis on patients in the new subgroup, and comparable patients in a European treatment registry, led to a sample size recalculation of 446 evaluable patients. As of January 11, 2016, Spectral reported that trial enrollment had reached 400 patients (90% complete) and was recruiting the last 46 patients in the trial. Spectral stated that it expects to complete the trial in 2016. Because of the lack of available therapies, there remains a significant medical need for improved treatments for sepsis.

Toray also markets its Hemofeel CH1.0 polymethylmethacrylate membrane (PMMA) in Japan and it has been used in several non-controlled, or historically controlled, clinical or case studies treating patients with sepsis, acute respiratory distress syndrome and pancreatitis. We are not aware of any prospective, randomized controlled studies using this PMMA hemofilter in patients with sepsis. Without such studies, it is difficult to assess the true impact of this technology in these conditions. Gambro AB launched its Prismaflex eXeed system in August 2009 and introduced the SepteX high molecular weight cutoff hemodialyzer in Europe, intended to treat patients with acute renal failure and the removal of inflammatory mediators from blood. Gambro also launched the oXiris dialyzer, based upon the AN60 CRRT membrane, to bind endotoxin. To our knowledge, neither are specifically approved for the treatment of sepsis. In September 2013, Baxter International, Inc. acquired Gambro AB. Fresenius has launched a similar high molecular weight cut off filter called the Ultraflux EMiC2. To our knowledge, there has been a lack of published data on the treatment of sepsis with these devices. Bellco S.R.L. also sells the CPFA (coupled plasma filtration and adsorption) system in Europe. This uses a sorbent cartridge to remove cytokines from plasma. However, because the sorbent cannot treat blood directly, it requires the cost and complexity of an additional plasma separator to treat blood. This system is similar to the I.M.P.A.C.T. System being currently commercialized outside of the U.S. by Hemolife Medical Inc., that requires a three-cartridge system and a proprietary blood pump. According to Hemolife, the product is in product registration in 32 countries with initial shipments to the EU and Asia Pacific in process. We believe that CytoSorb, which can treat whole blood directly, and which works with standard hemodialysis pumps already found in hospitals worldwide, has significant competitive advantages compared to these multi-cartridge sorbent systems.

Kaneka Corporation currently markets Lixelle™, a modified porous cellulosic bead, for the removal of beta$_2$–microglobulin during hemodialysis in Japan. Lixelle has been used in several small human pilot studies including a 5 patient pilot study in 2002 and a 4 patient pilot study in 2009. Though these studies correlate Lixelle use with cytokine reduction, they are not randomized, controlled studies and so do not control for natural cytokine clearance. To our knowledge, no large, randomized, controlled trials have been conducted with Lixelle as a treatment for sepsis. Kaneka has since developed a modified cellulosic resin called CTR that can also remove cytokines from experimental pre-clinical systems. In 2009, CTR was used in an 18-patient randomized, controlled trial in patients with septic shock with undisclosed improvements in APACHE II scores and IL-6 and IL-8. To our knowledge, Kaneka has not conducted or published any other study using CTR to treat human sepsis patients since then. Ube Industries, Ltd is currently developing an adsorbent resin called CF-X for the removal of cytokines. To our knowledge, Ube has not published any study using CF-X to treat human sepsis patients. CytoPherx Inc., has developed an extracorporeal system based on selective cytapheresis, or the inactivation or removal of activated leukocytes. It was enrolling a 344 patient pivotal trial that began in August 2011 and was expected to be completed by December 2014 in patients with acute kidney injury with or without severe sepsis, on continuous renal replacement therapy with the goal of reducing mortality. This system does not remove cytokines directly, but attempts to reduce the numbers of activated white blood cells that can produce cytokines or cause cell-mediated injury. The status of the trial and the company is unknown. ExThera Medical Corporation is a privately held company that has developed its Seraph™ (Selective Removal by Apheresis) platform that consists of heparin coated, solid polyethylene beads. Heparin has the ability to bind some, but not all viruses, bacteria, toxins and cytokines. In *in vitro* studies using 1 mL of human septic blood, there was no statistically different change in IL-6 or Interferon-gamma compared to control, but effected a ~50% reduction in TNF-alpha. This inability to remove a broad range of cytokines will likely limit its efficacy as a treatment in sepsis. It has repositioned Seraph™ as a pathogen removal technology, and plans to conduct a human trial in Germany in the future. In addition, it has partnered with BioBridge Global to apply its technology to pathogen reduction in transfused blood products. Other potential competitors include the now defunct Arbios Systems, Inc. and Hemocleanse Technologies, LLC. We believe our CytoSorb cartridge has significant competitive, technological, and economic advantages over systems by these other companies.

Acute Respiratory Distress Syndrome (ARDS)

Treatment of ARDS is predominantly supportive care using supplemental oxygen, careful fluid management and multiple modes of ventilation incorporating the concepts of low tidal volume, high frequency oscillation, and prone ventilation. Corticosteroids, nitric oxide, statins, non-steroidal anti-inflammatory drugs, and surfactant therapy have been tried, but are not indicated for the treatment of ARDS. We are not aware of any specific products approved to treat ARDS.

Severe Burn Injury

Modern management of severe burn injury patients involves a combination of therapies. From a burn standpoint, patients undergo active escharotomy and debridement of burns, the use of skin grafts and substitutes, anti-microbial dressings and negative pressure dressings. Tight fluid control, nutrition, prevention of hypothermia and infection are also priorities. Smoke and chemical inhalation injury in burn victims is also common and increasing as a cause of death in severe burn injury. Carbon monoxide and cyanide poisoning is also an issue. Supplemental oxygen and mechanical ventilation are often required and are the mainstay of supportive care treatment. Recently continuous renal replacement therapy has been used to treat patients with acute kidney injury with an improvement in survival compared to a historical control cohort. We believe CytoSorb therapy may yield improved results. We are not aware of any specific products approved to directly address inhalational lung injury or multiple organ failure in severe burn injury.

Trauma

Trauma management initially involves respiratory, hemodynamic and physical stabilization of the patient. However, in the days to weeks that ensue, the focus shifts to preventing or treating organ failure and preventing or treating infection. We are not aware of any specific therapies to prevent or treat multiple organ dysfunction or multiple organ failure in trauma. Rhabdomyolysis, or the breakdown of muscle fibers due to crush injury or other means, occurs in trauma and can lead to acute kidney injury or renal failure. Aggressive hydration, urine alkalinization, and forced diuresis are the main therapies to prevent renal injury. Continuous hemodiafiltration with super-high-flux membranes has demonstrated modest myoglobin clearance but was associated with albumin loss. In general, however, most extracorporeal therapies are not well-suited to remove myoglobin. We have developed a polymer resin that removes myoglobin efficiently without major losses of albumin. The US Army Medical Research and Materiel Command has funded the development of our polymer resins to treat trauma and rhabdomyolysis under a Phase I and Phase II SBIR grant awarded to us in December 2011 and September 2012, respectively. The US Air Force is also currently funding a 30 patient human pilot study to treat trauma and rhabdomyolysis patients with CytoSorb.

Severe Acute Pancreatitis

Treatment of severe acute pancreatitis is predominantly supportive care focused on aggressive hydration, enteral nutrition and pain control. Mechanical ventilation, hemodialysis and vasopressor use is common in cases of multiple organ failure. In cases where cholelithiasis or other obstruction is the underlying cause of the pancreatitis, endoscopic retrograde cholangiopancreatography and/or stent placement can be used to relieve the obstruction. Antibiotics are often instituted to prevent or treat infection. Surgery is sometimes indicated to remove or drain necrotic or infected portions of the pancreas. To our knowledge, there are no other specific treatments approved to treat severe acute pancreatitis or multiple organ failure that is caused by systemic inflammation in this disease.

Cardiopulmonary Bypass Surgery

There is currently a pre-existing market for the use of leukocyte reduction filters sold by Pall Corporation, Terumo Medical Corporation and others in the cardiopulmonary bypass circuit. The purpose of these devices is to reduce cytokine-producing white blood cells from blood. They do not remove cytokines free hemoglobin, or activated complement directly and are not considered by many to be an effective solution for the reduction of these substances. We are not aware of any practical competitive approaches for removing cytokines, free hemoglobin, activated complement, and a broad range of other inflammatory mediators in cardiopulmonary bypass patients. To our knowledge, CytoSorb is the only cytokine reduction therapy capable of being placed directly into a bypass circuit in the heart-lung machine and used during cardiopulmonary bypass without the need for another pump. Modified ultrafiltration is sometimes used after termination of cardiopulmonary bypass in cardiac surgery to remove excess fluid and inflammatory substances, but has had mixed benefit. Alternative therapies such as “off-pump” surgeries are available but “post-bypass” syndrome and cytokine production still remain a problem in this less invasive, but more technically challenging procedure. If successful, CytoSorb is expected to be useful in both on-pump and off-pump procedures. CytoSorb is also being used with a dialysis machine to treat the development of a post-cardiac surgery systemic inflammatory response syndrome, a deadly complication of open heart surgery that if left untreated, can lead to multiple organ dysfunction syndrome, multiple organ failure, and potentially death.

Radiocontrast Removal

ContrastSorb has demonstrated the rapid, high efficiency single pass removal of IV contrast. The use of low osmolar IV contrast, oral administration of N-acetylcysteine, and other agents to prevent CIN have demonstrated modest benefit in some clinical studies, but in many cases, the results across studies have been equivocal and inconsistent. Hydration of high risk patients pre-procedure is standard of care but has limited efficacy. PLC Medical Systems, Inc., received CE Mark approval for its RenalGuard system in 2007. RenalGuard encourages excretion of IV contrast and a reduction of CIN, by administering IV hydration that matches urine output in patients receiving a loop diuretic. Hemodialysis can remove IV contrast, but is relatively slow (46% at 1 hour, 65% at 2 hours, and 75% at 3 hours) in chronic renal failure patients who lack normal renal clearance. In high risk patients, the rapid and direct removal of IV contrast from the blood with ContrastSorb to prevent CIN represents a potentially more effective alternative.

Drug Removal

Treatment of patients suffering from drug overdose often involves a number of pharmacological treatments and mechanical interventions to detoxify and stabilize the patient. Mechanical interventions include procedures such as orogastric lavage, activated charcoal, whole bowel irrigation and extracorporeal blood purification. Each method has its own limitations, many of which are associated with the timing of administration following overdose. Blood purification with high flux dialyzers or with activated charcoal cartridges by Gambro, Fresenius, Nephros and others are typically efficient at removing hydrophilic drugs that are not protein bound. However, they are inefficient at removing drugs that have a large volume of distribution, or drugs that are hydrophobic or lipophilic. Many drugs of overdose fall into this category. Resin based hemoperfusion devices have been used to remove lipophilic drugs that are protein bound, but have historically had issues of biocompatibility. DrugSorb is a highly biocompatible resin-based hemoperfusion device that can remove a wide range of drugs of overdose *in vitro* very rapidly, with high single pass removal.

Chronic Dialysis

Although standard dialysis treatment effectively removes urea and creatinine from the blood stream (which are normally filtered by functioning kidneys), standard dialysis has not been effective in removing beta$_2$-microglobulin toxins from the blood of patients suffering from chronic kidney failure. High flux dialyzers by Gambro, Fresenius, Nephros and others are capable of removing some beta$_2$-microglobulin. However, we believe our technology would significantly improve clearance of this and other toxins. Kaneka markets Lixelle™, a cellulosic resin, outside the US to remove beta$_2$-microglobulin in dialysis patients. In March 2015, Lixelle received Humanitarian Device Exemption (HDE) approval in the U.S. for the treatment of beta-amyloidosis and removal of beta$_2$-microglobulin, a complication of chronic dialysis. HDE approval applies to the treatment of diseases with an* incidence of less than 4,000 cases a year in the U.S. annually. We know of no other device, medication or therapy considered directly competitive with our technology.

Treatment of Organ Dysfunction in Brain-Dead Organ Donors

We are not aware of any directly competitive products to address the application of our technology for the mitigation of organ dysfunction and failure resulting from severe inflammation following brain-death.

HemoDefend Purification Technology Platform for Transfused Blood Products

There are only a few directly competitive approved products to address the removal of substances from blood and blood products that can cause transfusion reactions. Leukoreduction (Pall Corporation, Terumo-BCT, Hemerus Corporation, others) is widely used in transfusion medicine and can remove the majority of white cells that can produce new cytokines but cannot eliminate those cytokines already in blood, and cannot otherwise remove other causative agents. Automated washing of pRBC is very effective at cleansing contaminants from blood, but is impractical due to the time, cost, materials, and logistics of washing each unit of blood and is not widely used. Blood filters that utilize affinity technologies are in development to remove certain substances such as antibodies from blood, but have other issues, such as cost and concern about the stability or leachability of the affinity technology. The HemoDefend platform represents a potentially superior alternative to these methods, as it can provide comprehensive removal of a wide variety of contaminants that can trigger transfusion reactions without washing blood, requires no additional equipment, energy source, or manipulation, and can be incorporated directly into the blood storage bag or used as an in-line blood filter.

Clinical Studies

Our first clinical studies were conducted in patients with chronic renal failure. The health of these patients is challenged by high levels of toxins circulating in their blood but, unlike sepsis patients, they are not at imminent risk of death. The toxins involved in chronic renal failure are generally different from those involved in sepsis, eroding health gradually over time. The treatment of patients with chronic renal failure is a significant target market for us, although not the current focus of our efforts and resources. Our clinical studies and product development work in this application functioned to obtain safety and treatment data without the need to put the patient at additional risk (e.g., placing a new temporary dialysis catheter) with direct benefit to the development of the critical care applications on which we are now focusing our efforts.

We are focusing our research efforts on critical care and cardiac surgery applications of our technology.

Sepsis

In 2011, the CytoSorb filter received EU regulatory approval under the CE Mark as an extracorporeal cytokine filter to be used in clinical situations where cytokines are elevated. As part of the CE Mark approval process, we completed our randomized, controlled, European Sepsis Trial amongst fourteen trial sites in Germany, with enrollment of 100 patients with sepsis and respiratory failure. The purpose of the trial was to demonstrate safety and the broad reduction of key cytokines such as IL-6 in critically-ill patients. Taking into account all 100 patients, the treatment was well-tolerated and considered safe in more than 300 human treatments in the trial. Although the trial was not powered to demonstrate significant reduction in other clinical endpoints such as mortality, these were also included as secondary and exploratory endpoints in the trial.

The first 22 patients in the study represented a sepsis pilot study. In the next 31 patients, a compromise of the manual randomization schedule at two trial sites led to an imbalance in the severity of illness between the control and treatment patient groups of the study. After a thorough review, the Scientific Advisory Board and the independent Data Safety Monitoring Board both recommended that due to this enrollment bias, these 31 patients should only be used for safety evaluation purposes and that new patients should be enrolled into the trial using electronic web-based randomization to randomly assign patients into either the control or treatment arms.

Excluding four patients that withdrew, the remaining 43 patients enrolled under electronic randomization were relatively balanced in terms of the severity of illness in treatment and control patients, confirming the findings of the Scientific Advisory Board and DSMB. An independent Contract Research Association, RCRI, Inc. (Minneapolis, MN),, analyzed these 43 patients the European Sepsis Trial and showed on a statistically significant basis ($p<0.05$), the ability of CytoSorb to reduce circulating levels of key cytokines from whole blood in treated patients on the average of 30% to 50% over the seven day treatment period. Additionally, post-hoc subgroup analyses of the clinical outcome data from patients enrolled under electronic randomization demonstrated statistically significant reduction in mortality in patients at high risk of death in sepsis, specifically in patients with:

- very high cytokine levels (IL-6 ≥ 1,000 pg/mL and/or IL-1ra ≥ 16,000 pg/mL) where 28-day mortality was 0% treated as compared to 63% control, p=0.03, n=14, and
- an age ≥ 65 (14-day mortality: 0% treated as compared to 36% control, p=0.04, n=21).

In patients aged ≥ 65 years old, however, seven days of treatment with CytoSorb was not adequate to extend the observed 14-day mortality benefit out to 28-days (40% as compared to 45% control, p=0.6, n=21). These critically ill patients carried two major mortality risk factors: multiple organ failure and age ≥ 65 years old, which itself confers a 2.3-fold relative risk of death. Treatment of life-threatening infections with antibiotics often requires seven to 14 days of treatment. We hypothesize that treatment of the “run-away” immune response should mirror treatment with antibiotics. We have completed enrollment of a dose ranging study (Dosing Study) in Germany amongst several clinical trial sites to evaluate the safety and efficacy of CytoSorb when used continuously for 7 days, each day with a new device and are conducting final statistical analysis of the data. Patients are being stratified for age, cytokine levels, and co-morbid illnesses in this matched pairs analysis.

At the end of 2013, we reported a clinical update on the first 28 treated patients that were enrolled in the first arm of the Dosing study (24 hours of treatment for seven days, each day with a new device). Treatment was safe and well-tolerated at flow rates up to 300 mL/min, with no serious device related adverse events. Twenty-four-hour treatment increased platelet reduction compared to six-hour treatment in the EST, but with no reported complications. Broad spectrum antibiotics, such as the carbapenem class, were compatible with CytoSorb, requiring only modest dose adjustments. IL-6 reduction continued throughout the entire 24-hour period, higher at the beginning of treatment when IL-6 levels are highest, and with an overall average instantaneous IL-6 reduction of 8% per pass. In this preliminary analysis, the overall 28-day all-cause mortality and 28-day all-cause mortality in patients 65 years and older was not statistically different from the treatment data reported in the EST (electronic randomized cohort). Severity of illness in the overall treatment groups were comparably high, with 50% or more of the treated patients (dosing > EST) having an APACHE II severity of illness score > 25 at the time of enrollment, predicting very high mortality of 55% or more. In comparison, the overall control patients reported in the EST (electronic randomization cohort) had a lower severity of illness with only 20% having an APACHE 2 score > 25. Once final statistical analysis of the data is completed, the principal investigator and writing committee expects to submit the data for publication.

In 2007, we received FDA approval of our Investigational Device Exemption (IDE) application to run a single center sepsis study in the U.S. Assuming availability of adequate and timely funding, and continued positive results from our clinical studies, we intend to continue commercializing our product in Europe while pursuing additional sepsis studies in both the U.S. and the EU.

Cardiac Surgery

In February 2015, the FDA approved our IDE application to commence a planned U.S. cardiac surgery safety and feasibility study called REFRESH I (REduction of FREe plaSma Hemoglobin) amongst 20 patients and three U.S. clinical sites. The FDA subsequently approved an amendment to the protocol, expanding the trial to be a 40 patient randomized controlled study (20 treatment, 20 control) in eight clinical centers. REFRESH I represents the first part of a larger clinical trial strategy intended to support the approval of CytoSorb in the U.S. for intra-operative use during cardiac surgery.

The study is designed to evaluate the safety of CytoSorb when used intra-operatively in a heart-lung machine to reduce plasma free hemoglobin and cytokines in patients undergoing complex cardiac surgery. The length, complexity and invasiveness of these procedures cause hemolysis and inflammation, leading to high levels of plasma free hemoglobin, cytokines, activated complement, and other substances. These inflammatory mediators directly correlate with the incidence of serious post-operative complications such as kidney injury and failure. The goal of CytoSorb is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications. As of March 4, 2016, the trial is approximately 35% enrolled and is expected to be completed by mid-2016.

Trauma

In June 2013, we announced that the U.S. Air Force would fund a 30 patient, single site, randomized controlled human pilot study in the U.S. amongst trauma patients with rhabdomyolysis most commonly associated with trauma. The primary endpoint is myoglobin removal. The FDA approved our IDE application for this study and we also received ethics committee approval, allowing the study to commence. However, because of the stringency of our inclusion criteria, and because of the patient mix seen at our single center, we have experienced difficulty in enrolling patients. We have subsequently modified one of the key inclusion criteria and have expanded the number of clinical trial sites to three in a revised protocol.

Other Critical Care Applications

There are currently more than 50 ongoing investigator initiated studies being planned, with 17 enrolling and four completed in our commercialized territories. These trials, which are funded and supported by renowned university hospitals and key opinion leaders, will provide invaluable information regarding the success of the device in the treatment of sepsis, cardiac surgery, trauma, burn injury, pancreatitis, liver failure, acute kidney injury, acute respiratory distress syndrome, and many other indications, and will be integral to helping us determine the ultimate course of our U.S. clinical trial pathway in critical care.

Even though we have obtained CE Mark approval, no assurance can be given that our CytoSorb product will work as intended in these studies or that we will be able to obtain FDA approval to sell CytoSorb in the U.S. Even though we have obtained CE Mark approval, there is no guarantee or assurance that we will be successful in obtaining FDA approval in the United States or approval in any other country or jurisdiction. Because of the limited studies we have conducted, we are subject to substantial risk that our technology will have little or no effect on the treatment of any indications that we have targeted.

Government Research Grants

Two government research grants by the National Institutes of Health (NIH) and the U.S. Department of Health and Human Services have been awarded to investigators at the University of Pittsburgh to explore the use of adsorbent polymers in the treatment of sepsis and organ transplant preservation. Under "SubAward Agreements" with the University of Pittsburgh, we have been developing polymers for use in these studies.

A grant of $1 million was awarded to the University of Pittsburgh Medical Center in 2003. The project seeks to improve the quantity and viability of organs donated for transplant by using CytoSorb to detoxify the donor's blood. The observational and dosing phases of the study, involving 30 viable donors and eight non-viable donors, respectively, have been completed. The next phase of this study, the treatment phase, will involve viable donors. We are not currently focusing our efforts on the commercialization of CytoSorb for application in organ donors. The treatment phase would be contingent upon further discussion with the FDA and HRSA regarding study design, as well as obtaining additional funding.

In addition, in September 2005, the University of Pittsburgh Medical Center was awarded a grant of approximately $7 million from NIH entitled "Systems Engineering of a Pheresis Intervention for Sepsis (SEPsIS)" to study the use of adsorbent polymer technology in the treatment of severe sepsis. The study, which lasted for a total of five years, commenced in September 2005. Under a SubAward Agreement, we worked with researchers at the University of Pittsburgh - Critical Care Medicine Department. We believe that the only polymers used in this study were polymers we have developed specifically for use in the study, which are similar to the polymers used in our devices. Under the SubAward Agreement, for our efforts in support of the grant during 2006 through 2010, we received approximately $402,000.

In October 2010, we were awarded a grant of approximately $489,000 from the federal Qualifying Therapeutic Discovery Project (QTDP) program for two products in our pipeline including the development of CytoSorb for the treatment of sepsis and other critical care illnesses. We received half of the grant in November 2010 and the second half in February 2011.

In December 2011, we were awarded a $100,000 Phase I SBIR contract, and subsequently a $50,000 Phase I extension, by the US Army Medical Research and Materiel Command to evaluate our technology for the treatment of trauma and burn injury in large animal models. In September 2012, we were awarded a Phase II SBIR contract which provided for a maximum funding of approximately $753,000 with the granting agency. This work is supported by the U.S. Army Medical Research and Material Command under an amendment to Contract W81XWH-12-C-0038. As of December 31, 2015, we received approximately $649,000 in funding under this contract and no further amounts are expected from this contract.

In August 2012, we were awarded a $3.8 million, five-year contract by DARPA for its "Dialysis-Like Therapeutics" (DLT), program to treat sepsis. DARPA has been instrumental in funding many of the major technological and medical advances since its inception in 1958, including development of the Internet, development of GPS, and robotic surgery. The DLT program in sepsis seeks to develop a therapeutic blood purification device that is capable of identifying the cause of sepsis (e.g., cytokines, toxins, pathogens, activated cells) and remove these substances in an intelligent, automated, and efficient manner. Our contract is for advanced technology development of our hemocompatible porous polymer technologies to remove cytokines and a number of pathogen and biowarfare toxins from blood. We are in Year 4 of the program and is currently working with the systems integrator, Battelle Laboratories, and its subcontractor NxStage Medical, who are responsible for integrating the technology developed by us and others into a final medical device design prototype, and evaluating this device in septic animals and eventually in human clinical trials in sepsis. Our work is supported by DARPA and SSC Pacific under Contract No. N66001-12-C-4199. As of December 31, 2015, we have received approximately $3,499,000 to date and have approximately $301,000 not yet billed under this contract.

In September 2012, we were awarded a Phase II SBIR contract by the US Army Medical Research and Materiel Command to evaluate our technology for the treatment of trauma and burn injury in large animal models. In 2013, we finalized the Phase II SBIR contract which provided for a maximum funding of approximately $753,000 with the granting agency. This work is supported by the U.S. Army Medical Research and Material Command under an amendment to Contract W81XWH-12-C-0038. As of December 31, 2015, we received approximately $649,000 in funding under this contract and no further amounts are expected from this contract.

In June 2013, we announced that the U.S. Air Force will fund a 30 patient, single site, randomized controlled human pilot study in the U.S. amongst trauma patients with rhabdomyolysis. The primary endpoint is myoglobin removal. The FDA approved our IDE application for this study and we also received ethics committee approval, allowing the study to commence. However, because of the stringency of our inclusion criteria, and because of the patient mix seen at our single center, we have experienced difficulty in enrolling patients. We have subsequently modified one of the key inclusion criteria and have expanded the number of clinical trial sites to three in a revised protocol. Though we do not expect to receive material direct funding from this $3 million budgeted program, the study may generate valuable data that can be used commercially or in future trauma studies.

In September 2013, the National Heart, Lung, and Blood Institute (NHLBI) awarded us a Phase I SBIR contract to further advance our HemoDefend blood purification technology for packed red blood cell (pRBC transfusions. The project, entitled "Elimination of blood contaminants from pRBCs using HemoDefend hemocompatible porous polymer beads," is valued at $203,351 over six months. The overall goal of this new program is to reduce the risk of potential side effects of blood transfusions, and help to extend the useful life of pRBCs. As of December 31, 2014, we successfully completed the Phase I program.

In October 2015, we were awarded a Phase II SBIR, contract by NHLBI, to help advance our HemoDefend blood purification technology towards commercialization for the purification of pRBC transfusions. The contract, entitled "pRBCs Contaminant Removal with Porous Polymer Beads", provides for maximum funding of approximately $1,520,000 over a two year period, with funding to begin in 2016.

Our business could be adversely impacted by automatic cuts in Federal spending. The American Taxpayer Relief Act (ATRA) of 2012, referred to generally as the fiscal cliff deal, that went into effect on March 1, 2013, enacted automatic spending cuts of nearly $1 trillion over the next 10 years (commonly known as sequestration) that were included under the Budget Control Act of 2011. Sequestration may delay payments under the DARPA and SBIR grant agreements, although no material delays have occurred to date. The short term and long term economic impact of the sequestration will not be known until the actual spending cuts are implemented and the economic impact of the changes in the budget and taxes are known. It will take an extended number of years to understand the impact of any changes brought about from the sequester.

These grants represent a substantial research cost savings to us and we believe demonstrate the strong interest of the medical and scientific communities in our technology.

Regulation

The medical devices that we manufacture are subject to regulation by numerous regulatory bodies, including the FDA and comparable international regulatory agencies. These agencies require manufacturers of medical devices to comply with applicable laws and regulations governing the development, testing, manufacturing, labeling, marketing and distribution of medical devices. Devices are generally subject to varying levels of regulatory control, the most comprehensive of which requires that a clinical evaluation program be conducted before a device receives approval for commercial distribution.

In the EU, medical devices are required to comply with the Medical Devices Directive and obtain CE Mark certification in order to market medical devices. The CE Mark certification, granted following approval from an independent Notified Body, is an international symbol of adherence to quality assurance standards and compliance with applicable European Medical Devices Directives. Distributors of medical devices may also be required to comply with other foreign regulations such as Ministry of Health Labor and Welfare approval in Japan. The time required to obtain these foreign approvals to market our products may be longer or shorter than that required in the U.S., and requirements for those approvals may differ from those required by the FDA.

In March 2011, we successfully completed our technical file review with our Notified Body, and received approval to apply the CE Mark to the CytoSorb device as an extracorporeal cytokine filter. We also achieved ISO 13485:2003 Full Quality Systems certification, an internationally recognized quality standard designed to ensure that medical device manufacturers have the necessary comprehensive management systems in place to safely design, develop, manufacture and distribute medical devices in the EU. In February 2015, we extended the coverage of our ISO 13485 Certificate with the inclusion of Canadian Quality Systems requirements. This additional level of certification will allow us to apply for product approvals in Canada in the future.

In the U.S., specific permission from FDA to distribute a new device is usually required (that is, other than in the case of very low risk devices), and we expect that some form of marketing authorization will be necessary for our devices. Marketing authorization is generally sought and obtained in one of two ways. The first process requires that a pre-market notification (510(k) Submission) be made to the FDA to demonstrate that the device is as safe and effective as, or "substantially equivalent" to, a legally marketed device that is not subject to pre-market approval (PMA). A legally marketed device is a device that (i) was legally marketed prior to May 28, 1976, (ii) has been reclassified from Class III to Class II or I, or (iii) has been found to be substantially equivalent to another legally marketed device following a 510(k) Submission. The legally marketed device to which equivalence is drawn is known as the "predicate" device. Applicants must submit descriptive data and, when necessary, performance data to establish that the device is substantially equivalent to a predicate device. In some instances, data from human clinical studies must also be submitted in support of a 510(k) Submission. If so, these data must be collected in a manner that conforms with specific requirements in accordance with federal regulations including the Investigational Device Exemption (IDE) and human subjects protections or "Good Clinical Practice" regulations. After the 510(k) application is submitted, the applicant cannot market the device unless FDA issues "510(k) clearance" deeming the device substantially equivalent. After an applicant has obtained clearance, the changes to existing devices covered by a 510(k) Submission which do not significantly affect safety or effectiveness can generally be made without additional 510(k) Submissions, but evaluation of whether a new 510(k) is needed is a complex regulatory issue, and changes must be evaluated on an ongoing basis to determine whether a proposed change triggers the need for a new 510(k), or even premarket approval (PMA). The 510(k) clearance pathway is not available for all devices: whether it is a suitable path to market depends on several factors, including regulatory classifications, the intended use of the device, and technical and risk-related issues for the device.

The second, more rigorous, process requires that an application for premarket approval (PMA) be made to the FDA to demonstrate that the device is safe and effective for its intended use as manufactured. This approval process applies to most Class III devices. A PMA submission includes data regarding design, materials, bench and animal testing, and human clinical data for the medical device. Again, clinical trials are subject to extensive FDA regulation. Following completion of clinical trials and submission of a PMA, the FDA will authorize commercial distribution if it determines there is reasonable assurance that the medical device is safe and effective for its intended purpose. This determination is based on the benefit outweighing the risk for the population intended to be treated with the device. This process is much more detailed, time-consuming, and expensive than the 510(k) process. Also, FDA may impose a variety of conditions on the approval of a PMA.

In the U.S., we believe that our potential devices, if we were to pursue marketing authorization, would likely fall under the classification for "Sorbent Hemoperfusion Systems" (21 C.F.R. § 876.5870). This category of device is Class II (subject to a 510(k) and special controls) when the device is intended for the treatment of poisoning and drug overdose, and Class III (subject to premarket approval) when the device is intended for the treatment of hepatic coma and metabolic disturbances or other life-threatening illnesses.

Both before and after a device for the U.S. market is commercially released, we would have ongoing responsibilities under FDA regulations. The FDA reviews design and manufacturing practices, labeling and record keeping, and manufacturers' required reports of adverse experiences and other information to identify potential problems with marketed medical devices. We would also be subject to periodic inspection by the FDA for compliance with the FDA's quality system regulations, which govern the methods used in, and the facilities and controls used for, the design, manufacture, packaging, and servicing of all finished medical devices intended for human use. In addition, the FDA and other U.S. regulatory bodies (including the Federal Trade Commission, the Office of the Inspector General of the Department of Health and Human Services, the Department of Justice (DOJ), and various state Attorneys General) monitor the manner in which we promote and advertise our products. Although physicians are permitted to use their medical judgment to employ medical devices for indications other than those cleared or approved by the FDA, we are prohibited from promoting products for such "off-label" uses, and can only market our products for cleared or approved uses. If the FDA were to conclude that we are not in compliance with applicable laws or regulations, or that any of our medical devices are ineffective or pose an unreasonable health risk, the FDA could require us to notify health professionals and others that the devices present unreasonable risks of substantial harm to the public health, order a recall, repair, replacement, or refund of such devices, detain or seize adulterated or misbranded medical devices, or ban such medical devices. The FDA may also impose operating restrictions, enjoin and/or restrain certain conduct resulting in violations of applicable law pertaining to medical devices, including a hold on approving new devices until issues are resolved to its satisfaction, and assess civil or criminal penalties against our officers, employees, or us. The FDA may also recommend prosecution to the DOJ. Conduct giving rise to civil or criminal penalties may also form the basis for private civil litigation by third-party payers or other persons allegedly harmed by our conduct.

The delivery of our devices in the U.S. market would be subject to regulation by the U.S. Department of Health and Human Services and comparable state agencies responsible for reimbursement and regulation of health care items and services. U.S. laws and regulations are imposed primarily in connection with the Medicare and Medicaid programs, as well as the government's interest in regulating the quality and cost of health care.

Federal health care laws apply when we or customers submit claims for items or services that are reimbursed under Medicare, Medicaid, or other federally-funded health care programs. The principal federal laws include: (1) the False Claims Act which prohibits the submission of false or otherwise improper claims for payment to a federally-funded health care program; (2) the Anti-Kickback Statute which prohibits offers to pay or receive remuneration of any kind for the purpose of inducing or rewarding referrals of items or services reimbursable by a Federal health care program; (3) the Stark law which prohibits physicians from referring Medicare or Medicaid patients to a provider that bills these programs for the provision of certain designated health services if the physician (or a member of the physician's immediate family) has a financial relationship with that provider; and (4) health care fraud statutes that prohibit false statements and improper claims to any third-party payer. There are often similar state false claims, anti-kickback, and anti-self referral and insurance laws that apply to state-funded Medicaid and other health care programs and private third-party payers. In addition, the U.S. Foreign Corrupt Practices Act can be used to prosecute companies in the U.S. for arrangements with physicians, or other parties outside the U.S. if the physician or party is a government official of another country and the arrangement violates the law of that country.

The laws applicable to us are subject to change, and subject to evolving interpretations. If a governmental authority were to conclude that we are not in compliance with applicable laws and regulations, we and our officers and employees could be subject to severe criminal and civil penalties including substantial fines and damages, and exclusion from participation as a supplier of product to beneficiaries covered by Medicare or Medicaid.

In Europe, our devices are classified as Class IIb, and will need to conform to the Medical Devices Directive.

The process of obtaining clearance to market products is costly and time-consuming in virtually all of the major markets in which we expect to sell products and may delay the marketing and sale of our products. Countries around the world have recently adopted more stringent regulatory requirements, which are expected to add to the delays and uncertainties associated with new product releases, as well as the clinical and regulatory costs of supporting those releases. No assurance can be given that any of our other medical devices will be approved on a timely basis, if at all, or that our CytoSorb® device will be approved for CE Mark labeling in other potential medical applications or that it will be approved for cytokine filtration in markets not covered by the CE Mark on a timely basis, or at all. In addition, regulations regarding the development, manufacture and sale of medical devices are subject to future change. We cannot predict what impact, if any, those changes might have on our business. Failure to comply with regulatory requirements could have a material adverse effect on our business, financial condition and results of operations.

Exported devices are subject to the regulatory requirements of each country to which the device is exported. Some countries do not have medical device regulations, but in most foreign countries medical devices are regulated. Frequently, device companies may choose to seek and obtain regulatory approval of a device in a foreign country prior to application in the U.S., as we have done, given the differing regulatory requirements. However, this does not ensure approval of a device in the U.S.

Sales and Marketing

In 2012, we established our European subsidiary, CytoSorbents Europe GmbH, a wholly-owned subsidiary of CytoSorbents Corporation. Following the completion of a controlled market release in late June 2012, CytoSorb was formally launched in Germany with reimbursement established at more than $500 per cartridge. We recruited Dr. Christian Steiner, MD as our Vice President of Sales and Marketing and hired three additional sales representatives who completed training in the third quarter of 2012. The fourth quarter of 2012 was the first full quarter of direct CytoSorb sales with our sales force in place. We began expansion into Austria, where reimbursement for CytoSorb is now available, and Switzerland. From the beginning of the controlled market release in the fourth quarter of 2011 through the end of December 31, 2015, we achieved cumulative sales of approximately $8,189,000 in sales of CytoSorb. At the end of 2015, we had hundreds of key opinion leaders (KOLs) worldwide who are either using CytoSorb or supporting its use in clinical practice and/or in clinical studies. These KOL relationships were an essential step in our initial goal of driving usage, adoption and reorders of CytoSorb as they facilitate ordering and reimbursement within the hospital, have a strong influential role within their department and amongst their peers and colleagues outside the hospital, and have the ability to conduct studies and generate data, papers and conference presentations that could drive awareness and demand.

We are approved to sell CytoSorb in all 28 countries in the EU and the countries in the European Economic Area, including Germany, the United Kingdom, Italy, France and Spain, and currently have either direct sales or distributor or strategic partnership in 32 countries worldwide. We plan to expand to other countries in the EU, and with registration, other countries outside the EU that will accept CE Mark approval with a mixed direct and independent distributor strategy, that can be augmented through strategic partnerships.

In 2013, we reached agreements with distributors in the United Kingdom, Ireland, Turkey, Russia, and the Netherlands. In April 2014, we announced distribution of CytoSorb in the Middle East, including Saudi Arabia, the United Arab Emirates, Kuwait, Qatar, Bahrain, and Oman (the Gulf Cooperative Council (GCC)) and Yemen, Iraq, and Jordan through an exclusive agreement with Techno Orbits. In August 2014, we announced exclusive distribution of CytoSorb in Taiwan with Hemoscien Corporation, which was subsequently terminated by us in March 2015 due to the complexity of Taiwanese FDA product registration. In December 2014, we entered into an exclusive agreement with Smart Medical Solutions S.R.L., to distribute CytoSorb for critical care applications in Romania and the neighboring Republic of Moldova. In 2015, we announced exclusive distribution agreements with Aferetica SRL to distribute CytoSorb in Italy, AlphaMedix Ltd. to distribute CytoSorb in Israel, TekMed Pty Ltd. to distribute CytoSorb in Australia and New Zealand, and Hoang Long Pharma to distribute CytoSorb in Vietnam.

We have been expanding the number and scope of our strategic partnerships. In September 2013, we entered into a strategic partnership with Biocon, Ltd., India's largest biotech company with an initial distribution agreement for India and select emerging markets, under which Biocon will have the exclusive commercialization rights for CytoSorb initially focused on sepsis. In September 2014, the Biocon partnership was expanded to include all critical care applications and cardiac surgery. In addition, Biocon committed to higher annual minimum purchases of CytoSorb to maintain distribution exclusivity and conduct and publish results from multiple investigator initiated studies and patient case studies.

In addition, in November 2014, we entered into an initial partnership agreement with a leading global medical device company in cardiac surgery and other cardiovascular diseases, to use CytoSorb intra-operatively during cardiac surgery in France. Following positive evaluation of the device during the term of the agreement, we are now in discussions with multiple potential cardiac surgery partners for distribution rights to CytoSorb in the field of cardiac surgery.

In December 2014, we entered into a multi-country strategic partnership with Fresenius Medical Care AG & CO KGaA to commercialize the CytoSorb therapy. Under the terms of the agreement, Fresenius Medical Care has exclusive rights to distribute CytoSorb for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership will allow Fresenius Medical Care to offer an innovative and easy to use blood purification therapy for removing cytokines in patients that are treated in the intensive care unit. To promote the success of CytoSorb, Fresenius will also engage in the ongoing clinical development of the product. This includes the support and publication of a number of small case series and patient case reports as well as the potential for future larger, clinical collaborations.

Intellectual Property and Patent Litigation

The medical device market in which we primarily participate is in large part technology driven. As a result, intellectual property rights, particularly patents and trade secrets, play a significant role in product development and differentiation. However, intellectual property litigation to defend or create market advantage is inherently complex, unpredictable and is expensive to pursue. Litigation often is not ultimately resolved until an appeal process is completed and appellate courts frequently overturn lower court patent decisions.

Moreover, competing parties frequently file multiple suits to leverage patent portfolios across product lines, technologies and geographies and to balance risk and exposure between the parties. In some cases, several competitors are parties in the same proceeding, or in a series of related proceedings, or litigate multiple features of a single class of devices. These forces frequently drive settlement not only of individual cases, but also of a series of pending and potentially related and unrelated cases. In addition, although monetary and injunctive relief is typically sought, remedies are generally not determined until the conclusion of the proceedings, and are frequently modified on appeal. Accordingly, the outcomes of individual cases are difficult to time, predict or quantify and are often dependent upon the outcomes of other cases in other forums, both domestic and international.

We rely on a combination of patents, trademarks, trade secrets and non-disclosure agreements to protect our intellectual property. We hold 32 issued U.S. patents, some of which have foreign counterparts, and additional patent applications pending worldwide that cover various aspects of our technology. The issued patents expire at various dates ranging from two to twelve years. The following table provides a brief description of our patents that have been issued in the U.S.:

Product Group	Description/Indications	Patent Term	Patent Expiration	Patent Type
CytoSorb	Material and Method of Producing: Hypercrosslinked Polystyrene Resins with Various Surface Modifications	20 Years	11/25/2016	Standard
CytoSorb	Method of Removing Beta-2 Microglobulin Using Hypercrosslinked Polystyrene-Type Resins	20 Years	7/30/2017	Standard
CytoSorb	Method of Removing Beta-2 Microglobulin Using Polymers with Surface-Exposed Vinyl Groups Modified for Biocompatibility	20 Years	7/30/2017	Standard
CytoSorb	Devices, Systems & Methods for Reducing Cytokines, Etc. in Plasma and Other Separated Blood Components	20 Years	7/30/2017	Standard
CytoSorb	Biocompatible Devices, Systems & Methods for Reducing levels of Pro-Inflammatory and Anti-Inflammatory Stimulators or mediators in Blood	20 Years	7/30/2017	Standard
CytoSorb	Methods for reducing levels of pro-inflammatory or anti-inflammatory stimulators or mediators in the blood	20 Years	7/30/2017	Standard
CytoSorb	Biocompatible Devices, Systems & Methods for Reducing levels of Pro-Inflammatory and Anti-Inflammatory Stimulators or mediators in Blood	20 Years	7/30/2017	Standard
CytoSorb	Biocompatible Devices, Systems, and Methods for Reducing Levels of Pro-Inflammatory or Anti-Inflammatory Stimulators or Mediators in the Blood	20 Years	7/30/2017	Standard
CytoSorb	Devices, Systems, and Methods for Reducing Levels of Pro-Inflammatory or Anti-Inflammatory Stimulators or Mediators in Blood Products	20 Years	7/30/2017	Standard
CytoSorb	Material for Purification: DVB Copolymer with Surface Vinyl Groups Modified to One of Four Functional Groups	20 Years	2/6/2018	Standard
CytoSorb	Method of Producing Material: Chloromethylated Styrene or DVB Polymers with Chlorine Replaced for Improved Biocompatibility	20 Years	2/6/2018	Standard
CytoSorb	Method of Purification Using DVB Copolymer with Surface-Exposed Vinyl Groups Modified for Biocompatibility	20 Years	2/6/2018	Standard
CytoSorb	Material and Method of Producing: Chloromethylated Styrene or DVB Polymers with Chlorine Replaced for Improved Biocompatibility	20 Years	2/6/2018	Standard
CytoSorb	Method of Producing Material: DVB Copolymer with No Endotoxin Contamination	20 Years	2/6/2018	Standard
CytoSorb	Material for Purification: DVB Copolymer with Surface Vinyl Groups Modified in Three Ways for Biocompatibility	20 Years	2/6/2018	Standard
CytoSorb	Method of Purification Using Chloromethylated Styrene or DVB Polymers with Chlorine Replaced for Improved Biocompatibility	20 Years	2/6/2018	Standard
CytoSorb	Method of Producing Material: Polymer with Modification of Surface-Exposed Vinyl Groups	20 Years	2/6/2018	Standard

CytoSorb	Material and Method of Producing: Chloromethylated Polymers with Chlorine Replaced for Improved Biocompatibility	20 Years	2/6/2018	Standard
CytoSorb	Method of Producing Material: Polymer with Modification of Surface-Exposed Vinyl Groups	20 Years	12/14/2018	Standard
CytoSorb	Method of and Device for Introducing Fluids into a Patient's Body	20 Years	2/14/2020	Standard
CytoSorb	Perfusion Device Combining Adsorbing Material and Hollow Fibers to Filter and Recombine Plasma	20 Years	4/17/2020	Standard
CytoSorb	Method of Peritoneal Dialysis	20 Years	4/27/2020	Standard
CytoSorb	Material and Method of Producing: Biocompatible Polymeric Adsorbents Using a One-Pot Process	20 Years	10/10/2020	Standard
CytoSorb	Protective clothing	20 Years	2/14/2021	Standard
CytoSorb	Devices, systems, and methods for reducing levels of pro-inflammatory or anti-inflammatory stimulators or mediators in the blood	20 Years	4/10/2021	Standard
CytoSorb	Method of Producing Devices	20 Years	4/25/2021	Standard
CytoSorb	Hemocompatible Coated Polymer and Related One-Step Methods	20 Years	10/18/2022	Standard
CytoSorb	Hemocompatible Coated Polymer and Related Methods	20 Years	10/18/2022	Standard
CytoSorb	Hemocompatible Coated Polymer and Related One-Step Methods	20 Years	10/18/2022	Standard
CytoSorb	Hemocompatible Polymer Systems And Related Devices	20 Years	10/18/2022	Standard
CytoSorb	Size-Selective Hemoperfusion Polymeric Adsorbents	20 Years	11/20/2026	Standard
CytoSorb	Size-Selective Hemoperfusion Polymeric Adsorbents	20 Years	11/20/2026	Standard

Certain of these patents also have foreign counterparts.

There can be no assurance that pending patent applications will result in issued patents, that patents issued to us will not be challenged or circumvented by competitors, or that such patents will be found to be valid or sufficiently broad to protect our technology or to provide us with a competitive advantage.

We also rely on non-disclosure and non-competition agreements with employees, consultants and other parties to protect, in part, trade secrets and other proprietary technology. There can be no assurance that these agreements will not be breached, that we will have adequate remedies for any breach, that others will not independently develop equivalent proprietary information or that third parties will not otherwise gain access to our trade secrets and proprietary knowledge.

Prior to the year 2000, we engaged in discussions with the Dow Chemical Company, (Dow), which had indicated a strong interest in being our polymer manufacturer. After a Dow representative on our Advisory Board resigned, Dow filed and received five patents naming our former Advisory Board member as an inventor. These patents, two of which subsequently lapsed for failure to pay maintenance fees, concern the area of coating high divinylbenzene-content polymers to render them hemocompatible, and using such coated polymers to treat blood or plasma. In management's view the Dow patents improperly incorporate our technology, are based on our proprietary technology, and should not have been granted to Dow. While we believe that our own patents would prevent Dow from producing our products as they are currently envisioned, Dow could attempt to assert its patents against us. To date, to our knowledge, Dow has not utilized their patents for the commercial manufacture of products that would be competitive with us, and we currently have no plans to challenge Dow's patents. However, the existence of these Dow patents could result in a potential dispute with Dow in the future and additional expenses for us.

We may find it necessary to initiate litigation to enforce our patent rights, to protect our trade secrets or know-how and to determine the scope and validity of the proprietary rights of others. Patent litigation can be costly and time-consuming, and there can be no assurance that our litigation expenses will not be significant in the future or that the outcome of litigation will be favorable to us. Accordingly, we may seek to settle some or all of our pending litigation described below. Settlement may include cross-licensing of the patents which are the subject of the litigation as well as our other intellectual property and may involve monetary payments to or from third parties.

Environmental Matters

We believe that there are no compliance issues associated with applicable environmental laws and regulations that would have a material adverse effect on us or our business. We incur waste removal costs in connection with both our solid and liquid wastes which are byproducts of our manufacturing process. We utilize the services of various qualified contractors to dispose of these waste products. These waste removal costs amounted to approximately $315,000 for the year ended December 31, 2015.

Employees

As of February 28, 2016 we had 54 full-time employees. We also utilize consultants and temporary service providers who are not our employees, as necessary. None of our employees are represented by a labor union or are subject to collective-bargaining agreements.

Item 1A. Risk Factors

Risks Related to our Business and our Industry

We have a history of losses and expect to incur substantial future losses, and the report of our auditor on our consolidated financial statements expresses substantial doubt about our ability to continue as a going concern.

We have experienced substantial operating losses since inception. As of December 31, 2015, we had an accumulated deficit of $132,525,858, which included net losses of $8,131,738 for the year ended December 31, 2015 and $9,321,672 for the year ended December 31, 2014. In part due to these losses, our audited consolidated financial statements have been prepared assuming we will continue as a going concern, and the auditors' report on those financial statements express substantial doubt about our ability to continue as a going concern. Our losses have resulted principally from costs incurred in the research and development of our polymer technology and general and administrative expenses. We intend to conduct significant additional research, development, and clinical study activities which, together with expenses incurred for the establishment of manufacturing arrangements and a marketing and distribution presence and other general and administrative expenses, are expected to result in continuing operating losses for the foreseeable future. The amount of future losses and when, if ever, we will achieve profitability are uncertain. Our ability to achieve profitability will depend, among other things, on successfully completing the development of our technology and commercial products, obtaining additional requisite regulatory approvals in markets not covered by the CE Mark and for potential label extensions of our current CE Mark, establishing manufacturing and sales and marketing arrangements with third parties, and raising sufficient funds to finance our activities. No assurance can be given that our product development efforts will be successful, that our current CE Mark will enable us to achieve profitability, that additional regulatory approvals in other countries will be obtained, that any of our products will be manufactured at a competitive cost and will be of acceptable quality, that we will be able to achieve profitability or that profitability, if achieved, can be sustained, or our ability to raise additional capital when needed or on terms acceptable to us. Our failure with respect to any or all of the matters would have a material adverse effect on our business, operating results, financial condition and prospects.

We will require additional capital in the future to fund our operations.

As of December 31, 2015, we had current assets of approximately $9,860,000 including cash on hand of approximately $5,317,000, short-term investments of approximately $2,192,000, and current liabilities of approximately $3,044,000. For the year ended December 31, 2015, our cash burn was approximately $10.3 million. Our current and historical cash burn is not necessarily indicative of our future use of cash and cash equivalents.

We will require additional financing in the future in order to complete additional clinical studies and to support the commercialization of our proposed products. There can be no assurance that we will be successful in our capital raising efforts. Our long-term capital requirements are expected to depend on many factors, including:

- continued progress and cost of our research and development programs;
- progress with pre-clinical studies and clinical studies;
- the time and costs involved in obtaining regulatory clearance in other countries and/or for other indications;
- costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims;
- costs of developing sales, marketing and distribution channels;
- market acceptance and reimbursement of our products; and
- cost for training physicians and other health care personnel.

Although we entered into a Controlled Equity Offering[SM] Sales Agreement with Cantor Fitzgerald & Co. in November 2015 for the offer and sale of up to an aggregate of $25,000,000 of shares of our common stock, we may need additional financing. Should the financing we require be unavailable or on terms unacceptable to us when we require it, the consequences could be a material adverse effect on our business, operating results, financial condition and prospects.

In addition, in the event that additional funds are obtained through arrangements with collaborative partners or other sources, we may have to relinquish economic and/or proprietary rights to some of our technologies or products under development that we would otherwise seek to develop or commercialize by ourselves.

We could be adversely affected by violations of the Foreign Corrupt Practices Act and similar worldwide anti-bribery laws.

We are subject to the Foreign Corrupt Practices Act (FCPA), which generally prohibits companies and their intermediaries from making payments to non-U.S. government officials for the purpose of obtaining or retaining business or securing any other improper advantage. We are also subject to anti-bribery laws in the jurisdictions in which we operate. Although we have policies and procedures designed to ensure that we, our employees and our agents comply with the FCPA and other anti-bribery laws, there is no assurance that such policies or procedures will protect us against liability under the FCPA or other laws for actions taken by our agents, employees and intermediaries with respect to our business or any businesses that we acquire. We do business in a number of countries in which FCPA violations have recently been enforced. Failure to comply with the FCPA, other anti-bribery laws or other laws governing the conduct of business with foreign government entities, including local laws, could disrupt our business and lead to severe criminal and civil penalties, including imprisonment, criminal and civil fines, loss of our export licenses, suspension of our ability to do business with the federal government, denial of government reimbursement for our products and/or exclusion from participation in government healthcare programs. Other remedial measures could include further changes or enhancements to our procedures, policies, and controls and potential personnel changes and/or disciplinary actions, any of which could have a material adverse effect on our business, financial condition, results of operations and liquidity. We could also be adversely affected by any allegation that we violated such laws.

Although historically we have been a research and development company, we are in the process of commercializing our products. There can be no assurance that we will be successful in developing and expanding commercial operations or balancing our research and development activities with our commercialization activities.

We have historically been engaged primarily in research and development activities and have generated limited revenues to date. With the launch of our CytoSorb product in the EU and abroad, there can be no assurance that we will be able to successfully manage the balance of our research and development operations with our planned commercial enterprise. Potential investors should be aware of the problems, delays, expenses and difficulties frequently encountered by an enterprise in balancing development, which include unanticipated problems relating to testing, product registration, regulatory compliance and manufacturing, with commercialization, which includes problems with market adoption, reimbursement, marketing problems and additional costs. Our products and product candidates will require significant additional research and testing, and we will need to overcome significant regulatory burdens prior to commercialization in other countries, such as the U.S., and for ongoing compliance for our CE Mark. We will also need to raise significant additional funds to complete additional clinical studies and obtain regulatory approvals in other countries before we can begin selling our products in markets not covered by our CE Mark. In addition, we may be required to spend significant funds on building out our commercial operations. There can be no assurance that after the expenditure of substantial funds and efforts, we will successfully develop and commercialize any products, generate any significant revenues or ever achieve and maintain a substantial level of sales of our products.

We depend upon key personnel who may terminate their employment with us at any time.

As of February 28, 2016 we currently have 54 full-time employees and several full-time temporary employees. Our success will depend to a significant degree upon the continued services of our key management team and advisors, including, Dr. Phillip Chan, our Chief Executive Officer; Kathleen P. Bloch, our Chief Financial Officer; Vincent Capponi, our Chief Operating Officer and Dr. Robert Bartlett, our Chief Medical Officer, who works with us on a consulting basis. Although these individuals have long-term employment and consulting agreements, there can be no assurance that key management personnel or other members of our management team and advisors will continue to provide services to us. In addition, our success will depend on our ability to attract and retain other highly skilled personnel. We may be unable to recruit such personnel on a timely basis, if at all. Management and other employees may voluntarily terminate their employment with us at any time. The loss of services of key personnel, or the inability to attract and retain additional qualified personnel, could result in delays in development or approval of our products, loss of sales and diversion of management resources.

Our Chief Medical Officer works with us on a consulting basis.

Our Chief Medical Officer, Dr. Robert Bartlett, works with us on a consulting basis. Because of the part time nature of his consulting agreement, Dr. Bartlett may not always be available to provide us with his services when needed by us in a timely manner.

Acceptance of our medical devices in the marketplace is uncertain, and failure to achieve market acceptance will prevent or delay our ability to generate revenues.

Our future financial performance will depend, at least in part, upon the introduction and customer acceptance of our products. Even with CE Mark approval for our CytoSorb device as a cytokine filter, our products and product candidates may not achieve market acceptance in the countries that recognize and accept the CE Mark. Additional approvals from other regulatory authorities (such as the FDA) will be required before we can market our device in countries not covered by the CE Mark. There is no guarantee that we will be able to achieve additional regulatory approvals, and even if we do, our products may not achieve market acceptance in the countries covered by such approvals. The degree of market acceptance will depend upon a number of factors, including:

- the receipt of regulatory clearance of marketing claims for the uses that we are developing;
- the establishment and demonstration of the advantages, safety and efficacy of our polymer technology;
- pricing and reimbursement policies of government and third-party payers such as insurance companies, health maintenance organizations and other health plan administrators;
- our ability to attract corporate partners, including medical device companies, to assist in commercializing our products; and
- our ability to effectively market our products.

Physicians, patients, payers or the medical community in general may be unwilling to accept, utilize or recommend any of our products. Approval of our CytoSorb device as a cytokine filter as well as the data we have gathered in our clinical studies to support device usage in this indication may not be sufficient for market acceptance in the medical community. We may also need to conduct additional clinical studies to gather additional data for marketing purposes. If we are unable to obtain regulatory approval or commercialize and market our products when planned, we may not achieve any market acceptance or generate revenue.

If we are unable to obtain and maintain patent protection for our products and product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and product candidates similar or identical to ours, and our ability to successfully commercialize our products and product candidates may be adversely affected.

Our commercial success will depend, in part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our products and product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our products and product candidates that are important to our business. We cannot be certain that patents will be issued or granted with respect to applications that are currently pending or that we apply for in the future with respect to one or more of our products and product candidates, or that issued or granted patents will not later be found to be invalid and/or unenforceable.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, distribution partners, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

The patent position of medical device companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued, and even if issued, the patents may not meaningfully protect our products or product candidates, effectively prevent competitors and third parties from commercializing competitive products or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative products in a non-infringing manner.

Changes in either the patent laws, implementing regulations or interpretation of the patent laws in the United States and other countries may also diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States, and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions.

We cannot be certain that our patents and patent rights will be effective in protecting our products, product candidates and technologies. Failure to protect such assets may have a material adverse effect on our business, operations, financial condition and prospects.

We may face litigation from third parties claiming that our products infringe on their intellectual property rights, or seek to challenge the validity of our patents.

Our future success is also dependent in part on the strength of our intellectual property, trade secrets and know-how, which have been developed from years of research and development. In addition to the "Purolite" litigation discussed below, we may be exposed to additional future litigation by third parties seeking to challenge the validity of our rights based on claims that our technologies, products or activities infringe the intellectual property rights of others or are invalid, or that we have misappropriated the trade secrets of others.

Since our inception, we have sought to contract with large, established manufacturers to supply commercial quantities of our adsorbent polymers. As a result, we have disclosed, under confidentiality agreements, various aspects of our technology with potential manufacturers. We believe that these disclosures, while necessary for our business, have resulted in the attempt by potential suppliers to improperly assert ownership claims to our technology in an attempt to gain an advantage in negotiating manufacturing rights.

We have previously engaged in discussions with the Brotech Corporation and its affiliate, Purolite International, Inc. (collectively referred to as Purolite), which had demonstrated a strong interest in being our polymer manufacturer. For a period of time beginning in December 1998, Purolite engaged in efforts to develop and optimize the manufacturing process needed to produce our polymer products on a commercial scale. However, the parties eventually decided not to proceed. In 2003, Purolite filed a lawsuit against us asserting, among other things, co-ownership and co-inventorship of certain of our patents. On September 1, 2006, the United States District Court for the Eastern District of Pennsylvania approved a Stipulated Order and Settlement Agreement under which we and Purolite agreed to the settlement of the action. The Settlement Agreement provides us with the exclusive right to use our patented technology and proprietary know how relating to adsorbent polymers for a period of 18 years. Under the terms of the Settlement Agreement, we have agreed to pay Purolite royalties of 2.5% to 5% on the sale of certain of our products if and when those products are sold commercially.

Several years ago we engaged in discussions with the Dow Chemical Company, which had indicated a strong interest in being our polymer manufacturer. After a Dow representative on our Advisory Board resigned, Dow filed and received several patents naming our former Advisory Board member as an inventor. In management's view the Dow patents improperly incorporate our technology and should not have been granted to Dow. The existence of these Dow patents could result in a potential dispute with Dow in the future. In the event such a dispute arises, we may be forced to spend significant time and resources to defending our position. There can be no assurances that such efforts will be successful and not have a material adverse effect on our business, operating results, financial condition and prospects.

The expiration or loss of patent protection may adversely affect our future revenues and operating earnings.

We rely on patent, trademark, trade secret and other intellectual property protection in the discovery, development, manufacturing, and sale of our products and product candidates. In particular, patent protection is important in the development and eventual commercialization of our products and product candidates. Patents covering our products and product candidates normally provide market exclusivity, which is important in order for our products and product candidates to become profitable.

Certain of our patents will expire in the next one to ten years. While we are seeking additional patent coverage which may protect the technology underlying these patents, there can be no assurances that such additional patent protection will be granted, or if granted, that these patents will not be infringed upon or otherwise held enforceable. Even if we are successful in obtaining a patent, patents have a limited lifespan. In the United States, the natural expiration of a utility patent typically is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our products and product candidates, we may be open to competition from generic versions of such methods and devices.

We have commenced the process of seeking regulatory approvals of our products and product candidates, but the approval process involves lengthy and costly clinical studies and is, in large part, not in our the control. The failure to obtain government approvals, internationally or domestically, for our products and product candidates, or to comply with ongoing governmental regulations could prevent, delay or limit introduction or sale of our products and result in the failure to achieve revenues or maintain our operations.

CytoSorb has already achieved EU regulatory approval under the CE Mark and the Medical Devices Directive. It is manufactured at our manufacturing facility in New Jersey under ISO 13485 Full Quality Systems certification. The manufacturing and marketing of our products will be subject to extensive and rigorous government regulation in the European market, the U.S., in various states and in other foreign countries. In the U.S. and other countries, the process of obtaining and maintaining required regulatory approvals is lengthy, expensive, and uncertain. There can be no assurance that we will ever obtain the necessary additional approvals to sell our products in the United States or other non EU countries. Even if we do ultimately receive FDA approval for any of our products, we will be subject to extensive ongoing regulation. While we have received approval from our Notified Body to apply the CE Mark to our CytoSorb device, we will be subject to extensive ongoing regulation and auditing requirements to maintain the CE Mark.

Our products will be subject to international regulation as medical devices under the Medical Devices Directive. In Europe, which we expect to provide the initial market for our products, the Notified Body and Competent Authority govern, where applicable, development, clinical studies, labeling, manufacturing, registration, notification, clearance or approval, marketing, distribution, record keeping, and reporting requirements for medical devices. Different regulatory requirements may apply to our products depending on how they are categorized by the Notified Body under these laws. Current international regulations classify our CytoSorb device as a Class IIb device. Even though we have received CE Mark certification of the CytoSorb device, there can be no assurance that we will be able to continue to comply with the required annual auditing requirements or other international regulatory requirements that may be applicable. In addition, there can be no assurance that government regulations applicable to our products or the interpretation of those regulations will not change. The extent of potentially adverse government regulation that might arise from future legislation or administrative action cannot be predicted. There can be no assurances that reimbursement will be granted or that additional clinical data will be required to establish reimbursement.

We have conducted limited clinical studies of our CytoSorb device. Clinical and pre-clinical data is susceptible to varying interpretations, which could delay, limit or prevent additional regulatory clearances.

To date, we have conducted limited clinical studies on our CytoSorb product. There can be no assurance that we will successfully complete additional clinical studies necessary to receive additional regulatory approvals in markets not covered by the CE Mark. While studies conducted by us and others have produced results we believe to be encouraging and indicative of the potential efficacy of our products and technology, data already obtained, or in the future obtained, from pre-clinical studies and clinical studies do not necessarily predict the results that will be obtained from later pre-clinical studies and clinical studies. Moreover, pre-clinical and clinical data are susceptible to varying interpretations and varying statistical analysis methodologies, which can affect interpretation and conclusions of the data and which could delay, limit or prevent additional regulatory approvals. A number of companies in the medical device and pharmaceutical industries have suffered significant setbacks in advanced clinical studies, even after promising results in earlier studies. The failure to adequately demonstrate the safety and effectiveness of an intended product under development could delay or prevent regulatory clearance of the device, resulting in delays to commercialization, and could materially harm our business. Even though we have received approval to apply the CE Mark to our CytoSorb device as a cytokine filter, there can be no assurance that we will be able to receive approval for other potential applications of CytoSorb, or that we will receive regulatory clearance from other targeted regions or countries.

We rely extensively on research and testing facilities at various universities and institutions, which could adversely affect us should we lose access to those facilities.

Although we have our own research laboratories and clinical facilities, we collaborate with numerous institutions, universities and commercial entities to conduct research and studies of our products. We currently maintain a good working relationship with these parties. However, should the situation change, the cost and time to establish or locate alternative research and development facilities could be substantial and delay gaining CE Mark for other potential applications of our products, our other product candidates or technologies, and/or FDA approval and commercializing our products.

We are and will be exposed to product liability risks, and clinical and preclinical liability risks, which could place a substantial financial burden upon us should we be sued.

Our business exposes us to potential product liability and other liability risks that are inherent in the testing, manufacturing and marketing of medical devices. We cannot be sure that claims will not be asserted against us. A successful liability claim or series of claims brought against us could have a material adverse effect on our business, financial condition and results of operations.

We cannot give assurances that we will be able to continue to obtain or maintain adequate product liability insurance on acceptable terms, if at all, or that such insurance will provide adequate coverage against potential liabilities. Claims or losses in excess of any product liability insurance coverage that we may obtain could have a material adverse effect on our business, financial condition and results of operations.

Certain university and other relationships are important to our business and may potentially result in conflicts of interests.

Dr. John Kellum and others are critical care advisors and consultants of ours and are associated with institutions such as the University of Pittsburgh Medical Center. Their association with these institutions may currently or in the future involve conflicting interests in the event they or these institutions enter into consulting or other arrangements with competitors of ours.

We have limited manufacturing experience, and once our products are approved, we may not be able to manufacture sufficient quantities at an acceptable cost, or without shut-downs or delays.

In March 2011, we received approval from our Notified Body to apply the CE Mark to our CytoSorb device for commercial sale as a cytokine filter. We also achieved ISO 13485:2003 Full Quality Systems certification, an internationally recognized quality standard designed to ensure that medical device manufacturers have the necessary comprehensive management systems in place to safely design, develop, manufacture and distribute medical devices in the European Union. We manufacture CytoSorb at our manufacturing facilities in New Jersey for sale in the EU and for additional clinical studies. Manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices (cGMP). As such, we are subject to continual review and periodic inspections to assess compliance with cGMP as required by our International notified body and those FDA regulations governing companies that export medical products for sale outside the United States. Accordingly, we must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We have limited experience in establishing, supervising and conducting commercial manufacturing. If we or the third-party manufacturers of our products fail to adequately establish, supervise and conduct all aspects of the manufacturing processes, we may not be able to commercialize our products.

While we currently believe we have established sufficient production capacity to supply potential near term demand for the CytoSorb device, we will need to scale up and increase our manufacturing capabilities in the future. No assurance can be given that we will be able to successfully scale up our manufacturing capabilities or that we will have sufficient financial or technical resources to do so on a timely basis or at all.

Due to our limited marketing, sales and distribution experience, we may be unsuccessful in our efforts to sell our products.

We expect to enter into agreements with third parties for the commercial marketing, and distribution of our products. There can be no assurance that parties we may engage to market and distribute our products will:

- satisfy their financial or contractual obligations to us;
- adequately market our products; or
- not offer, design, manufacture or promote competing products.

If for any reason any party we engage is unable or chooses not to perform its obligations under our marketing and distribution agreement, we would experience delays in product sales and incur increased costs, which would harm our business and financial results.

Our results of operations can be significantly affected by foreign currency fluctuations and regulations.

A significant portion of our revenues is currently derived in the local currencies of the foreign jurisdictions in which our products are sold. Accordingly, we are subject to risks relating to fluctuations in currency exchange rates. In the future, and especially as we further expand our sales efforts in international markets, our customers will increasingly make payments in non-U.S. currencies. Fluctuations in foreign currency exchange rates could affect our revenues, operating costs and operating margins. In addition, currency devaluation can result in a loss to us if we hold deposits of that currency. We cannot predict the effect of future exchange rate fluctuations on our operating results.

If we are unable to convince physicians and other health care providers as to the benefits of our products, we may incur delays or additional expense in our attempt to establish market acceptance.

Broad use of our products may require physicians and other health care providers to be informed about our products and their intended benefits. The time and cost of such an educational process may be substantial. Inability to successfully carry out this education process may adversely affect market acceptance of our products. We may be unable to educate physicians regarding our products in sufficient numbers or in a timely manner to achieve our marketing plans or to achieve product acceptance. Any delay in physician education may materially delay or reduce demand for our products. In addition, we may expend significant funds towards physician education before any acceptance or demand for our products is created, if at all.

The market for our products is rapidly changing and competitive, and new devices and drugs, which may be developed by others, could impair our ability to maintain and grow our business and remain competitive.

The medical device and pharmaceutical industries are subject to rapid and substantial technological change. Developments by others may render our technologies and products noncompetitive or obsolete. We also may be unable to keep pace with technological developments and other market factors. Technological competition from medical device, pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase. Many of these entities have significantly greater research and development capabilities and budgets than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us.

If users of our products are unable to obtain adequate reimbursement from third-party payers, or if new restrictive legislation is adopted, market acceptance of our products may be limited and we may not achieve anticipated revenues.

The continuing efforts of government and insurance companies, health maintenance organizations and other payers of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and collaborative partners and the availability of capital. For example, in certain foreign markets, pricing or profitability of medical devices is subject to government control. In the United States, given recent federal and state government initiatives directed at lowering the total cost of health care, the U.S. Congress and state legislatures will likely continue to focus on health care reform, the cost of medical devices and on the reform of the Medicare and Medicaid systems. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of these proposals could materially harm our business, financial condition and results of operations.

Our ability to commercialize our products will depend in part on the extent to which appropriate reimbursement levels for the cost of our products and related treatment are obtained by governmental authorities, private health insurers and other organizations, such as health maintenance organizations (HMOs). Third-party payers are increasingly challenging the prices charged for medical care. Also, the trend toward managed health care in the United States and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of health care services and medical devices, as well as legislative proposals to reform health care or reduce government insurance programs, may all result in lower prices for our products. The cost containment measures that health care payers and providers are instituting and the effect of any health care reform could materially harm our ability to operate profitably.

CytoSorb is currently reimbursable in Germany and Austria. We plan to seek reimbursement for our product in other EU and non-EU countries to help further adoption. There can be no assurance when, or if, this additional reimbursement might be approved.

Risks Connected to Our Securities

The price of our Common Stock has been highly volatile due to factors that will continue to affect the price of our stock.

On December 3, 2014, we effected a twenty-five-for-one (25:1) reverse split of our common stock. Immediately after the reverse stock split, on December 3, 2014 we changed our state of incorporation from the State of Nevada to the State of Delaware pursuant to an Agreement and Plan of Merger, dated December 3, 2014, whereby we merged with and into our recently formed, wholly-owned Delaware subsidiary. On December 17, 2014, we received approval for up-listing to The NASDAQ Capital Market and our common stock began trading on The NASDAQ Capital Market on December 23, 2014. Our Common Stock closed as high as $14.99 and as low as $5.20 per share between January 1, 2015 and December 31, 2015 on The NASDAQ Capital Market. On March 4, 2016 the closing price of our common stock, as reported on The NASDAQ Capital Market, was $4.72. Historically, medical device company securities such as our Common Stock have experienced extreme price fluctuations. Some of the factors leading to this volatility include, but are not limited to:

- fluctuations in our operating results;
- announcements of product releases by us or our competitors;
- announcements of acquisitions and/or partnerships by us or our competitors; and
- general market conditions.

Although shares of our common stock currently trade on the NASDAQ Capital Market under the symbol “CTSO”, there is no assurance that our stock will not continue to be volatile while listed on NASDAQ in the future.

Directors, executive officers and principal stockholders own a significant percentage of the shares of Common Stock, which will limit your ability to influence corporate matters.

Our directors, executive officers and principal stockholders together beneficially own a significant percentage of the voting control of the Common Stock on a fully diluted basis. Accordingly, these stockholders could have a significant influence over the outcome of any corporate transaction or other matter submitted to stockholders for approval, including mergers, consolidations and the sale of all or substantially all of our assets and also could prevent or cause a change in control. The interests of these stockholders may differ from the interests of our other stockholders. Third parties may be discouraged from making a tender offer or bid to acquire us because of this concentration of ownership.

Our Board of Directors may, without stockholder approval, issue and fix the terms of shares of preferred stock and issue additional shares of common stock adversely affecting the rights of holders of our common stock.

On December 3, 2014, we effected a twenty-five-for-one (25:1) reverse split of our common stock. Immediately after the reverse stock split, on December 3, 2014 we changed our state of incorporation from the State of Nevada to the State of Delaware pursuant to an Agreement and Plan of Merger, dated December 3, 2014, whereby we merged with and into our recently formed, wholly-owned Delaware subsidiary. Pursuant to the Agreement and Plan of Merger effecting the merger, we adopted the certificate of incorporation, as amended and restated, and bylaws of our Delaware subsidiary as our certificate of incorporation and bylaws at effective time of the merger. As a result, our certificate of incorporation, as amended and restated, authorizes the issuance of up to 5,000,000 shares of “blank check” preferred stock, with such designation rights and preferences as may be determined from time to time by the Board of Directors. Currently, our certificate of incorporation, as amended and restated, which was effective December 3, 2014, authorizes the issuance of up to 50,000,000 shares of common stock, of which approximately 24,593,944 shares remain available for issuance and may be issued by us without stockholder approval.

Anti-takeover provisions in our charter documents and under Delaware law could prevent or delay transactions that our stockholders may favor and may prevent stockholders from changing the direction of our business or our management.

After giving effect to our merger into our wholly-owned Delaware subsidiary, provisions of our certificate of incorporation, as amended and restated, and bylaws may discourage, delay or prevent a merger or acquisition that our stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares, and may also frustrate or prevent any attempt by stockholders to change the direction or management of us. For example, these provisions:

- authorize the issuance of "blank check" preferred stock without any need for action by stockholders;
- eliminate the ability of stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent; and
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

Compliance with changing corporate governance and public disclosure regulations may result in additional expense.

Keeping abreast of, and in compliance with, changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new SEC regulations will require an increased amount of management attention and external resources. In addition, prior to the merger, our current management team was not subject to these laws and regulations, as we were a private corporation. We intend to continue to invest all reasonably necessary resources to comply with evolving standards, which may result in increased general and administrative expense and a diversion of management time and attention from revenue-generating activities to compliance activities.

Our Common Stock is thinly traded on The NASDAQ Capital Market exchange and no assurances can be made about stock performance, liquidity, or maintenance of our NASDAQ listing.

Prior to December 23, 2014, our common stock was quoted on the OTCQB, which provided significantly less liquidity than a securities exchange (such as the New York Stock Exchange or the Nasdaq Stock Market). On December 17, 2014, our common stock was approved for trading on The NASDAQ Capital Market (NASDAQ). Beginning on December 23, 2014, our common stock began trading on NASDAQ under the symbol "CTSO." Although currently listed on NASDAQ, there can be no assurance that we will continue to meet NASDAQ's minimum listing requirements or that of any other national exchange. In addition, there can be no assurances that a liquid market will be created for our common stock. If we are unable to maintain listing on The NASDAQ or if a liquid market for our common stock does not develop, our common stock may remain thinly traded.

Future sales of our common stock could cause our share price to fall.

In November 2015, we entered into a sales agreement with Cantor Fitzgerald & Co. to offer shares of our common stock from time to time through "at-the-market" offerings, pursuant to which we offer and sell shares of our common stock for an aggregate offering price of up to $25 million. We are not obligated to make or continue to make any sale of shares of our common stock under the "at-the-market" offerings. Any sale of securities pursuant to the "at-the-market" offerings will result in dilution of our stockholders and could cause our share price to fall.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We currently operate a facility near Princeton, New Jersey with approximately 12,400 sq. ft., housing research laboratories, clinical manufacturing operations and administrative offices, under a lease agreement which expires in May 2017. We expect to secure new, expanded facilities upon expiration of this lease. In the opinion of management, the leased properties are adequately insured, are in good condition and suitable for the conduct of our business. We also collaborate with numerous institutions, universities and commercial entities who conduct research and testing of our products at their facilities. Our monthly base rent as of March 2016 is approximately $16,449 and additionally we reimburse the landlord for monthly operating expenses of approximately $13,795.

We also operate a small office facility in Berlin, Germany housing sales and administrative offices. We entered into a lease for this office on March 1, 2012. The lease expires on December 31, 2016. We rent this space for €1,200 per month or US $1,332 per month.

Item 3. Legal Proceedings.

We are from time to time subject to claims and litigation arising in the ordinary course of business. We intend to defend vigorously against any future claims and litigation. We are not currently a party to any legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Beginning on December 23, 2014, our Common Stock began trading on NASDAQ. From May 2010 to December 23, 2014, our Common Stock traded on the OTC Bulletin Board (OTCBB) and OTCQB under the symbol "CTSO." The OTCBB is a quotation service that displays real-time quotes, last-sale prices, and volume information in the OTC equity securities. An OTCBB equity security generally is any equity security that is not listed or traded on a national securities exchange. Prior to May 2010, our Common Stock traded on the OTCBB under the symbol "MSBT", but was changed to "CTSO" as part of our name change to CytoSorbents Corporation. Our common stock began trading on such market on August 9, 2006.

Price Range of Common Stock

The following table shows, for the periods indicated, the high and low bid prices per share of our common stock as reported by NASDAQ and the OTCBB quotation service. These bid prices represent prices quoted by broker-dealers on the OTCBB quotation service and The NASDAQ Capital Market. The quotations reflect inter-dealer prices, without retail mark-up, mark-down or commissions, and may not represent actual transactions.

	High	Low
2014		
First quarter	$ 8.75	$ 3.00
Second quarter	$ 6.47	$ 5.02
Third quarter	$ 7.75	$ 5.05
Fourth quarter	$ 12.87	$ 4.40
2015		
First quarter	$ 14.99	$ 7.89
Second quarter	$ 9.02	$ 5.20
Third quarter	$ 7.70	$ 5.80
Fourth quarter	$ 8.00	$ 5.57

Approximate Number of Equity Security Holders

As of February 28, 2016, there were approximately 5,900 stockholders. Because shares of our Common Stock are held by depositaries, brokers and other nominees, the number of beneficial holders of our shares is larger than the number of stockholders.

Dividends

We have not declared or paid any cash dividends on our common stock, and we do not anticipate declaring or paying cash dividends for the foreseeable future. We are not subject to any legal restrictions respecting the payment of dividends, except that we may not pay dividends if the payment would render us insolvent. Any future determination as to the payment of cash dividends on our common stock will be at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements and other factors that our board of directors considers to be relevant.

Stock Performance Graph.

Smaller reporting companies are not required to provide the information required by this item. As of June 30, 2015, the date on which our filer status was determined for the year ending December 31, 2016, we are no longer a smaller reporting company. In accordance with Item 10(f)(2)(i) of Regulation S-K, we are permitted to utilize the scaled disclosure requirements applicable to smaller reporting companies in this Annual Report on Form 10-K. We will be transitioning to the disclosure requirements applicable to accelerated filers beginning with our Quarterly Report on Form 10-Q for the quarterly period ending March 31, 2016.

Item 6. Selected Financial Data.

The following table summarizes our selected financial data for the periods and as of the dates indicated, which have been derived from our audited financial statements and related notes and should be read together with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and with our consolidated financial statements and related notes, which are included elsewhere in this Annual Report.

	Year Ended December 31,				
	2015	2014	2013	2012	2011
Revenue:					
Sales	$ 4,043,819	$ 3,135,387	$ 821,787	$ 151,574	$ 36,078
Grant income	735,863	978,271	1,600,880	1,191,362	-
Other revenue	11,934	9,167	-	-	-
Total revenue	4,791,616	4,122,825	2,422,667	1,342,936	36,078
Cost of revenue	2,212,546	2,133,888	1,911,565	319,298	11,760
Gross margin	2,579,070	1,988,937	511,102	1,023,638	24,318
Operating expenses:					
Research and development	3,871,069	2,431,759	1,738,938	2,532,489	2,888,245
Legal, financial and other consulting	1,089,145	896,847	908,644	627,245	342,651
Selling general and administrative	6.922,515	5,553,167	2,576,751	1,354,738	1,230,189
Total operating expenses	11,882,729	8,881,773	5,224,333	4,514,472	4,461,085
Loss from Operations	(9,303,659)	(6,892,836)	(4,713,231)	(3,490,834)	(4,436,767)
Other income (expense):					
Interest income/(expense), net	9,301	(310,024)	(422,843)	(564,428)	(1,044,881)
Foreign currency translation gain (loss)	(507,276)	(385,956)	-	-	-
Change in warrant liability	1,345,290	(2,118,498)	-	-	-
Total other income (expense), net	847,315	(2,814,478)	(422,843)	(564,428)	(1,044,881)
Loss before benefit from income taxes	(8,456,344)	(9,707,314)	(5,136,074)	(4,055,262)	(5,481,648)
Benefit from income taxes	324,606	385,642	458,279	391,756	-
Net loss	(8,131,738)	(9,321,672)	(4,677,795)	(3,663,506)	(5,481,648)
Preferred stock dividends	—	9,266,673	2,395,520	2,511,412	3,087,044
Net loss available to common stockholders, basic and diluted	(8,131,738)	(18,588,345)	(7,073,315)	(6,174,918)	(8,568,692)
Weighted average common shares outstanding, basic and diluted	24,885,809	14,382,813	9,440,763	7,929,132	6,409,412
Net loss per share, basic and dilute	(0.33)	(1.29)	(0.75)	(0.78)	(1.34)

	As of December 31,				
	2015	2014	2013	2012	2011
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 5,316,851	$ 3,605,280	$ 2,183,030	$ 1,729,344	$ 1,186,653
Short term investments	2,192,000	1,944,547	-	-	-
Working capital	6,816,548	3,101,564	422,035	862,852	169,532
Total assets	11,254,366	8,468,625	4,045,735	3,339,408	2,122,542
Preferred stock	-	-	15,246,350	12,887,817	10,408,371
Accumulated deficit	(132,525,858)	(124,394,120)	(105,805,775)	(98,732,460)	(92,557,542)
Total stockholders' equity	8,210,586	3,963,183	(14,265,547	(11,625,145)	(10,090,028)

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of the results of operations and financial condition for the fiscal years ended December 31, 2015 and 2014 should be read in conjunction with our financial statements, and the notes to those financial statements that are included elsewhere in this Report.

Overview

We are a leader in critical care immunotherapy commercializing our CytoSorb blood purification technology to reduce deadly uncontrolled inflammation in hospitalized patients around the world, with the goal of preventing or treating multiple organ failure in life-threatening illnesses. The technology is based upon biocompatible, highly porous polymer sorbent beads that are capable of extracting unwanted substances from blood and other bodily fluids. The technology is protected by 32 issued U.S. patents with multiple applications pending both in the U.S. and internationally. Our intellectual property consist of composition of matter, materials, methods of production, systems incorporating the technology and multiple medical uses with expiration dates ranging from one to 10 years.

In March 2011, our flagship product, CytoSorb, an extracorporeal cytokine filter indicated for use in clinical situations where cytokines are elevated was CE marked. The CE Mark demonstrates that a conformity assessment has been carried out and the product complies with the Medical Devices Directive 93/42/EEC in the EU. The goal of CytoSorb is to prevent or treat organ failure by reducing cytokine storm and the potentially deadly systemic inflammatory response syndrome in diseases such as sepsis, trauma, burn injury, acute respiratory distress syndrome, pancreatitis, liver failure, and many others. Organ failure is the leading cause of death in the intensive care unit, and remains a major unmet medical need, with little more than supportive care therapy (e.g., mechanical ventilation, dialysis, vasopressors, fluid support, etc.) as treatment options. By potentially preventing or treating organ failure, CytoSorb may improve clinical outcome, including survival, while reducing the need for costly intensive care unit treatment, thereby potentially saving significant healthcare costs.

Our CE Mark enables CytoSorb to be sold throughout all 28 countries of the EU and the countries in the European Economic Area. In addition, many countries outside the EU accept CE Mark approval for medical devices, but may also require registration with or without additional clinical studies. The broad approved indication enables CytoSorb to be used "on-label" in diseases where cytokines are elevated including, but not limited to, critical illnesses such as those mentioned above, autoimmune disease flares, cancer cachexia, and many other conditions where cytokine-induced inflammation plays a detrimental role.

As part of the CE Mark approval process, we completed our randomized, controlled, European Sepsis Trial amongst fourteen trial sites in Germany in 2011, with enrollment of 100 patients with sepsis and respiratory failure. The trial established that CytoSorb was safe in this critically-ill population, and that it was able to broadly reduce key cytokines in the blood of these patients. We plan to conduct larger, prospective studies in septic patients in the future to confirm the European Sepsis Trial findings.

In addition to CE Mark approval, we also achieved ISO 13485:2003 Full Quality Systems certification, an internationally recognized quality standard designed to ensure that medical device manufacturers have the necessary comprehensive management systems in place to safely design, develop, manufacture and distribute medical devices in the EU. We manufacture CytoSorb at our manufacturing facilities in New Jersey for sale in the EU and for additional clinical studies. We also established a reimbursement path for CytoSorb in Germany and Austria.

From September 2011 through June 2012, we began a controlled market release of CytoSorb in select geographic territories in Germany with the primary goal of preparing for commercialization of CytoSorb in Germany in terms of manufacturing, reimbursement, logistics, infrastructure, marketing, contacts, and other key issues.

In late June 2012, following the establishment of our European subsidiary, CytoSorbents Europe GmbH, we began the commercial launch of CytoSorb in Germany with the hiring of Dr. Christian Steiner as Vice President of Sales and Marketing and three additional sales representatives who joined us and completed their sales training in the third quarter of 2012. The fourth quarter of 2012 represented the first full quarter of direct sales with the full sales team in place. During this period, we expanded our direct sales efforts to include both Austria and Switzerland. At the end of 2015, we had hundreds of KOLs in our commercialized territories worldwide in critical care, cardiac surgery, and blood purification who were either using CytoSorb or supporting its use in clinical practice or clinical trials.

As of March 1, 2016, our sales force includes eight direct sales people, one contract sales person and nine sales support staff.

We have complemented our direct sales efforts with sales to distributors and/or corporate partners. In 2013, we reached agreements with distributors in the United Kingdom, Ireland, Turkey, Russia, and the Netherlands. In 2014, we announced distribution of CytoSorb in the Middle East, including Saudi Arabia, the United Arab Emirates, Kuwait, Qatar, Bahrain, and Oman (the Gulf Cooperative Council (GCC)) and Yemen, Iraq, and Jordan through an exclusive agreement with Techno Orbits, we entered into an exclusive agreement with Smart Medical Solutions S.R.L., to distribute CytoSorb for critical care applications in Romania and the neighboring Republic of Moldova. In 2015, we announced exclusive distribution agreements with Aferetica SRL to distribute CytoSorb in Italy, AlphaMedix Ltd. to distribute CytoSorb in Israel, TekMed Pty Ltd. to distribute CytoSorb in Australia and New Zealand, and Hoang Long Pharma to distribute CytoSorb in Vietnam.

We have been working to expand the number and scope of our strategic partnerships. In September 2013, we entered into a strategic partnership with Biocon, Ltd., India's largest biotech company, with an initial distribution agreement for India and select emerging markets, under which Biocon has the exclusive commercialization rights for CytoSorb initially focused on sepsis. In September 2014, the Biocon partnership was expanded to include all critical care applications and cardiac surgery. In addition, Biocon committed to higher minimum purchases of CytoSorb to maintain distribution exclusivity and to conduct and publish results from multiple investigator-initiated studies and patient case studies.

In addition, in November 2014, we entered into an initial partnership agreement with a leading global medical device company in cardiac surgery and other cardiovascular diseases, to use CytoSorb intra-operatively during cardiac surgery in France. Following a positive evaluation of the device during the term of the agreement, we are now in discussions with multiple potential cardiac surgery partners for distribution rights to CytoSorb in the field of cardiac surgery.

In December 2014, we entered into a multi-country strategic partnership with Fresenius Medical Care AG & CO KGaA to commercialize the CytoSorb therapy. Under the terms of the agreement, Fresenius Medical Care has exclusive rights to distribute CytoSorb for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership will allow Fresenius Medical Care to offer an innovative and easy to use blood purification therapy for removing cytokines in patients that are treated in the intensive care unit. To promote the success of CytoSorb, Fresenius will also engage in the ongoing clinical development of the product. This includes the support and publication of a number of small case series and patient case reports as well as the potential for future larger, clinical collaborations.

We are currently evaluating other potential distributor and strategic partner networks in other major countries where we are approved to market the device.

Concurrent with our commercialization plans, we intend to conduct or support additional clinical studies in sepsis, cardiac surgery, and other critical care diseases to generate additional clinical data to expend the scope of clinical experience for marketing purposes, to increase the number of treated patients, and to support potential future publications. We have completed a single arm, dose ranging trial in Germany amongst several clinical trial sites to evaluate the safety and efficacy of CytoSorb when used 24 hours per day for seven days, each day with a new device, and are conducting final statistical analysis of the data. Patients are being stratified for age, cytokine levels, and co-morbid illnesses in this matched pairs analysis.

In addition, we now have more than 50 investigator-initiated studies planned, with 17 enrolling and four completed around the world. Approximately 12 of these studies are currently enrolling patients. These trials, which are funded and supported by well-known university hospitals and KOLs, are the equivalent of Phase II clinical studies. They will provide invaluable information regarding the success of the device in the treatment of sepsis, cardiac pulmonary bypass surgery, trauma, and many other indications, and if successful, will be integral in helping to drive additional usage and adoption of CytoSorb.

In February 2015, the FDA, approved our Investigational Device Exemption (IDE) application to commence a planned U.S. cardiac surgery feasibility study called REFRESH I (REduction of FREe plaSma Hemoglobin) amongst 20 patients and three U.S. clinical sites. The FDA subsequently approved an amendment to the protocol, expanding the trial to be a 40 patient randomized controlled study (20 treatment, 20 control) in eight clinical centers. REFRESH I represents the first part of a larger clinical trial strategy intended to support the approval of CytoSorb in the U.S. for intra-operative use during cardiac surgery.

The study is designed to evaluate the safety of CytoSorb when used intra-operatively in a heart-lung machine to reduce plasma free hemoglobin and cytokines in patients undergoing complex cardiac surgery. The length, complexity and invasiveness of these procedures cause hemolysis and inflammation, leading to high levels of plasma free hemoglobin, cytokines, activated complement, and other substances. These inflammatory mediators directly correlate with the incidence of serious post-operative complications such as kidney injury and failure. The goal of CytoSorb is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications. As of March 4, 2016, the trial is approximately 35% enrolled and is expected to be completed by mid-2016.

The market focus of CytoSorb is prevention or treatment of organ failure in life-threatening conditions, including commonly seen illnesses in the intensive care unit such as infection and sepsis, trauma, burn injury, acute respiratory distress syndrome (ARDS), and others. Severe sepsis and septic shock, a potentially life-threatening systemic inflammatory response to a serious infection, accounts for approximately 10% to 20% of all ICU admissions and is one of the largest target markets for CytoSorb. Sepsis is a major unmet medical need with no approved products in the U.S. or Europe to treat it. As with other critical care illnesses, multiple organ failure is the primary cause of death in sepsis. When used with standard of care therapy, that includes antibiotics, the goal of CytoSorb in sepsis is to reduce the excessive levels of cytokines and other inflammatory toxins, to help reduce the systematic inflammatory response syndrome (SIRS) response and either prevent or treat organ failure.

In addition to the sepsis indication, we intend to conduct or support additional clinical studies in sepsis, cardiac surgery, and other critical care diseases where CytoSorb could be used, such as ARDS, trauma, sever burn injury, acute pancreatitis, and other acute conditions that may benefit by the reductions of cytokines in the bloodstream. Some examples include the prevention of post-operative complications of cardiac surgery (cardiopulmonary bypass surgery) and damage to organs for transplant prior to organ harvest. We intend to generate additional clinical data to expand the scope of clinical experience for marketing purposes, to increase the number of treated patients, and to support potential future publications.

Our proprietary hemocompatible porous polymer bead technology forms the basis of a broad technology portfolio. Some of our products include:

- CytoSorb - an extracorporeal hemoperfusion cartridge approved in the EU for cytokine removal, with the goal of reducing SIRS and preventing or treating organ failure.
- HemoDefend – a development-stage blood purification technology designed to remove contaminants in blood transfusion products. The goal of HemoDefend is to reduce transfusion reactions and improve the safety of older blood.
- ContrastSorb – a development-stage extracorporeal hemoperfusion cartridge designed to remove IV contrast from the blood of high risk patients undergoing CT imaging with contrast, or interventional radiology procedures such as cardiac catheterization. The goal of ContrastSorb is to prevent contrast-induced nephropathy.
- DrugSorb – a development-stage extracorporeal hemoperfusion cartridge designed to remove toxic chemicals from the blood (e.g., drug overdose, high dose regional chemotherapy).

- BetaSorb – a development-stage extracorporeal hemoperfusion cartridge designed to remove mid-molecular weight toxins, such as β2-microglobulin, that standard high-flux dialysis cannot remove effectively. The goal of BetaSorb is to improve the efficacy of dialysis or hemofiltration.

We have been successful in obtaining technology development contracts from agencies in the U.S. Department of Defense, including Defense Advanced Research Projects Agency , or DARPA, the U.S. Army, and the U.S. Air Force.

In October 2015, we were awarded a Phase II Small Business Innovation Research, or SBIR, contract by the National Heart, Lung, and Blood Institute (NHLBI), a division of the National Institutes of Health, to help advance our HemoDefend blood purification technology towards commercialization for the purification of packed red blood cell(pRBC) transfusions. The contract, entitled "pRBCs Contaminant Removal with Porous Polymer Beads", provides for maximum funding of approximately $1,520,000 over a two year period, with funding to begin in 2016.

In September 2013, the NHLBI awarded us a Phase I SBIR contract valued at $231,351 to further advance our HemoDefend blood purification technology for pRBC transfusions. The University of Dartmouth collaborated with us as a subcontractor on the project, entitled "Elimination of blood contaminants from pRBCs using HemoDefend hemocompatible porous polymer beads." The overall goal of this program is to reduce the risk of potential side effects of blood transfusions, and help to extend the useful life of pRBCs.

In June 2013, we announced that the U.S. Air Force will fund a 30 patient, single site, randomized controlled human pilot study in the United States amongst trauma patients with rhabdomyolysis. The primary endpoint is myoglobin removal. The FDA approved our IDE application for this study and we also received ethics committee approval, allowing the study to commence. However, because of the stringency of our inclusion criteria, and because of the patient mix seen at our single center, we have experienced difficulty in enrolling patients. We have subsequently modified one of the key inclusion criteria and have expanded the number of clinical trial sites to three in a revised protocol.

In September 2012, we were awarded a Phase II Small Business Innovation Research (SBIR) contract by the U.S. Army Medical Research and Materiel Command to evaluate our technology for the treatment of trauma and burn injury in large animal models. In 2013, we finalized the Phase II SBIR contract which provided for a maximum funding of approximately $753,000 with the granting agency. This work is supported by the U.S. Army Medical Research and Material Command under an amendment to Contract W81XWH-12-C-0038. As of December 31, 2015, we received approximately $649,000 in funding under this contract and no further amounts are expected from this contract.

In August 2012, we were awarded a $3.8 million, five-year contract by DARPA for our "Dialysis-Like Therapeutics" (DLT), program to treat sepsis. DARPA has been instrumental in funding many of the major technological and medical advances since its inception in 1958, including development of the Internet, development of GPS, and robotic surgery. The DLT program in sepsis seeks to develop a therapeutic blood purification device that is capable of identifying the cause of sepsis (e.g., cytokines, toxins, pathogens, activated cells) and remove these substances in an intelligent, automated, and efficient manner. Our contract is for advanced technology development of our hemocompatible porous polymer technologies to remove cytokines and a number of pathogen and biowarfare toxins from blood. We are in Year 4 of the program and are currently working with the recently announced systems integrator, Battelle Laboratories, and its subcontractor NxStage Medical, who are responsible for integrating the technology developed by us and others into a final medical device design prototype, and evaluating this device in septic animals and eventually in human clinical trials in sepsis. Our work is supported by DARPA and SSC Pacific under Contract No. N66001-12-C-4199. As of December 31, 2015, we have received approximately $3,499,000 to date and have approximately $301,000 not yet billed under this contract.

Results of Operations

Our financial statements have been presented on the basis that it is a going concern, which contemplates the realization of revenues from our subscriber base and the satisfaction of liabilities in the normal course of business. We have incurred losses from inception. These factors raise substantial doubt about our ability to continue as a going concern.

Comparison of the year ended December 31, 2015 and 2014

Revenues:

For the year ended December 31, 2015, we generated total revenue, which includes product revenue and grant income, of approximately $4,792,000 as compared to revenues of approximately $4,123,000 for the year ended December 31, 2014, an increase of approximately $669,000, or 16%. Revenue from product sales was approximately $4,044,000 for the year ended December 31, 2015, as compared to approximately $3,135,000 in the year ended December 31, 2014, an increase of 29%. This increase was driven by the continued growth in direct sales as well as the expansion of sales to our growing distributor network, which was offset by the negative impact of the decline in the exchange rate of the Euro relative to the U.S. dollar. The impact of the decline in the exchange rate of the Euro was approximately $637,000, or 16% of product sales, for the year ended December 31, 2015.

Grant income decreased by approximately $242,000 from $978,000 in 2014 to approximately $736,000 in 2015 as a result of the conclusion of several significant grants.

Cost of Revenue:

For the years ended December 31, 2015 and 2014, cost of revenue was approximately $2,213,000 and $2,134,000, respectively, an increase of approximately $79,000, or 4%. This increase is related to an increase in product cost of revenue of approximately $354,000 attributable to increased sales in 2015. This was offset by a decrease of approximately $292,000 of direct labor and other costs being deployed toward grant-funded activities in 2015, which has the effect of decreasing the amount of costs allocated to cost of revenue. Product gross margins were approximately 62% for the year ended December 31, 2015, as compared to approximately 63% for the year ended December 31, 2014.

Research and Development Expenses:

Our research and development costs were approximately $3,871,000 and $2,432,000 for the years ended December 31, 2015 and 2014, respectively, an increase of approximately $1,439,000, or 59%. This increase in research and development expenditures is related to an increase in costs related to our various clinical studies and trials of approximately $1,187,000 and an increase in salaries related to non-clinical research and development activities of approximately $134,000.

Legal, Financial and Other Consulting Expenses:

Our legal, financial and other consulting costs were approximately $1,089,000 and $897,000 for the years ended December 31, 2015 and 2014, respectively, an increase of approximately $192,000, or 21%. This increase is due to an increase in legal fees of approximately $112,000 related to general corporate and governance matters, an increase in accounting fees of approximately $87,000 due to the cost of compliance with the Sarbanes-Oxley Act of 2002, and an increase in employment related fees of approximately $10,000 related to the hiring of certain highly qualified personnel. These increases were offset by a decrease in consulting fees of approximately $17,000.

Selling, General and Administrative Expense:

Our selling, general and administrative expenses were approximately $6,923,000 and $5,553,000 for the years ended December 31, 2015 and 2014, respectively, an increase of approximately $1,370,000, or 25%. This increase was due to increases in salaries, commissions and related costs of approximately $959,000 due to the impact of employee hirings and approximately $110,000 of salary increases for named executive officers; additional sales and marketing costs, which include expenses relating to advertising and conferences of approximately $530,000; an increase in royalty and license expenses of approximately $107,000 due to higher sales in 2015; and an increase in travel and entertainment costs of approximately $73,000. These increases were offset be a decrease in stock compensation expense of approximately $296,000 due to certain milestone options earned and awarded by the Board of Directors in 2014 and a reduction in public relations expense of approximately $207,000.

Interest Expense:

For the year ended December 31, 2015, interest income was approximately $9,000, as compared to interest expense of approximately $310,000 for the year ended December 31, 2014. The decrease in net interest expense was solely due to the interest payable and amortization of financing costs related to our convertible notes which were converted to common stock during 2014.

Gain (Loss) on Foreign Currency Transactions:

For the year ended December 31, 2015, the loss on foreign currency transactions was approximately $507,000, as compared to $386,000 for the year ended December 31, 2014, an increase of approximately $121,000. This increase is directly related to the decline in the exchange rate of the Euro at December 31, 2015 as compared to December 31, 2014. The exchange rate of the Euro to the U.S. dollar was $1.09 per Euro at December 31, 2015, as compared to $1.22 per Euro at December 31, 2014.

Change in Warrant Liability:

We recognize warrants as liabilities at their fair value on the date of the grant because of price adjustment provisions in the warrants, then measure the fair value of the warrants on each reporting date, and record a change to the warrant liability as appropriate. The change in warrant liability resulted in other income of approximately $1,345,000 for the year ended December 31, 2015 and other expense of approximately $2,118,000 for the year ended December 31, 2014, The change in warrant liability was as a result of the change in the fair value of the warrant liability from December 31, 2014 to December 31, 2015 and from March 11, 2014 (the date of our $10,200,000 offering) to December 31, 2014. See the consolidated financial statements for details related to the calculation of the fair value of the warrant liability.

Benefit from Income Taxes:

Our benefit from income taxes was approximately $325,000 and $386,000 for the years ended December 31, 2015 and 2014, respectively. These benefits were realized by utilizing the New Jersey Technology Business Tax Certificate Transfer Program whereby we sold our net operating losses to the State of New Jersey.

History of Operating Losses:

We have experienced substantial operating losses since inception. As of December 31, 2015, we had an accumulated deficit of approximately $132,526,000, which included losses of approximately $8,132,000 and $9,322,000 for years ended December 31, 2015 and 2014, respectively. Historically, our losses have resulted principally from costs incurred in the research and development of our polymer technology, and selling, general and administrative expenses, which together were approximately $11,883,000 and $8,882,000 for the years ended December 31, 2015 and 2014, respectively.

Liquidity and Capital Resources

Since inception, our operations have been primarily financed through the private and public placement of our debt and equity securities. At December 31, 2015, we had current assets of approximately $9,860,000 including cash on hand of $5,317,000 and short-term investments of approximately $2,192,000, and had current liabilities of $3,044,000. In January 2016, we received approximately $325,000 in cash from the sale of our net operating losses to the State of New Jersey.

We believe that we have sufficient cash to fund our operations through 2016; however, we will need to raise additional funding to support our ongoing operations in the future. In addition, we will need to raise additional funds to support clinical trials in the U.S. and/or Germany. We will be better able to assess this need once the specific protocols of these trials are finalized.

Contractual Obligations

The following table summarizes our obligations with regard to our contractual obligations as of December 31, 2015, and the expected timing of maturities of those contractual obligations. This table should be read in conjunction with the notes to financial statements included elsewhere in this Annual Report on Form 10-K.

	1 Year	1-3 Years	3-5 Years	Over 5 Years
Operating Lease Obligations	$ 265,879	119,750	–	–

Effects of Recent Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board (FASB) issued ASU No. 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40). The ASU requires all entities to evaluate for the existence of conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the issuance date of the financial statements. The amendments in this update are effective for the annual period ending after December 15, 2016, and for annual periods and interim periods thereafter. Early application is permitted. We are currently evaluating the impact of the updated guidance. We do not believe that the adoption of ASU 2014-15 will have a significant impact on our consolidated financial statements, but the adoption of ASU 2014-15 may impact our footnote disclosures.

In May 2014, the FASB issued ASU 2014-09, "Revenue with Contracts from Customers." ASU 2014-09 supersedes the current revenue recognition guidance, including industry-specific guidance. The ASU introduces a five-step model to achieve its core principal of the entity recognizing revenue to depict the transfer of goods or services to customers at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods and services. In August 2014, the FASB issued ASU 2015-14 which deferred the effective date by one year. Accordingly, the updated guidance is effective for public entities for interim and annual periods beginning after December 15, 2017 and early adoption is permitted as of the beginning of an interim or annual reporting period beginning after December 31, 2016. We are currently evaluating the impact of the updated guidance, but we do not believe that the adoption of ASU 2014-09 will have a significant impact on our consolidated financial statements.

In July 2015, the FASB issued ASU 2015-11, "Inventory: Simplifying the Measurement of Inventory." ASU 2015-11 clarifies current guidance regarding the valuation of inventory. The ASU requires that inventory be measured at the lower of cost or net realizable value. This ASU does not apply to inventory that that is measured using the last-in, first-out (LIFO) or the retail inventory method. The updated guidance is effective for public entities for fiscal years beginning after December 15, 2016, and interim periods within fiscal years beginning after December 15, 2017. We are currently evaluating the impact of the updated guidance, but we do not believe that the adoption of ASU 2015-11 will have a significant impact on our consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, "Leases (Topic 842)". ASU 2016-02 outlines reporting requirements for Lessees to recognize a right-of-use asset and corresponding liability on the balance sheet for all leases covering a period of greater than 12 months. The liability is to be measured as the present value of the future minimum lease payments, plus any initial direct costs. The minimum payments are discounted using the rate implicit in the lease, or, if not known, the lessee's incremental borrowing rate. The Company is currently evaluating the impact of the updated guidance on the consolidated financial statements.

Critical Accounting Policies

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. We believe the following critical accounting policies have significant effect in the preparation of our consolidated financial statements.

Patents

Legal costs incurred to establish patents are capitalized. When patents are issued, capitalized costs are amortized on the straight-line method over the related patent term. In the event a patent is abandoned, the net book value of the patent is written off.

Revenue Recognition

Product Sales: Revenues from sales of products are recognized at the time when title and risk of loss passes to the customer. Recognition of revenue also requires reasonable assurance of collection of sales proceeds and completion of all performance obligations.

*Grant Revenue***:** Revenue from grant income is based on contractual agreements. Certain agreements provide for reimbursement of costs, while other agreements provide for reimbursement of costs and an overhead margin. Revenues are recognized when milestones have been achieved and revenues have been earned. Costs are recorded as incurred. Costs subject to reimbursement by these grants have been reflected as costs of revenue.

*Deferred Revenue***:** We defer revenue that has been received but not yet earned on government contracts. This revenue will be recognized as income in the period in which the revenue is earned. All deferred revenue is expected to be earned within a one year of the balance sheet date.

Research and Development

All research and development costs, payments to laboratories and research consultants are expensed when incurred.

Stock Based-Compensation

We account for our stock-based compensation under the recognition requirements of accounting standards for accounting for stock-based compensation, for employees and directors whereby each option granted is valued at fair market value on the date of grant. Under these accounting standards, the fair value of each option is estimated on the date of grant using the Black-Scholes option pricing model.

We also follow the guidance of accounting standards for accounting for equity instruments that are issued to other than employees for acquiring, or in conjunction with selling, goods or services for equity instruments issued to consultants.

Warrant Liability

We recognize the fair value of the warrants as of the date of the warrant grant using the binomial lattice valuation model. At each subsequent reporting date, we again measure the fair value of the warrants, and records a change to the warrant liability as appropriate, and the change is reported in the statement of operations.

Off-Balance Sheet Arrangements

We currently operate a facility near Princeton, New Jersey with approximately 12,400 sq. ft., housing research laboratories, clinical manufacturing operations and administrative offices, under a lease agreement, which expires in May 2017. We expect to renew this lease upon expiration. We also operate a small office facility in Berlin, Germany housing sales and administrative offices. We entered into a lease for this office on March 1, 2012. The lease expires on December 31, 2016. We rent this space for €1,200 per month or US $1,332 per month.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Smaller reporting companies are not required to provide the information required by this item. As of June 30, 2015, the date on which our filer status was determined for fiscal year 2016, we are no longer a smaller reporting company. In accordance with Item 10(f)(2)(i) of Regulation S-K, we are permitted to utilize the scaled disclosure requirements applicable to smaller reporting companies in this Annual Report on Form 10-K. We will be transitioning to the disclosure requirements applicable to accelerated filers beginning with our Quarterly Report on Form 10-Q for the quarterly period ending March 31, 2016.

Item 8. Financial Statements and Supplementary Data.

Our Financial Statements and notes thereto are included elsewhere in this Annual Report on Form 10-K and incorporated herein by reference. See Item 15 of Part IV.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures designed to ensure information required to be disclosed in Company reports filed under the Securities Exchange Act of 1934, as amended (the Exchange Act), is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures are designed to provide reasonable assurance that information required to be disclosed in Company reports filed under the Exchange Act is accumulated and communicated to management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) as of the end of the period covered by this report. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures as of the end of the period covered by this report are functioning effectively to provide reasonable assurance that the information required to be disclosed by us in reports filed under the Securities Exchange Act of 1934 is (i) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (ii) accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate to allow timely decisions regarding disclosures. A controls system, no matter how well designed and operated, cannot provide absolute assurance that the objectives of the controls system are met, and no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within a company have been detected.

Management's Report on Internal Control Over Financial Reporting

Our management's report on internal control over financial reporting procedures (as defined in Rule 13a-15(f) under the Exchange Act) is included with the financial statements reflected in Item 8 of this Annual Report on Form 10-K and is incorporated herein by reference.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting occurred during the fiscal quarter ended December 31, 2015 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Control Persons; Compliance with Section 16(a) of the Exchange Act.

Information required to be disclosed by this Item with respect to our executive officers is incorporated in this Annual Report on Form 10-K by reference from the section entitled "Officers and Key Employees" contained in our definitive proxy statement for our 2016 annual meeting of stockholders scheduled to be held on June 7, 2016, which we intend to file within 120 days of the end of our fiscal year.

Information required to be disclosed by this Item about our board of directors is incorporated in this Annual Report on Form 10-K by reference from the section entitled "Nomination and Election of Directors" contained in our definitive proxy statement for our 2016 annual meeting of stockholders scheduled to be held on June 7, 2016, which we intend to file within 120 days of the end of our fiscal year.

Information required to be disclosed by this Item about the Section 16(a) compliance of our directors and executive officers is incorporated in this Annual Report on Form 10-K by reference from the section entitled "Section 16(a) Beneficial Ownership Reporting Compliance" contained in our definitive proxy statement for our 2016 annual meeting of stockholders scheduled to be held on June 7, 2016, which we intend to file within 120 days of the end of our fiscal year.

Information required to be disclosed by this Item about our board of directors, the audit committee of our board of directors, our audit committee financial expert, our Code of Business Conduct and Ethics, and other corporate governance matters is incorporated in this Annual Report on Form 10-K by reference from the section entitled "Board of Directors and Corporate Governance Matters" contained in our definitive proxy statement for our 2016 annual meeting of stockholders scheduled to be held on June 7, 2016, which we intend to file within 120 days of the end of our fiscal year.

The text of our Code of Business Conduct and Ethics, which applies to our directors and employees (including our principal executive officer, principal financial officer, and principal accounting officer or controller, and persons performing similar functions), is posted in the "Corporate Governance" section of our website, www.cytosorbents.com. A copy of the Code of Business Conduct and Ethics can be obtained free of charge on our website. We intend to disclose on our website any amendments to, or waivers from, our Code of Business Conduct and Ethics that are required to be disclosed pursuant to the rules of the Securities and Exchange Commission and The NASDAQ Stock Market.

The information presented on our website is not a part of this Annual Report on Form 10-K and the reference to our website is intended to be an inactive textual reference only.

Item 11. Executive Compensation

Information required to be disclosed by this Item is incorporated in this Annual Report on Form 10-K by reference from the sections entitled "Executive Compensation," "Director Compensation" and "Board of Directors and Corporate Governance Matters" contained in our definitive proxy statement for our 2016 annual meeting of stockholders scheduled to be held on June 7, 2016, which we intend to file within 120 days of the end of our fiscal year.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Information required to be disclosed by this Item is incorporated in this Annual Report on Form 10-K by reference from the sections entitled "Principal Stockholders," "Stock Ownership of Directors, Nominees for Director, and Executive Officers" and "Equity Compensation Plan Information" contained in our definitive proxy statement for our 2016 annual meeting of stockholders scheduled to be held on June 7, 2016, which we intend to file within 120 days of the end of our fiscal year.

Item 13. Certain Relationships and Related Transactions and Director Independence

The information required to be disclosed by this Item is incorporated in this Annual Report on Form 10-K by reference from the section(s) entitled "Certain Relationships and Related Party Transactions" and "Board of Directors and Corporate Governance Matters," "Compensation for Executive Officers and Directors, "Compensation Committee Interlocks and Insider Participation" and "Compensation Committee Report" contained in our definitive proxy statement for our 2016 annual meeting of stockholders scheduled to be held on June 7, 2016, which we intend to file within 120 days of the end of our fiscal year.

Item 14. Principal Accounting Fees and Services

This information required to be disclosed by this Item is incorporated in this Annual Report on Form 10-K by reference from the section entitled "Audit and Other Fees" contained in our definitive proxy statement for our 2016 annual meeting of stockholders scheduled to be held on June 7, 2016, which we intend to file within 120 days of the end of our fiscal year.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) Financial Statements and Schedules:

1. Financial Statements

The following financial statements and reports of independent registered public accounting firm are included herein:

2. Financial Statement Schedules

Not applicable.

3. List of Exhibits

Exhibit No.	Description
3.1	First Amended and Restated Certificate of Incorporation, dated December 3, 2014 (incorporated by reference to Exhibit 3(i).4 to the Registrant's Current Report on Form 8-K filed on December 4, 2014).
3.2	Bylaws of CytoSorbents Corporation (incorporated by reference to Exhibit 3(ii).1 to the Registrant's Current Report on Form 8-K filed on December 4, 2014).
4.1	Form of Convertible Note for sale of stock that occurred June 21, 2013 (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on June 27, 2013).
4.2	Form of Warrant for sale of stock that occurred June 21, 2013 (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K filed on June 27, 2013).

4.3	Form of Convertible Note for sale of stock that occurred September 30, 2013 (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on October 10, 2013).
4.4	Form of Warrant for sale of stock that occurred September 30, 2013 (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K filed on October 10, 2013).
4.5	Form of Underwriter Warrant (incorporated by reference to Exhibit 4.5 to the Registrant's Registration Statement on Form S-1/A (Commission File Number 333-199762) filed on December 30, 2014).
10.1	Employment Agreement with Dr. Phillip P. Chan Effective January 1, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on July 15, 2015).+
10.2	Employment Agreement with Vincent Capponi Effective January 1, 2015 (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on July 15, 2015).+
10.3	Employment Agreement with Kathleen P. Bloch Effective January 1, 2015 (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K filed on July 15, 2015).+
10.4	Consulting Agreement with Dr. Robert Bartlett Effective January 1, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on February 9, 2016).+
10.5	Lease Agreement between Princeton Corporate Plaza LLC and the Registrant dated as of March 9, 2000 (incorporated by reference to Exhibit 10.4 to the Registrant's Annual Report on Form 10-K filed on March 31, 2015).
10.6	Third Amendment to Lease Agreement between Princeton Corporate Plaza LLC and the Registrant dated as of December 12, 2014 (incorporated by reference to Exhibit 10.5 to the Registrant's Annual Report on Form 10-K filed on March 31, 2015).
10.7	Royalty Agreement between Guillermina Vega Montiel and the Registrant dated as of August 11, 2003 (incorporated by reference to Exhibit 10.6 to the Registrant's Annual Report on Form 10-K filed on March 31, 2015).
10.8	Stipulated Order and Settlement Agreement between Bro-Tech Corporation, Purolite International Ltd. And the Registrant, dated August 7, 2006 (incorporated by reference to Exhibit 10.1 to the Registrant's current report on Form 8-K filed on September 8, 2006).
10.9	Distribution Agreement between Biocon Limited and the Registrant dated as of September 20, 2013 (incorporated by reference to Exhibit 10.8 to the Registrant's Annual Report on Form 10-K filed on March 31, 2015).†
10.10	First Amendment to the Distribution Agreement between Biocon Limited and the Registrant, dated October 30, 2014 (incorporated by reference to Exhibit 10.9 to the Registrant's Annual Report on Form 10-K filed on March 31, 2015).†
10.11	Controlled Equity Offering Sales Agreement, dated November 4, 2015, by and among the Registrant and Cantor Fitzgerald & Co. (incorporated by reference to Exhibit 1.1 to the Registrant's Current Report on Form 8-K filed on November 5, 2015).
10.12	CytoSorbents Corporation 2006 Long-Term Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Current Report on Form 8-K filed on July 6, 2006).+
10.13	Amendment No. 1 to the CytoSorbents Corporation 2006 Long-Term Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's registration statement on Form S-8, filed on November 4, 2014).+
10.14	CytoSorbents Corporation 2014 Long-Term Incentive Plan (incorporated by reference to Exhibit 99.1 to the Registrant's Post-Effective Amendment No. 1 to Form S-8, filed on October 8, 2015).+

21.1	List of Subsidiaries.*
23.1	Consent of WithumSmith+Brown, PC.*
31.1	Certification of the Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.*
31.2	Certification of the Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.*
32.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.*
32.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.*
101	The following materials from CytoSorbents Form 10-K for the fiscal year ended December 31, 2015, formatted in Extensible Business Reporting Language (XBRL): (1) Consolidated Balance Sheets at December 31, 2015 and December 31, 2014, (iii) Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2015 and December 31, 2014, (iii) Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficiency) for the years ended December 31, 2015 and December 31, 2014, (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2015 and December 31, 2014, and (v) Notes to the Consolidated Financial Statements.

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* Filed or furnished herewith.

\+ Management contract or compensatory plan or arrangement of the Registrant required to be filed as an exhibit to this Annual Report.

† Confidential treatment has been requested for certain portions of this exhibit. The confidential portions of this exhibit have been omitted and filed separately with Securities and Exchange Commission.

In accordance with SEC Release 33-8238, Exhibits 32.1 and 32.2 are being furnished and not filed.

SIGNATURES

In accordance with Section 13 or 15(d) of the Exchange Act, CytoSorbents Corporation has caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on this 9th day of March, 2016.

CYTOSORBENTS CORPORATION

By: */s/ Dr. Phillip P. Chan*
Dr. Phillip P. Chan
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Dr. Phillip P. Chan Dr. Phillip P. Chan	President and Chief Executive Officer (Principal Executive Officer) and Director	March 9, 2016
/s/ Kathleen P. Bloch Kathleen P. Bloch	Chief Financial Officer (Principal Financial and Accounting Officer)	March 9, 2016
/s/ Al Kraus Al Kraus	Chairman of the Board	March 9, 2016
/s/ Alan D. Sobel Alan D. Sobel	Director	March 9, 2016
/s/ Edward R. Jones Edward R. Jones	Director	March 9, 2016
/s/Michael G. Bator Michael G. Bator	Director	March 9, 2016

FINANCIAL STATEMENTS

Management's Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act. The Company's internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles in the United States of America. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Further, because of changes in conditions, effectiveness of internal control over financial reporting may vary over time. Management, with the participation of the Chief Executive Officer and the Chief Financial Officer, working with an external consultant, conducted an evaluation of the effectiveness of internal control over financial reporting based on the framework in *Internal-Control –Integrated Framework* issued in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this evaluation, management concluded that internal control over financial reporting was effective as of December 31, 2015.

WithumSmith+Brown, PC, the independent registered public accounting firm that audited the Company's financial statements included in this Annual Report on Form 10-K, has issued an attestation report on the Company's internal control over financial reporting, which is included herein.

/s/ Dr. Phillip P. Chan	*/s/ Kathleen P. Bloch*
Dr. Phillip P. Chan	Kathleen P. Bloch
President and Chief Executive Officer	Chief Financial Officer
(Principal Executive Officer)	(Principal Financial Officer)

March 9, 2016

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders,

CytoSorbents Corporation:

We have audited the accompanying consolidated balance sheets of CytoSorbents Corporation as of December 31, 2015 and 2014, and the related consolidated statements of operations and comprehensive loss, changes in redeemable convertible preferred stock and stockholders' equity (deficiency), and cash flows for each of the years then ended. These financial statements are the responsibility of the entity's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of CytoSorbents Corporation as of December 31, 2015 and 2014, and the results of its operations and its cash flows for each of the years then ended, in conformity with accounting principles generally accepted in the United States of America.

The accompanying financial statements have been prepared assuming that the entity will continue as a going concern. As discussed in Note 1 to the financial statements, the entity has suffered recurring losses from operations and has a net capital deficiency that raises substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), CytoSorbents Corporation's internal control over financial reporting as of December 31, 2015, based on criteria established in *Internal Control – Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) and our report dated March 9, 2016 expressed an unqualified opinion thereon.

/s/ WithumSmith+Brown, PC
New Brunswick, New Jersey
March 9, 2016

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders,

CytoSorbents Corporation:

We have audited CytoSorbents Corporation's internal control over financial reporting as of December 31, 2015, based on the criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework), (the COSO criteria*)*. CytoSorbents Corporation's management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the entity's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

An entity's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America. An entity's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the entity; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the entity are being made only in accordance with authorizations of management and directors of the entity; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the entity's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, CytoSorbents Corporation maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015 based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of CytoSorbents Corporation as of December 31, 2015 and 2014, and the related consolidated statements of operations and comprehensive loss, changes in redeemable convertible preferred stock and stockholders' equity (deficiency), and cash flows for each of the years then ended and our report dated March 9, 2016 expressed an unqualified opinion thereon.

/s/ WithumSmith+Brown, PC
New Brunswick, New Jersey
March 9, 2016

CYTOSORBENTS CORPORATION
CONSOLIDATED BALANCE SHEETS

December 31,	2015	2014
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 5,316,851	$ 3,605,280
Short-term investments	2,192,000	1,944,547
Grants and accounts receivable, net of allowance for doubtful accounts of $3,275 and $3,756 at December 31, 2015 and 2014, respectively	648,869	819,151
Inventories	1,190,681	537,566
Prepaid expenses and other current assets	511,927	700,462
Total current assets	9,860,328	7,607,006
Property and equipment – net	557,289	245,821
Other assets	836,749	615,798
Total long-term assets	1,394,038	861,619
Total Assets	$ 11,254,366	$ 8,468,625
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 684,633	$ 698,307
Accrued expenses and other current liabilities	723,018	824,884
Deferred revenue	—	833
Warrant liability at fair value	1,636,128	2,981,418
Total current liabilities	3,043,779	4,505,442
Stockholders' Equity:		
Common Stock, Par Value $0.001, 50,000,000 shares authorized; 25,397,056 and 23,304,640 shares issued and outstanding at December 31, 2015 and 2014, respectively	25,397	23,305
Additional paid-in capital	140,126,731	128,106,297
Accumulated other comprehensive income	584,317	227,701
Accumulated deficit	(132,525,858)	(124,394,120)
Total stockholders' equity	8,210,587	3,963,183
Total Liabilities and Stockholders' Equity	$ 11,254,366	$ 8,468,625

The Notes to Consolidated Financial Statements are an integral part of these statements

CYTOSORBENTS CORPORATION
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Year ended December 31, 2015	Year ended December 31, 2014
Revenue:		
Sales	$ 4,043,819	$ 3,135,387
Grant income	735,863	978,271
Other revenue	11,934	9,167
Total revenue	4,791,616	4,122,825
Cost of revenue	2,212,546	2,133,888
Gross profit	2,579,070	1,988,937
Operating expenses:		
Research and development	3,871,069	2,431,759
Legal, financial and other consulting	1,089,145	896,847
Selling, general and administrative	6,922,515	5,553,167
Total operating expenses	11,882,729	8,881,773
Loss from operations	(9,303,659)	(6,892,836)
Other income (expense):		
Interest income (expense), net	9,301	(310,024)
Gain (loss) on foreign currency transactions	(507,276)	(385,956)
Change in warrant liability	1,345,290	(2,118,498)
Total other income (expense), net	847,315	(2,814,478)
Loss before benefit from income taxes	(8,456,344)	(9,707,314)
Benefit from income taxes	324,606	385,642
Net loss	(8,131,738)	(9,321,672)
Preferred stock dividends	—	9,266,673
Net loss available to common shareholders	$ (8,131,738)	$ (18,588,345)
Basic and diluted net loss per common share	$ (0.33)	$ (1.29)
Weighted average number of shares of common stock outstanding	24,885,809	14,382,813
Comprehensive loss:		
Net loss	$ (8,131,738)	$ (9,321,672)
Other comprehensive income:		
Currency translation adjustment	356,616	283,688
Comprehensive loss	$ (7,775,122)	$ (9,037,984)

The Notes to Consolidated Financial Statements are an integral part of these statements.

CYTOSORBENTS CORPORATION
CONSOLIDATED STATEMENTS OF CHANGES REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIENCY)
FOR THE YEARS ENDED DECEMBER 31, 2015 and 2014

	Series B Redeemable Convertible Preferred Stock		Common Stock		Preferred Stock A			Accumulated Other		Stockholders'
	Shares	Amount	Shares	Par value	Shares	Par Value	Paid-In Capital	Comprehensive Income	Accumulated Deficit	Equity (Deficit)
Balance at December 31, 2013	79,337	$ 15,246,350	10,052,782	$ 10,053	1,759,666	$ 1,760	$ 91,584,402	$ (55,987)	$ (105,805,775)	$ (14,265,547)
Stock based compensation - employees, consultants and directors	—	—	—	—	—	—	695,841	—	—	695,841
Issuance of Series A Preferred Stock as dividends	—	—	—	—	135,303	135	238,178	—	(238,313)	—
Issuance of Series B Preferred Stock as dividends	14,500	9,028,360	—	—	—	—	—	—	(9,028,360)	(9,028,360)
Issuance of common stock for services rendered	—	—	44,922	45	—	—	180,055	—	—	180,100
Conversion of Series A and Series B Preferred into Common	(93,837)	(24,274,710)	10,472,062	10,472	(1,894,969)	(1,895)	24,266,131	—	—	24,274,708
Issuance of common stock for cash	—	—	99,336	99	—	—	299,901	—	—	300,000
Issuance of common stock for cash - offering	—	—	1,632,000	1,632	—	—	10,198,368	—	—	10,200,000
Cost of raising capital	—	—	—	—	—	—	(748,545)	—	—	(748,545)
Conversion of convertible notes to common	—	—	701,309	702	—	—	1,989,738	—	—	1,990,440
Proceeds from exercise of warrants	—	—	20,000	20	—	—	156,230	—	—	156,250
Cashless exercise of warrants	—	—	165,435	165	—	—	(165)	—	—	—

	Series B Redeemable Convertible Preferred Stock		Common Stock		Preferred Stock A			Accumulated Other		Stockholders'
	Shares	Amount	Shares	Par value	Shares	Par Value	Paid-In Capital	Comprehensive Income	Accumulated Deficitb	Equity (Deficit)
Additional shares issued related to the round-up of fractional shares as a result of stock split	—	—	151	—	—	—	—	—	—	—
Cashless exercise of stock options	—	—	991	1	—	—	(1)	—	—	—
Proceeds from exercise of stock options	—	—	115,652	116	—	—	109,084	—	—	109,200
Other comprehensive income foreign translation adjustment	—	—	—	—	—	—	—	283,688	—	283,688
Warrant Liability	—	—	—	—	—	—	(862,920)	—	—	(862,920)
Net loss	—	—	—	—	—	—	—	—	(9,321,672)	(9,321,672)
Balance at December 31, 2014	—	—	23,304,640	23,305	—	—	128,106,297	227,701	(124,394,120)	3,963,183
Stock based compensation - employees, consultants and directors	—	—	—	—	—	—	382,284	—	—	382,284
Issuance of common stock - offerings, net of fees incurred			1,278,880	1,279	—	—	9,522,804	—	—	9,524,083
Proceeds from exercise of warrants	—	—	447,178	447	—	—	1,704,986	—	—	1,705,433
Cashless exercise of warrants	—	—	51,810	52	—	—	(52)	—	—	—
Cashless exercise of stock options	—	—	22,736	23	—	—	(23)	—	—	—
Proceeds from exercise of stock options	—	—	291,812	291	—	—	410,435	—	—	410,726

	Series B Redeemable Convertible Preferred Stock		Common Stock		Preferred Stock A			Accumulated Other	Deficit Accumulated	Stockholders'
	Shares	Amount	Shares	Par value	Shares	Par Value	Paid-In Capital	Comprehensive Income	Development Stage	Equity (Deficit)
Other comprehensive income foreign translation adjustment	—	—	—	—	—	—	—	356,616	—	356,616
Net loss	—	—	—	—	—	—	—	—	(8,131,738)	(8,131,738)
Balance at December 31, 2015	—	—	25,397,056	$ 25,397	—	—	$ 140,126,731	$ 584,317	$ (132,525,858)	$ 8,210,587

The Notes to Consolidated Financial Statements are an integral part of these statements.

CYTOSORBENTS CORPORATION
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31, 2015	Year ended December 31, 2014
Cash flows from operating activities:		
Net loss	$ (8,131,738)	$ (9,321,672)
Adjustments to reconcile net loss to net cash used by operating activities:		
Issuance of common stock to consultants for services	—	180,100
Depreciation and amortization	112,969	65,547
Amortization of debt discount	—	198,644
Bad debt expense	—	4,106
Change in warrant liability	(1,345,290)	2,118,498
Foreign currency transaction losses	386,435	—
Stock-based compensation	382,284	695,841
Changes in operating assets and liabilities:		
Grants and accounts receivable	131,970	(412,118)
Inventories	(632,535)	(303,129)
Prepaid expenses and other current assets	178,107	(108,153)
Other assets	(7,134)	(4,784)
Accounts payable and accrued expenses	(83,169)	497,453
Deferred revenue	(833)	(271,526)
Net cash used by operating activities	(9,008,934)	(6,661,193)
Cash flows from investing activities:		
Purchases of property and equipment	(403,608)	(153,157)
Patent costs	(239,839)	(214,165)
Proceeds from sale of short-term investments	5,430,547	4,745,000
Purchases of short-term investments	(5,678,000)	(6,689,547)
Net cash used by investing activities	(890,900)	(2,311,869)
Cash flows from financing activities:		
Equity contributions - net of fees incurred	9,524,083	9,751,456
Proceeds from exercise of stock options	410,726	109,200
Proceeds from exercise of warrants	1,705,433	156,250
Net cash provided by financing activities	11,640,242	10,016,906
Effect of exchange rates on cash	(28,837)	378,406

The Notes to Consolidated Financial Statements are an integral part of these statements.

	Year ended December 31, 2015	Year ended December 31, 2014
Net change in cash and cash equivalents	1,711,571	1,422,250
Cash and cash equivalents at beginning of period	3,605,280	2,183,030
Cash and cash equivalents at end of period	$ 5,316,851	$ 3,605,280
Supplemental schedule of noncash financing activities:		
Fair value of warrant liability upon issuance	$ —	$ 862,920
Fair value of shares issued as costs of raising capital	$ —	7,137
Note payable principal and interest conversion to equity	$ —	$ 1,990,440
Costs paid from proceeds in conjunction with issuance of common stock	$ 1,019,207	$ 748,545
Preferred stock dividends	$ —	$ 9,266,673

During the year ended December 31, 2014, 93,836.50 Series B Preferred Shares were converted into 10,244,450 Common Shares. During the year ended December 31, 2014, 1,894,969 Series A Preferred Shares were converted into 103,332 Common Shares.

The Notes to Consolidated Financial Statements are an integral part of these statements.

1. BASIS OF PRESENTATION:

The accompanying consolidated financial statements include the results of CytoSorbents Corporation (the "Parent"), CytoSorbents Medical Inc., its wholly-owned operating subsidiary (the "Subsidiary"), and CytoSorbents Europe GmbH, its wholly-owned European subsidiary (the "European Subsidiary"), collectively referred to as "the Company."

The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. Based on its projections, the Company believes it may have to raise additional capital to fund its planned operations over the next twelve month period.

As of December 31, 2015, the Company had an accumulated deficit of $132,525,858, which included net losses of $8,131,738 for the year ended December 31, 2015 and $9,321,672 for the year ended December 31, 2014. The Company's losses have resulted principally from costs incurred in the research and development of its polymer technology and selling, general and administrative expenses. The Company intends to continue to conduct significant additional research, development, and clinical study activities which, together with expenses incurred for the establishment of manufacturing arrangements and a marketing and distribution presence and other selling, general and administrative expenses, are expected to result in continuing operating losses for the foreseeable future. The amount of future losses and when, if ever, the Company will achieve profitability are uncertain. CytoSorbents' ability to achieve profitability will depend, among other things, on successfully completing the development of its technology and commercial products, obtaining additional requisite regulatory approvals in markets not covered by the CE Mark and for potential label extensions of the Company's current CE Mark, establishing manufacturing and sales and marketing arrangements with third parties, and raising sufficient funds to finance our activities. No assurance can be given that the Company will be able to raise funds required to sustain its working capital needs or that funds will be available at favorable terms. In addition, no assurance can be given that the Company's product development efforts will be successful, that the expiration of certain patents may adversely affect the company, that its current CE Mark will enable it to achieve profitability, that additional regulatory approvals in other countries will be obtained, that any of the Company's products will be manufactured at a competitive cost and will be of acceptable quality, or that the Company will be able to achieve profitability or that profitability, if achieved, can be sustained. These matters raise substantial doubt about the Company's ability to continue as a going concern. These consolidated financial statements do not include any adjustments related to the outcome of this uncertainty.

2. PRINCIPAL BUSINESS ACTIVITY AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES:

Nature of Business

The Company is a leader in critical care immunotherapy commercializing its CytoSorb blood purification technology to reduce deadly uncontrolled inflammation in hospitalized patients around the world, with the goal of preventing or treating multiple organ failure in life-threatening illnesses. The Company, through its subsidiary CytoSorbents Medical Inc. (formerly known as CytoSorbents, Inc.), is engaged in the research, development and commercialization of medical devices with its blood purification technology platform which incorporates a proprietary adsorbent, porous polymer technology. The Company, through its European Subsidiary, conducts sales and marketing related operations for the CytoSorb device. CytoSorb **,** **t**he Company's flagship product, is approved in the European Union and marketed in and distributed in thirty-two countries around the world, as a safe and effective extracorporeal cytokine absorber, designed to reduce the "cytokine storm" that could otherwise cause massive inflammation, organ failure and death in common critical illnesses such as sepsis, burn injury, trauma, lung injury, and pancreatitis. CytoSorb is also being used during and after cardiac surgery to remove inflammatory mediators, such as cytokines and free hemoglobin, which can lead to post-operative complications, including multiple organ failure. In March 2011, the Company received CE Mark approval for its CytoSorb device.

The technology is based upon biocompatible, highly porous polymer sorbent beads that can actively remove toxic substances from blood and other bodily fluids by pore capture and surface absorption. The Company has numerous products under development based upon this unique blood purification technology, which is protected by 32 issued U.S. patents and multiple applications pending, including HemoDefend, ContrastSorb, DrugSorb, and others, with multiple patent applications pending both in the United States and internationally. The Company's intellectual property consists of composition of matter, materials, method of production systems incorporating the technology, and multiple medical uses with expiration dates ranging from 1 to 10 years.

Corporate Actions

On December 1, 2014, the Company received stockholder approval authorizing our Board of Directors to (i) amend our Articles of Incorporation, as amended, to effect a reverse split of our Common Stock, with a reverse split ratio of twenty-five-to-one (25:1); (ii) amend its Articles of Incorporation, as amended, to reduce the total number of authorized shares of Common Stock from 800,000,000 to 50,000,000, after giving effect to the reverse stock split; (iii) amend its Articles of Incorporation, as amended, to reduce the total number of authorized shares of undesignated preferred stock from 100,000,000 to 5,000,000, after giving effect to the reverse stock split; (iv) implement the form, terms and provisions of the CytoSorbents Corporation 2014 Long-Term Incentive Plan; and (v) change its domicile from the State of Nevada to the State of Delaware through our merger with and into a newly-organized subsidiary organized under the laws of the State of Delaware.

On December 3, 2014, the Company effected the aforementioned twenty-five-for-one (25:1) reverse split of its common stock. As a result of the twenty-five-for-one (25:1) reverse stock split, shares of its common stock outstanding were reduced by approximately 96%. Immediately after the reverse split, on December 3, 2014 the Company changed its state of incorporation from the State of Nevada to the State of Delaware pursuant to an Agreement and Plan of Merger, dated December 3, 2014, whereby the Company merged with and into the recently formed, wholly-owned Delaware subsidiary. Pursuant to the Agreement and Plan of Merger, the Company adopted the certificate of incorporation, as amended and restated, and bylaws of its Delaware subsidiary as its certificate of incorporation and bylaws at effective time of the merger. At the effective time of the merger, (i) the Company merged with and into its Delaware subsidiary, (ii) separate corporate existence in Nevada ceased to exist, (iii) the Delaware subsidiary became the surviving corporation, and (iv) each share of common stock, $0.001 par value per share outstanding immediately prior to the effective time was converted into one fully-paid and non-assessable share of common stock of CytoSorbents Corporation, a Delaware corporation, $0.001 par value per share. The reverse stock split, the merger and the Agreement and Plan of Merger were approved by the Board of Directors and stockholders representing a majority of the outstanding common stock.

Reverse Stock Split

As discussed above, the Company's twenty-five-for-one reverse stock split became effective on December 3, 2014. As a result of this action, funds were shifted from the common stock account to the additional paid in capital account to reflect the par value of the reduced number of shares. All share, option and warrant information presented in these financial statements and accompanying footnotes has been retroactively adjusted to reflect the reduced number of shares resulting from this action.

Stock Market Listing

On December 17, 2014 the Company's common stock was approved for listing on The NASDAQ Capital Market ("NASDAQ"), and it began trading on NASDAQ on December 23, 2014 under the symbol "CTSO". Previously, the Company's common stock traded in the over-the-counter-market on the OTC Bulletin Board.

Basis of Consolidation and Foreign Currency Translation

The consolidated financial statements include the accounts of the Parent, CytoSorbents Corporation, and its wholly-owned subsidiaries, CytoSorbents Medical, Inc. and CytoSorbents Europe GmbH. All significant intercompany transactions and balances have been eliminated in consolidation.

Translation gains and losses resulting from the process of remeasuring into the United States of America dollar, the foreign currency financial statements of the European subsidiary, for which the United States of America dollar is the functional currency, are included in operations. Foreign currency transaction losses included in net loss amounted to approximately $507,000 and $386,000 for the years ended December 31, 2015 and 2014, respectively. The Company translates assets and liabilities of the European subsidiary, whose functional currency is their local currency, at the exchange rate in effect at the balance sheet date. The Company translates revenue and expenses at the daily average exchange rates. The Company includes accumulated net translation adjustments in stockholders' equity as a component of accumulated other comprehensive income.

Cash and Cash Equivalents

The Company considers all highly liquid instruments purchased with an original maturity of three months or less to be cash equivalents.

Short-Term Investments

Short-term investments include certificates of deposit with original maturities of greater than three months. The cost of the certificates of deposit approximates fair value. The Company classifies these investments as held-to-maturity securities in accordance with the provisions of ASC-320-10.

Grants and Accounts Receivable

Grants receivable represent amounts due from U.S. government agencies and are included in Grants and Accounts Receivable.

Accounts receivable are unsecured, non-interest bearing customer obligations due under normal trade terms. The Company sells its devices to various hospitals and distributors. The Company performs ongoing credit evaluations of customers' financial condition. Management reviews accounts receivable periodically to determine collectability. Balances that are determined to be uncollectible are written off to the allowance for doubtful accounts. The allowance for doubtful accounts contains a general accrual for estimated bad debts and amounted to $3,275 and $3,756 at December 31, 2015 and December 31, 2014, respectively.

Inventories

Inventories are valued at the lower of cost or market. Cost is determined using a first-in first-out ("FIFO") basis. At December 31, 2015 and December 31, 2014 the Company's inventory was comprised of finished goods, which amounted to $382,099 and $142,693, respectively, work in process which amounted to $758,562 and $326,047, respectively and raw materials which amounted to $50,020 and $68,826, respectively. Devices used in clinical trials or for research and development purposes are removed from inventory and charged to research and development expenses at the time of their use.

Property and Equipment

Property and equipment are recorded at cost less accumulated depreciation. Depreciation of property and equipment is provided for by the straight-line method over the estimated useful lives of the related assets. Leasehold improvements are amortized over the lesser of their economic useful lives or the term of the related leases. Gains and losses on depreciable assets retired or sold are recognized in the statements of operations in the year of disposal. Repairs and maintenance expenditures are expensed as incurred.

Patents

Legal costs incurred to establish patents are capitalized. When patents are issued, capitalized costs are amortized on the straight-line method over the related patent term. In the event a patent is abandoned, the net book value of the patent is written off.

Impairment or Disposal of Long-Lived Assets

The Company assesses the impairment of patents and other long-lived assets under accounting standards for the impairment or disposal of long-lived assets whenever events or changes in circumstances indicate that the carrying value may not be recoverable. For long-lived assets to be held and used, the Company recognizes an impairment loss only if its carrying amount is not recoverable through its undiscounted cash flows and measures the impairment loss based on the difference between the carrying amount and fair value.

Warrant Liability

The Company recognizes the fair value of the warrants as of the date of the warrant grant using the binomial lattice valuation model. At each subsequent reporting date, the Company again measures the fair value of the warrants, and records a change to the warrant liability as appropriate, and the change is reported in the statement of operations.

Revenue Recognition

Product Sales: Revenues from sales of products, all of which are in Europe and Asia, are recognized when title and risk of loss passes to the customer. Recognition of revenue also requires reasonable assurance of collection of sales proceeds and completion of all performance obligations.

*Grant Revenue***:** Revenue from grant income is based on contractual agreements with United States government agencies. Certain agreements provide for reimbursement of costs, while other agreements provide for reimbursement of costs and an overhead margin. Revenues are recognized when milestones have been achieved and revenues have been earned. Costs are recorded as incurred. Costs subject to reimbursement by these grants have been reflected as costs of revenue.

*Deferred Revenue***:** The Company defers revenue that has been received but not yet earned on government contracts and product sales. This revenue will be recognized as income in the period in which the revenue is earned. All deferred revenue is expected to be earned within a one year of the balance sheet date.

Research and Development

All research and development costs, payments to laboratories and research consultants are expensed when incurred.

Advertising Expenses

Advertising costs are charged to activities when incurred. Advertising expense amounted to approximately $282,000 and $142,000 in 2015 and 2014, respectively, and is included in selling, general, and administrative expenses on the consolidated statement of operations.

Income Taxes

Income taxes are accounted for under the asset and liability method prescribed by accounting standards for accounting for income taxes. Deferred income taxes are recorded for temporary differences between financial statement carrying amounts and the tax basis of assets and liabilities. Deferred tax assets and liabilities reflect the tax rates expected to be in effect for the years in which the differences are expected to reverse. A valuation allowance is provided if it is more likely than not that some or all of the deferred tax asset will not be realized. Under Section 382 of the Internal Revenue Code the net operating losses generated prior to the previously completed reverse merger may be limited due to the change in ownership. Additionally, net operating losses generated subsequent to the reverse merger may be limited in the event of changes in ownership.

The Company follows the accounting standards associated with uncertain tax provisions. The Company had no unrecognized tax benefits at December 31, 2015 or 2014. The Company files tax returns in the U.S. federal and state jurisdictions. The Company currently has no open years prior to December 31, 2012 and has no income tax related penalties or interest for the periods presented in these financial statements.

The Company utilizes the Technology Business Tax Certificate Transfer Program to sell a portion of its New Jersey Net Operating Loss tax carryforwards to an industrial company.

Our European subsidiary, CytoSorbents Europe GmbH annually files a corporate tax return, a VAT return, and a trade tax return in Germany.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities. Actual results could differ from these estimates. Significant estimates in these financials are the valuation of options granted, the valuation of preferred shares issued as stock dividends, valuation methods used to determine the fair value of the warrant liability and valuation methods used in determining any debt discount associated with the convertible securities.

Concentration of Credit Risk

The Company maintains cash balances, at times, with financial institutions in excess of amounts insured by the Federal Deposit Insurance Corporation. Management monitors the soundness of these institutions in an effort to minimize its collection risk of these balances.

As of December 31, 2015, three distributors accounted for approximately 48 percent of outstanding grant and accounts receivable. As of December 31, 2014, a U.S. Government agency accounted for approximately 66 percent of outstanding accounts receivable. For the year ended December 31, 2015, approximately 14 percent of revenue was from one U.S. government grant agency. For the year ended December 31, 2014, approximately 24 percent of revenue was from two U.S. government grant agencies and approximately 12 percent of revenues was from one distributor.

Financial Instruments

The carrying values of cash and cash equivalents, accounts receivable, accounts payable and other debt obligations approximate their fair values due to their short-term nature.

Net Loss per Common Share

Basic earnings per share is computed by dividing income (loss) available to common stockholders by the weighted average number of common shares outstanding during the period. Diluted earnings per common share is computed using the treasury stock method on the basis of the weighted-average number of shares of common stock plus the dilutive effect of potential common shares outstanding during the period. Dilutive potential common shares include outstanding warrants, stock options and restricted shares. The computation of diluted earnings per share does not assume conversion, exercise or contingent exercise of securities that would have an anti-dilutive effect on earnings. (See Note 11).

Stock-Based Compensation

The Company accounts for its stock-based compensation under the recognition requirements of accounting standards for accounting for stock-based compensation for employees and directors whereby each option granted is valued at fair market value on the date of grant. Under these accounting standards, the fair value of each option is estimated on the date of grant using the Black-Scholes option pricing model.

The Company also follows the guidance of accounting standards for accounting for equity instruments that are issued to other than employees for acquiring, or in conjunction with selling, goods or services for equity instruments issued to consultants.

Effects of Recent Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board ("FASB") issued ASU No. 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40). The ASU requires all entities to evaluate for the existence of conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the issuance date of the financial statements. The amendments in this update are effective for the annual period ending after December 15, 2016, and for annual periods and interim periods thereafter. Early application is permitted. The Company is currently evaluating the impact of the updated guidance, but the Company does not believe that the adoption of ASU 2014-15 will have a significant impact on its consolidated financial statements but may impact the Company's footnote disclosures.

In May 2014, the FASB issued ASU 2014-09, "Revenue with Contracts from Customers." ASU 2014-09 supersedes the current revenue recognition guidance, including industry-specific guidance. The ASU introduces a five-step model to achieve its core principal of the entity recognizing revenue to depict the transfer of goods or services to customers at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods and services. In August 2014, the FASB issued ASU 2015-14 which deferred the effective date by one year. Accordingly, the updated guidance is effective for public entities for interim and annual periods beginning after December 15, 2017 and early adoption is permitted as of the beginning of an interim or annual reporting period beginning after December 31, 2016. The Company is currently evaluating the impact of the updated guidance, but the Company does not believe that the adoption of ASU 2014-09 will have a significant impact on its consolidated financial statements.

In July 2015, the FASB issued ASU 2015-11, "Inventory: Simplifying the Measurement of Inventory." ASU 2015-11 clarifies current guidance regarding the valuation of inventory. The ASU requires that inventory be measured at the lower of cost or net realizable value. This ASU does not apply to inventory that is measured using the last-in, first-out (LIFO) or the retail inventory method. The updated guidance is effective for public entities for fiscal years beginning after December 15, 2016, and interim periods within fiscal years beginning after December 15, 2017. The Company is currently evaluating the impact of the updated guidance, but the Company does not believe that the adoption of ASU 2015-11 will have a significant impact on its consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, "Leases (Topic 842)". ASU 2016-02 outlines reporting requirements for Lessees to recognize a right-of-use asset and corresponding liability on the balance sheet for all leases covering a period of greater than 12 months. The liability is to be measured as the present value of the future minimum lease payments, plus any initial direct costs. The minimum payments are discounted using the rate implicit in the lease, or, if not known, the lessee's incremental borrowing rate. The Company is currently evaluating the impact of the updated guidance on the consolidated financial statements.

Shipping and Handling Costs

The cost of shipping product to customers and distributors is typically borne by the customer or distributor. The Company records shipping and handling costs in Research and Development. Total freight costs amounted to approximately $145,000 and $103,000 for the years ended December 31, 2015 and 2014 respectively.

Reclassifications

Certain reclassifications have been made to the December 31, 2014 financial statements in order to conform to the 2015 financial statement presentation. There was no change in the reported amount of the accumulated deficit as a result of these reclassifications.

3. PROPERTY AND EQUIPMENT, NET:

Property and equipment - net, consists of the following:

December 31,	2015	2014	Depreciation/ Amortization Period
Furniture and fixtures	$ 205,019	$ 186,121	7 years
Equipment and computers	2,287,305	2,000,821	3 to 7 years
Leasehold improvements	605,939	515,515	Lesser of term of lease or estimated useful life
	3,098,263	2,702,457	
Less accumulated depreciation and amortization	2,540,974	2,456,636	
Property and Equipment, Net	$ 557,289	$ 245,821	

Depreciation expense for the years ended December 31, 2015 and 2014 amounted to $87,397 and $48,429, respectively.

4. OTHER ASSETS:

Other assets consist of the following:

December 31,	2015	2014
Intangible assets, net	$ 771,795	$ 557,528
Security deposits	64,954	58,270
Total	$ 836,749	$ 615,798

Intangible assets consist of the following:

December 31,	**2015**		**2014**	
	Gross Amount	Accumulated Amortization	Gross Amount	Accumulated Amortization
Patents	$ 938,969	$ 167,174	$ 706,796	$ 149,268

Amortization expense amounted to $25,573 and 17,118 for the years ended December 31, 2015 and 2014, respectively.

Amortization expense for the next five years will be approximately $25,500 for the year ended December 31, 2016; approximately $18,500 for the year ended December 31, 2017; approximately $10,500 for the year ended December 31, 2018; approximately $10,500 for the year ended December 31, 2019; and approximately $9,600 for the year ended December 31, 2020.

5. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES:

Accrued expenses and other current liabilities consist of the following:

	2015	**2014**
Professional fees	$ 150,121	$ 293,758
Travel and entertainment	219,627	107,542
Clinical study costs	-	36,465
Sales, payroll and income taxes payable	22,592	64,745
Accrued salaries and commissions	141,606	204,515
Accrued royalties	102,586	45,200
Customer deposits	30,000	30,000
Board of Director fees	19,250	11,250
Other	37,236	31,409
	$ 723,018	$ 824,884

6. CONVERTIBLE NOTES:

On June 21, 2013 (the "June Closing Date"), the Company issued convertible notes to certain accredited investors (the "June Purchasers"), whereby the Company agreed to sell and the June Purchasers agreed to purchase the convertible notes in the aggregate principal amount of $1,098,000 (the "June Notes"). The June Notes were to mature one (1) year from the June Closing Date (the "June Maturity Date"), bear interest at an annual rate of 8%, and automatically convert into shares of the Company's Common Stock at a conversion price of $3.125 at maturity or earlier at the option of the June Purchaser. In connection with the issuance of the June Notes, the Company issued warrants to purchase shares of Common Stock, providing 50% coverage, exercisable at $3.75 per share (the "June Warrants"). On June 21, 2014, all outstanding June Notes were converted into 379,469 shares of Common Stock, consisting of 351,360 shares related to the principal value of the June Notes and 28,109 shares of Common Stock for payment of interest earned on the June Notes.

On September 30, 2013 (the "September Closing Date"), the Company issued convertible notes to certain accredited investors (the "September Purchasers"), whereby the Company agreed to sell and the September Purchasers agreed to purchase the convertible notes in the aggregate principal amount of $745,000 (the "September Notes"). The September Notes were to mature one (1) year from the September Closing Date (the "September Maturity Date"), bear interest at an annual rate of 8%, and automatically convert into shares of Common Stock at a conversion price of $2.50 at maturity, or earlier at the option of the September Purchaser. In connection with the issuance of the September Notes, the Company issued warrants to purchase shares of Common Stock, providing 50% coverage, exercisable at $3.125 per share (the "September Warrants"). On September 30, 2014, all outstanding September Notes were converted into 298,000 shares of Common Stock related to the principal value of the September Notes and 23,840 shares of Common Stock for payment of interest earned on the September Notes.

The Company allocates the proceeds associated with the issuance of convertible notes based on the relative fair value of the convertible notes and warrants. Additionally, the Company evaluates if the embedded conversion option results in a beneficial conversion feature by comparing the relative fair value allocated to the convertible notes to the market value of the underlying Common Stock subject to conversion. In connection with the convertible note issuances during the years ended December 31, 2013, the Company received proceeds of $1,843,000. The Company allocated the proceeds in accordance with FASB Codification Topic 470 based on the related fair value as follows: $1,511,883 was allocated to the convertible notes and $171,012 to the warrants. Additionally, the embedded conversion feature resulted in a beneficial conversion feature in the amount of $160,105. The value assigned to the warrants resulting from the relative fair value calculation as well as the value of the beneficial conversion feature is recorded as a debt discount and is presented in the consolidated balance sheets. The debt discount has been amortized to interest expense over the term of the convertible notes. During the years ended December 31, 2015 and 2014, debt discount of approximately $-0- and $199,000, respectively, was charged to interest expense.

7. INCOME TAXES:

The Company accounts for income taxes under FASB ASC 740 ("ASC 740"). Deferred income tax assets and liabilities are determined based upon differences between financial reporting and tax bases of assets and liabilities, which are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

The Company's consolidated loss before income taxes was $ (8,456,344) and $ (9,707,314) for the years ended December 31, 2015 and 2014, respectively.

The provision for income taxes consists of the following:

	Year Ended December 31,	
	2015	2014
State Tax, including sale of New Jersey losses & credits	$ (324,606)	$ (385,642)
Foreign tax provision	-	-
	$ (324,606)	$ (385,642)

As of December 31, 2015, the Company had federal net operating loss ("NOL") carry forwards of $31,663,000, state NOL carry forwards of $7,451,680, and foreign NOL carry forwards of $6,174,035 which are available to reduce future taxable income. The NOL carry forwards, if not utilized, will begin to expire at various dates starting in 2021. As of December 31, 2015, the Company had Federal and state research and development tax credit carryforwards of $1,113,151 and $182,717, respectively, available to reduce future tax liabilities which will begin to expire at various dates starting in 2022.

The NOL carry forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. The NOLs may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Section 382 of the Internal Revenue Code of 1986, as amended, as well as similar state tax provisions. This could limit the amount of NOLs that the Company can utilize annually to offset future taxable income or tax liabilities. The amount of the annual limitation, if any, will generally be determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

Sale of Net Operating Losses (NOLs)

The Company may be eligible, from time to time, to receive cash from the sale of its Net Operating Losses and R&D tax credits under the State of New Jersey Technology Business Tax Certificate Transfer Program.

In January 2016, the Company received a net cash amount of $324,606 from the sale of the 2014 state NOL and research and development credits.

The principal components of the Company's deferred tax assets and liabilities are as follows:

	Year Ended December 31,	
	2015	2014
Current and long term deferred tax assets:		
Net operating loss carryforward	$ 13,041,156	$ 11,073,004
Stock Options	486,726	
Warrants	120,329	-
Research and development credit carryforward	1,113,151	
Accruals and others	(12,065)	-
Gross deferred tax assets	14,749,297	11,073,004
Less valuation allowance	(14,746,091)	(11,073,004)
	3,206	-
Deferred tax liability:		
Fixed Assets	(3,206)	-
Net deferred tax assets	$ -	$ -

In assessing the realization of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. Management considers the scheduled reversal of deferred tax liabilities, projected future taxable income and tax planning strategies in making this assessment. Based on this assessment, management has established a full valuation allowance against all of the deferred tax assets for each period because it is more likely than not that all of the deferred tax assets will not be realized.

The increases in valuation allowance for the years ended December 31, 2015 and 2014 were $3,673,088 and $2,771,746, respectively.

A reconciliation of income tax (expense) benefit at the statutory federal income tax rate and income taxes as reflected in the financial statements is as follows:

	Year Ended December 31,	
	2015	2014
Federal statutory rate	(34.0)%	(34.0)%
State taxes, net of federal benefit	(3.1)	-
Foreign rate differential	1.5	-
Permanent items	(2.9)	1.0
Rate change and true-up	(5.1)	-
Timing differences	-	(1.0)
Change in valuation allowance	43.4	34.0
R&D credit	(3.6)	-
Effective income tax rate	(3.8)%	-%

8. WARRANT LIABILITY:

In connection with its March 11, 2014 offering, the Company issued warrants to purchase 816,000 shares of Common Stock. The Company recognizes these warrants as liabilities at their fair value on the date of grant, then measures the fair value of the warrants on each reporting date, and records a change to the warrant liability as appropriate. The warrants have certain pricing provisions which apply if the Company sells or issues Common Stock or Common Stock equivalents at a price that is less than the exercise price of the warrants, over the life of the warrants, excluding certain exempt issuances.

The Company recognized an initial warrant liability for the warrants issued in connection with the Offering completed in March 2014. The initial warrant liability recognized on the related warrants totaled $862,920, which was based on the March 11, 2014 five-day weighted average closing price per share of the Company's Common Stock of $6.00. On December 31, 2015, the five day weighted average closing price per share of Common Stock was $5.85. Due to the fluctuations in the market value of the Company's Common Stock from December 31, 2014 through December 31, 2015, the Company recorded a change in the fair value of the warrant liability of $1,345,290 during the year ended December 31, 2015. Due to fluctuations in the market value of the Company's Common Stock from March 11, 2014 through December 31, 2014, the Company recorded a change in the fair value of the warrant liability of $2,118,498 during the year ended December 31, 2014.

The assumptions used in connection with the valuation of warrants issued utilizing the binomial lattice valuation model were as follows:

	2015	2014
Number of shares underlying the warrants	736,000	816,000
Exercise price	$ 7.8125	$ 7.8125
Volatility	66.5%	28.3%
Risk-free interest rate	1.35%	1.43%
Expected dividend yield	0	0
Expected warrant life (years)	3.19	4.19
Stock price	$ 5.85	$ 10.22

9. COMMITMENTS AND CONTINGENCIES:

The Company is obligated under non-cancelable operating leases for office space expiring at various dates through May 2017. The aggregate minimum future payments under these leases are approximately as follows:

Year ending December 31,		
2016	$	265,879
2017		119,750
Total	$	385,629

The preceding data reflects existing leases through the date of this report and does not include replacements upon their expiration. In the normal course of business, operating leases are normally renewed or replaced by other leases.

Rent expense for the years ended December 31, 2015 and 2014 amounted to approximately $411,000 and $328,000, respectively.

Employment Agreements

On July 14, 2015, CytoSorbents Corporation entered into executive employment agreements with its principal executives, Dr. Phillip P. Chan, President and Chief Executive Officer, Vincent Capponi, Chief Operating Officer, and Kathleen P. Bloch, Chief Financial Officer. Each of these agreements has an initial term of three years, and is retroactively effective as of January 1, 2015. These agreements provide for base salary and other customary benefits which include participation in group insurance plans, paid time off and reimbursement of certain business related expenses, including travel and continuing educational expenses, as well as bonus and/or equity awards at the discretion of the Board of Directors. In addition, the agreements provide for certain termination benefits in the event of termination without Cause or voluntary termination of employment for "Good Reason", as defined in each agreement. The agreements also provide for certain benefits in the event of a Change in Control of the Company, as defined in each agreement.

Litigation

The Company is, from time to time, subject to claims and litigation arising in the ordinary course of business. The Company intends to defend vigorously against any future claims and litigation. The Company is not currently a party to any legal proceedings.

Royalty Agreements

Pursuant to an agreement dated August 11, 2003, an existing investor agreed to make a $4 million equity investment in the Company. These amounts were received by the Company in 2003. In connection with this agreement the Company granted the investor a future royalty of 3% on all gross revenues received by the Company from the sale of its CytoSorb device. For the years ended December 31, 2015 and 2014 the Company recorded royalty expenses of approximately $118,000 and $93,000 respectively.

License Agreements

In an agreement dated September 1, 2006, the Company entered into a license agreement which provides the Company the exclusive right to use its patented technology and proprietary know how relating to adsorbent polymers for a period of 18 years. Under the terms of the agreement, the Company has agreed to pay royalties of 2.5% to 5% on the sale of certain of its products if and when those products are sold commercially for a term not greater than 18 years commencing with the first sale of such product. For the years ended December 31, 2015 and 2014 per the terms of the license agreement the Company recorded licensing expenses of approximately $158,000 and $77,000 respectively.

10. STOCKHOLDERS' EQUITY:

Preferred Stock

In December 2014, the Company amended its articles of incorporation to reduce the total number of authorized shares of preferred stock after giving effect to the reverse stock split (see Note 2). The amended articles of incorporation authorize the issuance of up to 5,000,000 shares of "blank check" preferred stock, with such designation rights and preferences as may be determined from time to time by the Board of Directors.

Conversion of Series A and Series B Preferred Stock into Common Stock.

On October 9, 2014, the Company filed with the Nevada Secretary of State an Amendment (the "Series A Amendment") to the Certificate of Designation, as amended (the "Series A Certificate of Designation") of the Series A Preferred Stock. The Series A Amendment, which became effective on October 9, 2014, (i) amended the Series A Certificate of Designation to allow the stockholders representing eighty percent (80%) of the issued and outstanding shares of Series A Preferred Stock to elect to convert all issued and outstanding shares of Series A Preferred Stock into Common Stock of the Company, $0.001 par value per share (the "Common Stock"), at the then-effective "Conversion Price," as defined in the Series A Certificate of Designation, and (ii) as consideration for approving such amendment, amended the Conversion Price from $31.25 per share to $19.25 per share, except with respect to the shares of Series A Preferred Stock covered by that certain Agreement and Consent dated as of June 25, 2008 by and among the Company and certain holders of Series A Preferred Stock. The fair value of the reduction in the conversion price was determined based on the five day volume weighted average price of the Series A common stock equivalent immediately before and immediately after the reduction in conversion price. Immediately following effectiveness of the Series A Amendment, the stockholders representing over 88 percent (88%) of the then-issued and outstanding Series A Preferred Stock elected to convert all issued and outstanding Series A Preferred Stock into Common Stock at the Conversion Price, as amended. As a result of this election by the holders of Series A Preferred Stock, 1,894,969 shares of Series A Preferred Stock were converted into 103,332 post-split shares of Common Stock.

In addition, on October 9, 2014, the Company also filed with the Nevada Secretary of State an Amendment (the "Series B Amendment") to the Certificate of Designation (the "Series B Certificate of Designation") of the Series B Preferred Stock. The Series B Amendment, which became effective on October 9, 2014, amended the Series B Certificate of Designation to allow the holders of a majority of the Series B Preferred Stock, including NJTC Investment Fund, LP, to elect to convert all issued and outstanding shares of Series B Preferred Stock into Common Stock. Immediately following effectiveness of the Series B Amendment, the stockholders representing over 93 percent (93%) of the then-issued and outstanding Series B Preferred Stock elected to convert all issued and outstanding Series B Preferred Stock into Common Stock. Each share of Series B Preferred Stock had a stated value of $100.00 (the "Series B Stated Value"), and was convertible into that number of shares of Common Stock equal to the Series B Stated Value at a conversion price of $0.90. As consideration for approving the Series B Amendment, the holders of Series B Preferred Stock received a one-time dividend equal to ten percent (10%) of the shares of Series B Preferred Stock then held. As a result of this election by the holders of Series B Preferred Stock, 84,283.99 shares of Series B Preferred Stock were issued a dividend of 10% and then the 92,712.27 shares were converted into 10,244,450 post-split shares of Common Stock. As a result of the conversion, the carrying value of the Series B stock was reclassified to permanent equity.

After giving effect to the conversions of the Series A Preferred Stock and Series B Preferred Stock described above, there are no shares of Preferred Stock of the Company issued and outstanding as of December 31, 2015 and December 31, 2014.

During the year ended December 31, 2014, the Company issued 135,303 shares of Series A Preferred Stock respectively as payment of stock dividends at the stated value of $1.00 per share. The fair value of the non-cash stock dividends, including the value of the conversion price reduction, amounted to $238,313 for the year ended December 31, 2014.

During the year ended December 31, 2014, the Company issued 14,499.96 shares of Series B Preferred Stock respectively as payment of stock dividends at the stated value of $100.00 per share. The fair value of the non-cash stock dividends, which includes the one-time dividend disclosed above, amounted to $9,028,360 for the year ended December 31, 2014.

Determination of Stock Dividend Fair Value

The Company utilizes a five day volume weighted average price of actual closing market prices for the Company's Common Stock as its basis for estimating the fair value of the preferred stock dividends.

Common Stock

Shelf Registration

On July 29, 2015, the Company's registration statement on Form S-3, as filed with the SEC on July 23, 2015, was declared effective using a "shelf" registration process. Under this shelf registration statement, the Company may issue, in one or more offerings, any combination of common stock, preferred stock, senior or subordinated debt securities, warrants, or units, up to a total dollar amount of $100 million.

November 4, 2015 Controlled Equity Offering

On November 4, 2015, the Company entered into a Controlled Equity Offering[SM] Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald and Co., as agent ("Cantor "), pursuant to which the Company may offer to sell, from time to time through Cantor, shares of the Company's common stock, par value $0.001 per share (the "Common Stock"), having an aggregate offering price of up to $25,000,000 (the "Shares") Any shares offered and sold will be issued pursuant to the Company's shelf registration statement on Form S-3 (Registration No. 333-205806), and the related prospectus previously declared effective by the Securities and Exchange Commission (the "SEC") on July 29, 2015 (the "Registration Statement"), as supplemented by a prospectus supplement, dated November 4, 2015, which the Company filed with the SEC pursuant to Rule 424(b)(5) under the Securities Act.

Under the Sales Agreement, Cantor may sell Shares by any method permitted by law and deemed to be an "at the market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on The NASDAQ Capital Market, on any existing trading market for the Common Stock or to or through a market maker. In addition, under the Sales Agreement, Cantor may sell the Shares by any other method permitted by law, including in privately negotiated transactions. The Company may instruct Cantor not to sell Shares if the sales cannot be effected at or above the price designated by the Company from time to time.

The Company is not obligated to make any sales of Shares under the Sales Agreement, and if it elects to make any sales, the Company can set a minimum sales price for the Shares. The offering of Shares pursuant to the Sales Agreement will terminate upon the earlier of (a) the sale of all the shares subject to the Sales Agreement of (b) the termination of the Sales Agreement by Cantor or the Company, as permitted therein. In the fourth quarter of 2015, the Company sold 28,880 shares at an average selling price of $8.02 per share, generating net proceeds of approximately $225,000 under the Sales Agreement.

The Company pays a commission rate of 3.0% of the aggregate gross proceeds from each sale of Shares and has agreed to provide Cantor with customary indemnification and contribution rights. The Company has also reimbursed Cantor $50,000 for certain specified expenses in connection with entering into the Sales Agreement.

The Company intends to use the net proceeds raised through "at the market" sales for research and development activities, which include the funding of additional clinical studies and costs of obtaining regulatory approvals in countries not covered by the CE Mark, capital expenditures and other costs necessary to expand production capacity, support of various sales and marketing efforts, product development and general working capital purposes.

January 14, 2015 Public Offering

On January 14, 2015, the Company closed an underwritten public offering (the "Offering") consisting of 1,250,000 shares of common stock at a price of $8.25 per share for an aggregate price of $10,312,500. The Company received net proceeds from the Offering of approximately $9,409,000. The net proceeds received by the Company from the Offering are being used to fund clinical studies, expand production capacity, support various sales and marketing efforts, product development and general working capital purposes.

The Company conducted the Offering pursuant to a registration statement on Form S-1 (File No. 333-199762), which was declared effective by the U.S. Securities and Exchange Commission (the "SEC") on January 8, 2015. The Company filed a final prospectus on January 9, 2015, disclosing the final terms of the Offering.

In connection with the Offering, on January 8, 2015, the Company entered into underwriting agreements with Brean Capital, LLC and H.C. Wainwright & Co., LLC (the "Representatives"), who acted as book-running managers and as representatives of the underwriters in the Offering.

In connection with the successful completion of the Offering, the underwriters received aggregate discounts and commissions of 6% of the gross proceeds of the sale of the shares in the Offering. In addition, the Company agreed to issue warrants to the Representatives (the "Representatives' warrants") that allow for the purchase of 30,000 shares of the Company's common stock. These warrants had a fair value of approximately $30,000 on the date of the closing. The Representatives' warrants are exercisable at any time for a period of five years, commencing on the date of the effectiveness of the registration statement, at a price per share equal to 120% of the public offering price per share of the common stock in the Offering. The Company also agreed to reimburse the underwriters for actual out-of-pocket expenses related to the Offering, which amounted to approximately $85,000. The Company also granted the Representatives a right of first refusal to participate in any subsequent offering or placement of the Company's securities that takes place within nine months following the effective date of the registration statement.

March 7, 2014 Offering

On March 7, 2014, the Company entered into subscription agreements with certain investors providing for the issuance and sale by the Company, or the March 2014 Offering, of 1,632,000 units, or the Units, for an aggregate purchase price of $10,200,000. Each Unit is comprised of one share of the Company's common stock, priced at $6.25 per share, par value $0.001 per share and a warrant to purchase 0.50 shares of common stock at an exercise price of $7.8125 per share. The warrants are convertible into a total of 816,000 shares of common stock. Each warrant is exercisable for a period of five (5) years beginning on March 11, 2014, the date of the closing of the sale of these securities, and are only exercisable for cash if at the time of exercise there is an effective registration statement registering the warrants and shares underlying the warrants.

The Company received net proceeds from the March 2014 Offering of approximately $9,451,000. The net proceeds received by the Company from the March 2014 Offering will be used for building additional sales and marketing infrastructure, clinical studies, working capital and general corporate purposes.

The Company conducted the March 2014 Offering pursuant to a registration statement on Form S-1 (File No. 333-193053) which was declared effective by the Securities and Exchange Commission on February 14, 2014 and an additional registration statement on Form S-1 (File No. 333-194394) to register an additional amount of securities having a proposed maximum aggregate offering price of $2,762,500, which increased the total registered amount to $16,575,000 assuming the full cash exercise of the warrants for cash. The Company filed a final prospectus on March 7, 2014, disclosing the final terms of the March 2014 Offering.

In connection with the March 2014 Offering, on March 7, 2014, the Company entered into a placement agency agreement with Brean Capital, LLC pursuant to which the placement agent agreed to act as the Company's exclusive placement agent for the March 2014 Offering and sale of the Units.

In connection with the successful completion of the March 2014 Offering, the placement agent received an aggregate cash placement agent fee equal to 6% of the gross proceeds of the sale of the Units in the Offering and a warrant to purchase 48,960 shares of Common Stock at an exercise price of $7.50 per share exercisable for five years from the effective date of the placement agency agreement. The placement agent warrant contains piggy-back registration rights which expire on the fifth anniversary of the effective date of the registration statement. We have also agreed to reimburse the placement agent for actual out-of-pocket expenses up to a maximum of 2% of gross proceeds from the transaction. We also granted the placement agent a right of first refusal to participate in any subsequent offering or placement of our securities that takes place within twelve months following the effective date of the registration statement.

Reverse Stock Split

In December 2014, the Company amended its articles of incorporation to reduce the total number of authorized shares of common stock after giving effect to the reverse stock split (see Note 2). The amended articles of incorporation authorize the issuance of up to 50,000,000 shares with a par value of $0.001 per share.

Purchase Agreement

In May 2010, the Company executed a purchase agreement, or the Purchase Agreement, and a registration rights agreement, or the Registration Rights Agreement, with Lincoln Park Capital Fund, LLC ("LPC"). Under the Purchase Agreement, LPC is obligated, under certain conditions, to purchase from the Company up to $6 million of our Common Stock, from time to time over a 750 day (twenty-five (25) monthly) period.

The Company had the right, but not the obligation, to direct LPC to purchase up to $6,000,000 of its Common Stock in amounts up to $50,000 as often as every two business days under certain conditions. The Company could also accelerate the amount of its common stock to be purchased under certain circumstances. No sales of shares could occur at a purchase price below $2.50 per share or without a registration statement having been declared effective. The purchase price of the shares will be based on the market prices of our shares at the time of sale as computed under the Purchase Agreement without any fixed discount. The Company may at any time at its sole discretion terminate the Purchase Agreement without fee, penalty or cost upon one business days' notice.

The Company issued 46,154 shares of our Common Stock to LPC as a commitment fee for entering into the agreement, and was obligated to issue up to an additional 46,154 shares pro rata as LPC purchases up to $6,000,000 of its Common Stock as directed by the Company. LPC may not assign any of its rights or obligations under the Purchase Agreement. During the years ended December 31, 2015 and 2014 the Company issued a total of -0- and 99,336 shares of Common Stock, which includes the commitment shares per the terms of the Purchase Agreement with LPC at an average price of approximately $3.09 and $2.80 per share of Common respectively. The fair value of the Commitment shares has been recorded as a cost of raising capital.

In December 2011, the Company terminated the Purchase Agreement and executed a new purchase agreement, or the New Purchase Agreement, and a registration rights agreement, or the New Registration Rights Agreement, with Lincoln Park Capital Fund, LLC ("LPC"). Under the New Purchase Agreement, LPC is obligated, under certain conditions, to purchase from the Company up to $8.5 million of our Common Stock, from time to time over a thirty-two (32) month) period.

The Company had the right, but not the obligation, to direct LPC to purchase up to $8,500,000 of its Common Stock in amounts up to $50,000 as often as every two business days under certain conditions. The Company could also accelerate the amount of its common stock to be purchased under certain circumstances. No sales of shares could occur at a purchase price below $2.50 per share or without a registration statement having been declared effective. The purchase price of the shares was based on the market prices of our shares at the time of sale as computed under the Purchase Agreement without any fixed discount. The Company could at any time at its sole discretion terminate the Purchase Agreement without fee, penalty or cost upon one business days' notice.

There was no up-front commitment fee paid to LPC for entering into the new agreement, however the Company is obligated to issue up to an additional 65,385 shares pro rata as LPC purchases up to $8,500,000 of its Common Stock as directed by the Company. LPC could not assign any of its rights or obligations under the Purchase Agreement.

The Company has not sold any shares of its Common Stock under the New Purchase Agreement since January 17, 2014. The New Purchase Agreement expired pursuant to its terms in August 2014. At the time of expiration, $2,400,000 remained unused under the New Purchase Agreement with LPC.

Stock Option Plans

As of December 31, 2015, the Company had two Long Term Incentive Plans (the "2014 Plan" and the "2006 Plan") to attract, retain, and provide incentives to employees, officers, directors, and consultants. The Plans generally provide for the granting of stock, stock options, stock appreciation rights, restricted shares, or any combination of the foregoing to eligible participants.

A total of 3,100,000 and 1,600,000 shares of common stock are reserved for issuance under the 2014 Plan and the 2006 Plan, respectively. As of December 31, 2015 there were outstanding options to purchase approximately 253,000 and 272,000 shares of common stock reserved under the 2014 Plan and the 2006 Plan, respectively.

The 2014 and 2006 Plans as well as grants issued outside of the Plan are administered by the Board of Directors. The Board is authorized to select from among eligible employees, directors, advisors and consultants those individuals to whom incentives are to be granted and to determine the number of shares to be subject to, and the terms and conditions of the options. The Board is also authorized to prescribe, amend and rescind terms relating to options granted under the Plans. Generally, the interpretation and construction of any provision of the Plans or any options granted hereunder is within the discretion of the Board.

The Plan provides that options may or may not be Incentive Stock Options (ISOs) within the meaning of Section 422 of the Internal Revenue Code. Only employees of the Company are eligible to receive ISOs, while employees and non-employee directors, advisors and consultants are eligible to receive options, which are not ISOs, i.e. "Non-Qualified Options." Because the Company has not yet obtained shareholder approval of the 2006 Plan, all options granted thereunder to date are "Non-Qualified Options" and until such shareholder approval is obtained, all future options issued under the 2006 Plan will also be "Non-Qualified Options."

In December 2014, the Company's received shareholder approval authorizing the Board of Directors to implement the form, terms and provisions of the 2014 Plan. Accordingly, any options issued to employees under the 2014 Plan will be ISOs within the meaning of Section 422 of the Internal Revenue Code.

Stock-based Compensation

Total share-based employee, director, and consultant compensation for the years ended December 31, 2015 and 2014 amounted to approximately $382,000 and $696,000, respectively. These amounts are included in the statement of operations under the captions research and development ($126,000 and $144,000) and general and administrative ($256,000 and $552,000), respectively.

The summary of the stock option activity for the years ended December 31, 2015 and 2014 is as follows:

	Shares	Weighted Average Exercise per Share	Weighted Average Remaining Contractual Life (Years)
Outstanding January 1, 2014	1,916,951	$ 5.00	5.1
Granted	732,800	$ 5.02	8.7
Forfeited	(227,810)	$ 3.26	—
Expired	(2,502)	$ 45.80	—
Exercised	(117,252)	$ 0.97	—
Outstanding, December 31, 2014	2,302,187	$ 5.37	6.1
Granted	681,000	$ 7.88	9.0
Forfeited	(166,287)	$ 5.19	8.2
Expired	—	$ —	—
Exercised	(339,621)	$ 1.74	3.2
Outstanding, December 31, 2015	2,477,279	$ 6.56	6.2

The fair value of each stock option was estimated using the Black Scholes pricing model which takes into account as of the grant date the exercise price (ranging from $5.20 to $11.48 per share) and expected life of the stock option (ranging from 3 to 10 years), the current price of the underlying stock and its expected volatility (ranging from 28.3 to 77.9 percent), expected dividends (-0- percent) on the stock and the risk free interest rate (.86 to 1.95 percent) for the term of the stock option.

The intrinsic value is calculated at the difference between the market value as of December 31, 2015 of $5.57 and the exercise price of the shares.

Options Outstanding				
Range of Exercise Price	Number Outstanding at December 31, 2015	Weighted Average Exercise Price	Weighted Average Remaining Life (Years)	Aggregate Intrinsic Value
$0.88 - $166.00	2,477,279	$ 6.56	6.2	$ 3,634,961

Options Exercisable		
Number Exercisable at December 31, 2015	Weighted Average Exercise Price	Aggregate Intrinsic Value
1,682,571	$ 6.18	$3,491,056

The summary of the status of the Company's non-vested options for the year ended December 31, 2015 is as follows:

	Shares	Weighted Average Grant Date Fair Value
Non-vested, January 1, 2015	874,530	$ 1.37
Granted	681,000	3.33
Forfeited	(178,446)	0.18
Vested	(582,576)	0.21
Non-vested, December 31, 2015	794,708	$ 2.72

As of December 31, 2015, the Company had approximately $393,000 of total unrecognized compensation cost related to stock options which will be amortized over 0.74 years. In April 2015, the Board of Directors granted options to purchase 566,000 shares of common stock to the Company's employees which will vest upon achievement of certain specific, predetermined milestones. The grant date fair value of these unvested options amounted to approximately $1,388,000. Due to the uncertainty over whether these options will vest, which only occurs if the Company meets the predetermined milestones, no charge for these options has been recorded in the consolidated statements of operations for the year ended December 31, 2015. The Company is currently evaluating the probability and likelihood that any of these predetermined performance milestones being achieved and will accrue charges as it becomes likely that they will be achieved.

In addition, in April 2015, the Board of Directors also granted 960,000 restricted stock units, valued at $7,747,200, to Company employees and 240,000 restricted stock units, valued at $1,936,000, to the members of the Board of Directors, which will only vest upon a Change in Control of the Company, as defined in the Company's 2014 Long-Term Incentive Plan. Due to the uncertainty over whether these restricted stock units will vest, which only happens upon a Change in Control, no charge for these restricted stock units has been recorded in the consolidated statement of operations for the year ended December 31, 2015.

As of December 31, 2015, the Company has the following warrants to purchase common stock outstanding:

Number of Shares To be Purchased		Warrant Exercise Price per Share	Warrant Expiration Date
8,000	$	3.125	February 15, 2016
6,667	$	3.750	February 15, 2016
9,605	$	31.250	October 24, 2016
40,001	$	4.375	February 10, 2017
117,600	$	3.750	June 21, 2018
118,000	$	3.125	September 30, 2018
48,960	$	7.500	March 11, 2019
736,000	$	7.8125	March 11, 2019
30,000	$	9.9000	January 14, 2020
1,114,833			

11. NET LOSS PER SHARE:

Basic earnings per share and diluted earnings per share for the years ended December 31, 2015 and 2014 have been computed by dividing the net loss for each respective period by the weighted average number of shares outstanding during that period. All outstanding warrants and options representing approximately 3,592,000 and 3,915,000 incremental shares at December 31, 2015 and 2014, respectively, have been excluded from the computation of diluted loss per share as they are anti-dilutive.

12. RETIREMENT PLAN:

In June 2014, the Company formed the CytoSorbents 401(k) Plan. The plan is a defined contribution plan as described in section 401(k) of the Internal Revenue Code ("IRC") covering substantially all full time employees. Employees are eligible to participate in the plan on the first day of the calendar quarter following three full months of employment. Participants may defer up to 100% of their eligible compensation subject to certain IRC limitations. In addition, the Company provides for a matching contribution of twenty percent of the participants' contribution on a maximum of a five percent compensation contribution. Matching contributions amounted to approximately $26,400 and $10,500 for the years ended December 31, 2015 and December 31, 2014, respectively.

13. SUBSEQUENT EVENTS:

The Company has evaluated subsequent events occurring after the balance sheet date which include the following:

As an approved participant of the Technology Business Tax Certificate Transfer Program sponsored by the New Jersey Economic Development Authority in January 2016 the Company received $324,606 from the 2015 sale of our prior unused net operating loss carryovers.

14. QUARTERLY FINANCIAL RESULTS (UNAUDITED):

Summarized quarterly data for 2015 and 2014 are as follows:

	For the Quarters Ended			
	March 31	June 30	September 30	December 31
2015:				
Total revenue	$ 723,074	$ 963,939	$ 1,343,625	$ 1,760,978
Gross margin	418,593	498,508	704,795	957,174
Loss from operations	(2,711,629)	(2,227,459)	(2,150,296)	(2,214,275)
Net Income (loss) available to common stockholders	(4,716,942)	1,434,318	(2,847,441)	(2,001,674)
Net loss per share, basic	(0.19)	0.06	(0.11)	(0.08)
Net loss per share, diluted	(0.19)	0.05	(0.11)	(0.08)
2014:				
Total revenue	1,062,172	1,024,655	1,162,347	873,660
Gross margin	399,635	358,504	686,457	544,342
Loss from operations	(1,154,194)	(1,363,389)	(1,483,553)	(2,891,700)
Net loss available to common stockholders	(2,089,599)	(3,227,847)	(2,779,408)	(10,491,491)
Net loss per share, basic and diluted	(0.20)	(0.27)	(0.22)	(0.84)

Exhibit 21.1

CytoSorbents Corporation

List of Subsidiaries

Name	**Jurisdiction**
CytoSorbents Medical, Inc.*	Delaware
CytoSorbents Europe GmbH*	Germany

* Wholly-owned subsidiary

Exhibit 23.1

CONSENT OF REGISTERED INDEPENDENT PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference of our reports dated March 9, 2016 relating to the consolidated financial statements of Cytosorbents Corporation (the "Company") as of and for the years ended December 31, 2015 and 2014 and the effectiveness of the Company's internal control over financial reporting which appears in this annual report on Form 10-K into the Company's previously filed Registration Statements on Forms S-3 (Registration Nos. 333-194394, 333-193053, and 333-205806) and Forms S-8 (Registration Nos. 333-199852 and 333-203244) and to the reference to our Firm under the caption "Experts".

/s/ Withum Smith+Brown, PC
New Brunswick, New Jersey
March 9, 2016

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE
SARBANES-OXLEY ACT OF 2002

I, Phillip Chan, certify that:

1. I have reviewed this annual report on Form 10-K of CytoSorbents Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal controls over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation;

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the registrant's board of directors (or persons performing the equivalent function):

a) all significant deficiencies and material weaknesses in the design or operation of internal controls over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls over financial reporting.

Dated: March 9, 2016

By: /s/ Dr. Phillip P. Chan
Dr. Phillip P. Chan
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL AND ACCOUNTING OFFICER
PURSUANT TO SECTION 302 OF THE
SARBANES-OXLEY ACT OF 2002

I, Kathleen P. Bloch, certify that:

1. I have reviewed this annual report on Form 10-K of CytoSorbents Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal controls over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation;

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the registrant's board of directors (or persons performing the equivalent function):

a) all significant deficiencies and material weaknesses in the design or operation of internal controls over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls over financial reporting.

Dated: March 9, 2016

By: /s/ Kathleen P. Bloch
Kathleen P. Bloch
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of CytoSorbents Corporation (the "Company") on Form 10-K for the year ended December 31, 2015 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Dr. Phillip P. Chan, President and Chief Executive Officer of the Company, certifies, pursuant to 18 U.S.C. section 1350 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 9, 2016

By: /s/ Dr. Phillip P. Chan
Dr. Phillip P. Chan
President and Chief Executive Officer
(Principal Executive Officer)

A signed original of this written statement required by Section 906, or other document authenticating, acknowledging, or otherwise adopting the signature that appears in typed form within the electronic version of this written statement has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of CytoSorbents Corporation (the "Company") on Form 10-K for the year ended December 31, 2015 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Kathleen P. Bloch, Chief Financial Officer of the Company, certifies, pursuant to 18 U.S.C. section 1350 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 9, 2016

By: /s/ Kathleen P. Bloch
Kathleen P. Bloch
Chief Financial Officer
(Principal Financial and Accounting Officer)

A signed original of this written statement required by Section 906, or other document authenticating, acknowledging, or otherwise adopting the signature that appears in typed form within the electronic version of this written statement has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.