Cytosorbents Corp
Form 10-K
March 07, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D. C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2018

or

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

Commission file number 001-36792

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	**The 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 þ 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 þ 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.

þ Yes ¨ No

Indicate by check mark whether the registrant has submitted electronically 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 such files).

Yes þ 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. þ

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

Large Accelerated Filer ¨	Accelerated Filer þ
Non-accelerated Filer ¨	Smaller reporting company þ
	Emerging growth company ¨

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act.)

¨ Yes þ No

The aggregate market value of the common stock of the registrant held by non-affiliates as of June 30, 2018 was approximately $320,079,293. As of February 28, 2019 there were outstanding 31,855,099 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

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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," "exp "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 the applicable Report or public statement. All subsequent written and oral forward-looking statements concerning other matters addressed in this Report or public statement 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™, HemoDefend™, unKrol™, and VetResQ™, 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 our 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, investigating and 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 and cardiac surgery. Organ failure is the cause of nearly half of all deaths in the intensive care unit ("ICU"), with little to improve clinical outcome. CytoSorb, our flagship product, is approved in the European Union ("EU") 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 May 2018, the Company received a label extension for CytoSorb covering use of the device for the removal of bilirubin and myoglobin in the treatment of liver disease and trauma, respectively. In addition, CytoSorb is used during and after cardiac surgery to remove inflammatory mediators, such as cytokines, activated compliment and free hemoglobin, that can lead to post-operative complications, such as acute kidney injury, lung injury, shock and stroke. CytoSorb has the potential to be used in many other inflammatory conditions, including the treatment of autoimmune disease flares, cytokine release syndrome in cancer immunotherapy, and other applications in cancer, such as cancer cachexia. CytoSorb has been used globally in more than 56,000 human treatments to date in critical illnesses and in cardiac surgery. 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 product candidates under development based upon this unique blood purification technology, which is protected by 19 issued U.S. patents and multiple international patents, with applications pending both in the U.S. and internationally, including HemoDefend, ContrastSorb, DrugSorb, and others.

In March 2011, CytoSorb, was "CE marked" in the EU as an extracorporeal cytokine filter indicated for use in clinical situations where cytokines are elevated, allowing for commercial marketing. The CE mark demonstrates that a conformity assessment has been carried out and the product complies with the Medical Devices Directive. 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 ICU, 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 ICU treatment, thereby potentially saving significant healthcare costs.

Our CE Mark enables CytoSorb to be sold throughout the European Union and member states of the European Economic Area. In addition, many countries outside the EU accept the CE Mark for medical devices, but may also require registration with or without additional clinical studies. The broad indication for which CytoSorb is CE marked allows it 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.

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 ICU, 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.

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As part of the CE Mark 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 and published in PLOS ONE. In the European Sepsis Trial, the treatment was well-tolerated with no serious device related adverse events reported. The trial also demonstrated the ability of CytoSorb to reduce cytokines such as IL-6. The trial was not powered to demonstrate significant reduction in other clinical endpoints such as mortality.

In addition to CE marking, 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 commercial sales abroad and for additional clinical studies. In September 2016, we were granted a two-year renewal for the CytoSorb CE Mark. In June 2018, we received clearance from our notified body to begin production in our new manufacturing facility. In July 2018, we successfully completed an audit upgrade from an ISO 13485:2003 certification to an ISO 13485:2016 certification.

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 year 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. We believe our relationships with KOLs are essential to drive adoption and recurrent usage of CytoSorb, facilitate purchases by hospital administration, arrange reimbursement, and generate data for papers and presentations. As of, the end of 2018, 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.

In March 2016, we established CytoSorbents Switzerland GmbH, a wholly-owned subsidiary of CytoSorbents Europe GmbH, to conduct marketing and direct sales in Switzerland. This subsidiary began operations during the second quarter of 2016. In 2017, we further expanded our direct sales efforts into Belgium and Luxembourg.

In May 2018, the approved uses of CytoSorb in the EU were expanded to include the removal of bilirubin in liver disease, and the removal of myoglobin in trauma.

In the second quarter of 2018, we officially opened a new expanded CytoSorb manufacturing facility in New Jersey that quadruples manufacturing capacity and is expected to improve product gross margins in the future.

On March 5, 2019, the Company announced the expansion of direct sales of CytoSorb for all applications to Poland and the Netherlands, and critical care applications to Sweden, Denmark and Norway. As part of this effort, the Company established CytoSorbents Poland Sp. z.o.o., a wholly-owned subsidiary of CytoSorbents Europe GmbH.

In addition, we now have more than 50 investigator-initiated studies in various stages of planning, enrollment, or completion in Germany, Austria, Switzerland, the Netherlands, Hungary, the United Kingdom, France, India, Italy and Slovenia. Approximately 20 of these studies are currently enrolling patients. Others have been completed. These studies are being supported by our European Medical Director. As of February 15, 2019, we had increased our European sales, marketing and clinical support team to 29 direct sales people, one contract sales person, and 22 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, 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 s.r.l. 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. In June 2016, we announced an exclusive distribution agreement with Palex Medical SA to distribute CytoSorb in Spain and Portugal. In September 2016, we announced an exclusive agreement with Armaghan Salamat Kish Group (Arsak) to distribute CytoSorb in Iran. In April 2017, we entered into a distribution agreement with KRA Technical Services to distribute CytoSorb in Qatar. In July 2017, we announced an exclusive agreement with Droguería, Ramón, González, Revilla (DRGR) S.A. to distribute CytoSorb in Panama. In April 2018, we entered into exclusive agreements with Pharmaworld and Chong Lap (H.K.) Co. Ltd. to distribute CytoSorb in Lebanon and Hong Kong, respectively. As of the third quarter of 2018, we had expanded distribution to include Bosnia, Herzegovina, and Croatia with Medis, d.o.o.; Estonia, Latvia, and Lithuania with SIA Scanmed; and Montenegro and Serbia with Mar Medica, d.o.o. and Cardiotec Vascular Ltda., in Chile. CytoSorb is also distributed in the United Kingdom by Chalice Medical, Ltd., which focuses its efforts in England and Ireland.

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. ("Biocon"), India's largest biopharmaceuticals 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 October 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 December 2017, the Biocon partnership was further expanded to include exclusive distribution of CytoSorb in Malaysia. Under the terms of the agreement, Biocon has committed to minimum annual purchases in Malaysia to maintain exclusivity this territory. In addition, the term of the original agreement was extended to December 2022.

In December 2014, we entered into a multi-country strategic partnership with Fresenius Medical Care AG & Co KGaA (together with its affiliates, as appropriate, "Fresenius") to commercialize the CytoSorb therapy. Under the agreement reflecting the terms of the partnership, Fresenius was granted exclusive rights to distribute CytoSorb for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership allows Fresenius to offer an innovative and easy way to use blood purification therapy for removing cytokines in patients that are treated in the ICU. To promote the success of CytoSorb, Fresenius agreed to 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. In May 2016, Fresenius launched the product in the six countries for which it was granted exclusive distribution rights. In January 2017, the Fresenius partnership was expanded pursuant to a revised three year agreement. The terms of the revised agreement extended Fresenius' exclusive distributorship of CytoSorb for all critical care applications in their existing territories through 2019 and include guaranteed minimum quarterly orders and payments, evaluable every one and a half years.

At the same time, we entered into a comprehensive co-marketing agreement with Fresenius. Under the terms of the co-marketing agreement, CytoSorbents and Fresenius agreed to jointly market CytoSorb to Fresenius' critical care customer base in all countries where CytoSorb is being actively commercialized. CytoSorb continues to be sold by our direct sales force or through our international network of distributors and partners, while Fresenius sells all ancillary products to their customers. Fresenius further provides written endorsements of CytoSorb for use with their multiFiltrate and multiFiltratePRO acute care dialysis machines that can be used by us and our distribution partners to promote CytoSorb worldwide. Training and preparation for this co-marketing program began in five initial countries in 2017 and is continuing, with implementation of the co-marketing program in additional countries planned for the future.

In December 2018, the Fresenius agreement signed in December 2014 was amended, to grant Fresenius exclusive distribution rights for the Czech Republic and Finland and all critical care medicine and ICU applications on dialysis or ECMO machines for France. In addition, starting in 2019, Poland, Sweden, Denmark, and Norway will be transitioned into the co-marketing program. Finally, the guaranteed minimum quarterly purchases and payments requirements were removed for 2019.

In addition, also in December 2018, we entered into agreements to expand the partnership with Fresenius into South Korea and Mexico. Under the terms of these agreements, Fresenius has exclusive rights to distribute CytoSorb for acute care and other hospital applications in South Korea and Mexico. Commercial sales of CytoSorb are expected to commence after securing market registration clearance from the South Korean and Mexican health authorities. These multi-year agreements include an initial stocking order and are subject to annual minimum purchases of CytoSorb to maintain exclusivity.

In September 2016, we entered into a multi-country strategic partnership with Terumo Cardiovascular Group (“Terumo”) to commercialize CytoSorb for cardiac surgery applications. Under the terms of the agreement, Terumo has exclusive rights to distribute the CytoSorb cardiopulmonary bypass (CPB”) procedure pack for intra-operative use during cardiac surgery in France, Sweden, Denmark, Norway, Finland and Iceland. Terumo launched the product in these six countries in December 2016.

In March 2017, we entered into a partnership with Dr. Reddy’s Laboratories Ltd. for the South African market. Under the terms of the agreement, Dr. Reddy’s has the exclusive right to distribute CytoSorb for intensive care, cardiac surgery, and other hospital applications in South Africa. This is a multi-year agreement and is subject to annual minimum purchases of CytoSorb to maintain exclusivity.

Overall, we have established either direct sales or distribution (via distributors or strategic partners) of CytoSorb in 55 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 several 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. 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. Outside of the EU, CytoSorb is distributed in Turkey, India, Sri Lanka, Australia, New Zealand, Russia, South Africa, Serbia, Norway, Vietnam, Malaysia, Hong Kong, Chile, Iceland, Iran, Panama, Saudi Arabia and other Middle Eastern countries, Mexico and South Korea. We 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 continuously evaluate other

potential distributor and strategic partner networks in other 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 ICU 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 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.

In 2014, we 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. 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 Europe and abroad. Approximately 20 of these studies are currently enrolling. These trials, which are funded and supported by well-known university hospitals and KOLs, are the equivalent of Phase 2 clinical studies. They will provide invaluable information regarding the success of the device in the treatment of sepsis, cardio-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 addition to sepsis and other critical care applications, cardiac surgery is an important application for CytoSorb in the European market. There are approximately one million cardiac surgery procedures performed annually in the U.S. and EU combined 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 activation of complement, and cause hemolysis, leading to the release of toxic plasma free hemoglobin. These can lead to post-operative complications such as respiratory failure, circulatory 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 (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 Hemoglobin) amongst 20 patients and three U.S. clinical sites. The FDA subsequently approved an amendment to the protocol, expanding the trial to a 40 patient randomized controlled study (20 treatment, 20 control) in eight clinical centers. REFRESH I represented 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 REFRESH I study was designed to evaluate the safety and feasibility of CytoSorb when used intra-operatively with a heart-lung machine to reduce plasma free hemoglobin (pfHb) and cytokines in patients undergoing complex cardiac surgery. The study was not powered to measure effect on clinical outcomes. 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 are correlated with the incidence of serious post-operative complications such as kidney injury, renal failure and other organ dysfunction. The goal of CytoSorb is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications. Enrollment was completed with 46 patients. A total of 38 patients were evaluable for pfHb and completed all aspects of the study.

The primary safety and efficacy endpoints of the study were the assessment of serious device related adverse events and the change in plasma free hemoglobin levels, respectively. On October 5, 2016, we announced positive top-line safety data. In addition, following a detailed review of all reported adverse events in a total of 46 enrolled patients, the independent Data Safety Monitoring Board ("DSMB") found no serious device related adverse events with the CytoSorb device, achieving the primary safety endpoint of the trial. In addition, the therapy was well-tolerated and technically feasible, implementing easily into the cardiopulmonary bypass circuit without the need for an additional external blood pump. This study represents the first randomized controlled trial demonstrating the safety of intra-operative CytoSorb use in patients undergoing high risk cardiac operations.

Investigators of the REFRESH I trial submitted an abstract with data, including free hemoglobin data, from the REFRESH I trial which was selected for a podium presentation at the American Association of Thoracic Surgery conference on May 1, 2017. On May 5, 2017, we announced additional REFRESH I data, including data from the study on the reduction of pfHb and activated complement, and disclosed that investigators of the study have submitted a manuscript of the REFRESH I trial for publication.

In December 2017, the FDA approved our IDE application for our REFRESH 2-AKI study, permitting us to conduct this pivotal trial designed to provide the key safety and efficacy data needed to support United States regulatory approval for CytoSorb in cardiac surgery, which we plan to pursue via the premarket approval (PMA) pathway. The REFRESH 2-AKI trial is a randomized, controlled, multi-center, clinical trial designed to evaluate intraoperative CytoSorb use as a therapy to reduce the incidence and severity of AKI, as measured by Kidney Disease Improving Global Outcomes (KDIGO) criteria, following complex cardiac surgery. Postoperative AKI following cardiac surgery is common and is associated with 1-5 year mortality, and is a risk factor for developing chronic kidney disease requiring hemodialysis in the future. The trial will enroll up to 400 patients at increased risk of cardiovascular surgery-associated AKI, undergoing elective, non-emergent open-heart surgery for either valve replacement, or aortic reconstruction with hypothermic cardiac arrest. In April 2018, we announced the first patient enrollment into the pivotal U.S. REFRESH 2-AKI trial. Based on the recommendations of key clinical advisors, a protocol amendment was submitted to the FDA on July 18, 2018 to improve operational aspects of the patient screening process and expand the inclusion criteria. It was the preference of clinical trial sites to defer enrollment until the amendment was approved by the FDA, which occurred on August 17, 2018. Following the subsequent ethics committee approvals of the amended protocol at all trial sites, as of March 6, 2019, the trial had 21 initiated sites and another 8 sites that were undergoing approvals, contracting and initiation. As of March 6, 2019, the trial had enrolled 56 patients. We anticipate that patient enrollment in the REFRESH 2-AKI trial will be complete by 2020, but this could take longer if enrollment challenges or other factors causing delays are encountered. If the trial is successful, we plan to submit a PMA application in 2021.

The German government, via the German Federal Ministry of Education and Research, is funding a 250 patient, multi-center randomized, controlled study ("REMOVE") using CytoSorb during valve replacement open heart surgery in patients with infective endocarditis. The study enrolled its first patient in January 2018. As of February 28, 2019, the trial had enrolled 130 patients at 13 sites. A planned interim analysis of the first 50 patients has been completed. On February 4, 2019, Prof. Dr. med. Frank Brunkhorst, Director of the Center for Clinical Studies at Jena University Hospital, who is providing management and oversight to the REMOVE trial, and Prof. Dr. med. Torsten Doenst,

Director of the Clinic for Cardiac and Thoracic Surgery at the University of Jena, provided the following joint statement, “The Scientific Advisory Board (SAB) of the Center of Sepsis Control and Care (CSCC) and the Data Safety Monitoring Board (DSMB) of the REMOVE study recommended continuation of the study, based upon results of a pre-specified interim analysis that analyzed cytokine and vasoactive mediator levels as an indicator of the mechanistic mode of action of the device in 28 CytoSorb-treated patients and 22 control patients. There were no device-associated adverse events in the CytoSorb group.”

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. See the section entitled "Government Research Grants" of this Item 1 of this Report for information regarding the specific grants.

In January 2017, we launched VetResQ™ for the United States veterinary market, following registration with the FDA. VetResQ is a broad spectrum blood purification adsorber designed to help treat deadly inflammation and toxic injury in animals with critical illnesses such as septic shock, toxic shock syndrome, severe systemic inflammation, toxin-mediated diseases, pancreatitis, trauma, liver failure, and drug intoxication. Based upon cumulative studies, VetResQ is capable of reducing a broad range of excessive inflammatory mediators and toxins that could otherwise cause direct tissue injury or serious systemic inflammation that can rapidly lead to instability, organ failure, and death. VetResQ is manufactured in the United States for the treatment of cats, dogs, horses, and animals of comparable size. VetResQ is compatible with standard hemodialysis, continuous renal replacement therapy ("CRRT"), and hemoperfusion blood pumps. VetResQ is available only for veterinary animal usage and is not for human use. We do not expect VetResQ to be a significant source of revenue for us.

In addition to CytoSorb and VetResQ, we are developing other products utilizing our adsorbent polymer technology that have not yet received regulatory approval including HemoDefend, CytoSorb-XL, 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. CytoSorb-XL is a development-stage, next-generation product to CytoSorb, adding endotoxin removal capability to cytokine, exotoxin, and other inflammatory mediator removal. 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. Continued development of the product is being supported through a $3.0 million Phase IIB Bridge SBIR contract funded by the National Heart, Lung and Blood Institute (NHLBI) – a division of the National Institutes of Health ("NIH"), and in the past, by NHLBI and U.S. Special Operations Command (USSOCOM). 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 one hundred million packed red blood cell units 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. A 24 patient pivotal trial, which is being partially funded by NHLBI, is expected to begin in the second half of 2019. This trial is designed to measure the recovery of radiolabeled blood cells 24 hours after infusion, and additionally to show that red blood cell are not harmed by the filtration. The goal is to achieve FDA approval of HemoDefend.

CytoSorb-XL is a development-stage, porous polymer bead technology that combines lipopolysaccharide endotoxin removal with the robust cytokine, toxin, and inflammatory mediator reduction achieved by CytoSorb. CytoSorb-XL and its novel endotoxin binding chemistry is the subject of a broad composition of matter patent application, intended to protect the technology worldwide for the next two decades. In a head-to-head comparison with the leading endotoxin adsorber, Toraymyxin (Toray, Japan), CytoSorb-XL matched the level of endotoxin reduction in an *in vitro* plasma recirculation system on a comparable volume basis. CytoSorb-XL is expected to replace stand-alone endotoxin specific filters by offering superior performance in the removal of not just endotoxin, but a much broader array of inflammatory mediators that drive uncontrolled deadly inflammation, organ failure, and death in sepsis. The expected market for CytoSorb-XL is similar in size and scope as for CytoSorb.

K$^+$ontrol is a development-stage polymer sorbent technology designed to treat severe hyperkalemia, by directly reducing high levels of potassium in the blood. Trauma, crush injury to soft tissue, burn injury, ischemia, and toxic drugs are just some causes of rapid cell death and the release of intracellular potassium into the bloodstream. In compromised patients, particularly those with kidney failure, very high levels of potassium in the blood, or severe hyperkalemia, can result, and lead to dangerously irregular heartbeats called arrhythmias, and sudden cardiac death. Dialysis has been the definitive treatment of severe hyperkalemia, but requires a large dialysis machine, an electrical wall socket, bags of dialysate, a skilled technician, and prolonged treatment times that are not practical in certain situations, such as treatment in remote locations, mass casualty situations, and prolonged field care in combat. K$^+$ontrol has demonstrated the ability to reduce potassium in several large animal models with minimal technology and is currently being optimized prior to human clinical testing.

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, called MedaSorb Technologies, Inc. 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., 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, 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. Our website address is http://www.cytosorbents.com. We have included our website address as an inactive textual reference only. We make available free of charge through our website our Annual Reports on Form 10-K, our Quarterly Reports on Form 10-Q, our Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material, or furnish it to the SEC. We also similarly make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. We are not including the information contained at http://www.cytosorbents.com, or at any other website address, as part of, or incorporating it by reference into, this Annual Report on Form 10-K.

We have been engaged in research and development since our inception and have raised approximately $130 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.

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

Shelf Registration

On July 29, 2015, the Company’s registration statement on Form S-3, as filed with the SEC on July 23, 2015 (the “2015 Shelf”), was declared effective using a “shelf” registration process. On July 26, 2018, in anticipation of the expiration of the 2015 Shelf, the Company filed a new registration statement on Form S-3 with the SEC (as amended, the “2018 Shelf”). The 2018 Shelf, which was declared effective on August 7, 2018, enables the Company to offer and sell, in one or more offerings, any combination of common stock, preferred stock, senior or subordinated debt securities, warrants and units, up to a total dollar amount of $150 million.

April 5, 2017 Equity Offering

On April 5, 2017, the Company closed on the sale of an aggregate of 2,222,222 shares of common stock pursuant to the Company's 2015 Shelf. The Company received gross proceeds of approximately $10,000,000 from the sale of such shares based on a public offering price of $4.50 per share. On April 11, 2017, the Company closed the sale of an

additional 333,333 shares of the Company's common stock, pursuant to the underwriters' full exercise of an over-allotment option. The Company received gross proceeds of approximately $1,500,000 from the exercise of the option. As a result, the Company received total gross proceeds of $11,500,000 from the offering, and, after deducting the underwriting discounts and commissions and related expenses, the Company received total net proceeds of approximately $10,300,000.

As a result of this offering, the exercise price of the warrants issued in connection with the Company's March 11, 2014 public offering was reduced to $4.50 in accordance with the pricing provisions of those warrants. There was no change in the number of warrants which were repriced. As a result of the repricing of the warrants which occurred in connection with the April 2017 equity offering, the Company recorded a dividend of $335,731 during the year ended December 31, 2017.

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 & 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 (the "Shares"). Any Shares hereafter offered and sold will be issued pursuant to the Company's 2018 Shelf, and the related prospectus which the Company filed with the SEC pursuant to Rule 424(b)(5) under the Securities Act.

On July 26, 2018, the Company entered into that certain Amendment No. 1 to the Sales Agreement (the "Sales Agreement Amendment") to extend the term of the Sales Agreement until the expiration of the 2018 Shelf. The other provisions of the Sales Agreement remain unchanged. References herein to "Sales Agreement" shall refer to the Sales Agreement, as amended by the Sales Agreement Amendment.

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 (the "Securities Act"), including sales made directly on The Nasdaq Capital Market ("Nasdaq"), 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 expiration of the 2018 Shelf or (b) the termination of the Sales Agreement by Cantor or the Company, as permitted therein. From November 4, 2015 through December 31, 2015, the Company sold 28,880 shares, generating net proceeds of approximately $225,000 under the Sales Agreement. There were no sales during the year ended December 31, 2016. During the year ended December 31, 2017, the Company sold 550,000 shares at an average price of $6.31 per share, generating net proceeds of approximately $3,367,000. During the year ended December 31, 2018, the Company sold 1,515,260 shares at an average cost of $9.61 per share, generating net proceeds of approximately $14,127,000. In the aggregate, the Company has sold 2,094,140 shares at an average selling price of $8.72 per share, generating net proceeds of approximately $17,718,000 under the terms of 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 intends to use the net proceeds raised through "at the market" sales to fund clinical studies in the United States and abroad, expand production capacity, support its sales and marketing efforts, further develop its products, and for general working capital purposes.

Research and Development

We have been engaged in research and development since inception. Since 2012, we have been awarded an aggregate of approximately $14.1 million in grants and contracts from DARPA ($3.8M over 5 years), the U.S. Army ($100K Phase I SBIR; $50K Phase I option, $803K Phase II SBIR, $443K Phase II enhancement), the Congressionally Directed Medical Research Program Office, ("CDRMP"), $718K, the National Heart, Lung and Blood Institute and USSOCOM ($203K Phase I SBIR; $1.5M Phase II SBIR; $3.0M Bridge SBIR), the Joint Program Executive Office – Chemical and Biological Defense, (JPEO-CBD), ($150K Phase I and Phase I option, $1.0M Phase II) ,the U.S. Army Peritoneal dialysis/mesh packing for hyperkalemia ($150K Phase I SBIR, $1.0M Phase II), Universal Plasma ($150K Phase I and 1.0M Phase II) to further develop our technologies for sepsis, trauma and burn injury, and blood transfusions, respectively. Some payments are based on achieving certain technology milestones.

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, animal-targeted VetResQ, and other product candidates under development, including CytoSorb XL, 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, acute liver disease and severe acute pancreatitis. In the U.S., an estimated $110 billion or 0.7% of the U.S. gross domestic product is spent annually on critical care medicine. In 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. These 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. In May 2018, the approved indications for use of CytoSorb in the EU were expanded to include the

removal of bilirubin in liver disease, and the removal of myoglobin in trauma.

In addition to critical care, CytoSorb is used in many applications related to cardiac surgery. Intra-operatively, CytoSorb is either used to help stabilize patients with serious conditions such as infective endocarditis, or to prevent post-operative complications such as acute kidney injury, vasoplegia, respiratory failure, infection, and others. Post-operatively, CytoSorb is used in the intensive care unit to treat the post-operative systemic inflammatory response syndrome (post-op SIRS), sepsis, and other complications.

Together the total addressable market for these numerous critical care and cardiac surgery applications with CytoSorb is estimated to be in excess of $20 billion worldwide.

Sepsis

Sepsis is characterized by a systemic inflammatory response triggered by a severe infection. It is commonly seen in the ICU, 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 there are more than 30 million cases per year with approximately 6-9 million deaths. According to the 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, obesity, 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 H3N2 or 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 ICU. Severe sepsis has a mortality rate of approximately 20% to 25% despite the use of antibiotics and the highest level of available care. 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%, and up to 80-100% if it is refractory to vasopressors and other therapies.

In sepsis, there are two major problems: the infection and the body's immune response to the infection. Antibiotics are the 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. Recently, the 3rd International Consensus Definition Task Force defined sepsis as "life-threatening organ dysfunction due to a dysregulated host response to infection." 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 E.U. 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 to 7 days.

The only treatment that had been approved to treat sepsis in the U.S. or EU was Xigris from 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 many other experimental therapies has been discontinued, including Eritoran from Eisai, CytoFab from BTG/Astra Zeneca, Talactoferrin from Agennix, tranexemic acid from Leading Biosciences, and others.

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Since January 1, 2013, there have been three Phase 1, one Phase 1/2, nine Phase 2, four Phase 2/3, three Phase 3, and five Phase 4 interventional drug trials posted on clinicaltrials.gov for sepsis-related indications (sepsis, late-onset sepsis, severe sepsis, septic shock, systemic inflammatory response). Of these studies, three are not yet recruiting, nine are currently recruiting, five have been completed, and five have been terminated. Three additional studies were scheduled to be completed at this time, but their current status is unknown.

The sponsors for these studies include the following industry and academic organizations:

- Asahi Kasei Pharma America Corporation
- Baxter Healthcare Corporation
- Bristol-Myers Squibb
- Exponential Biotherapies Inc.
- Ferring Pharmaceuticals
- Fresenius Kabi
- Hamad Medical Corporation
- HK Surgical, Inc.
- Jafron
- Inotrem
- Kaneka Pharma America LLC
- Leading BioSciences, Inc
- Merck Sharp & Dohme Corp.
- Octapharma
- Pfizer
- PRA Health Sciences
- Revimmune
- Sanofi
- SciClone Pharmaceuticals
- Shionogi, Shionogi Inc.
- Techpool Bio-Pharma Co., Ltd.
- Tianjin Chasesun Pharmaceutical Co., LTD
- Yuria-Pharm

Primary outcomes of the investigational drug trials include safety and pharmacokinetic/pharmacodynamic primary outcome measures such as adverse event rates, maximum tolerated dose, clearance rates, and distribution. Additional primary outcomes for these trials include:

- # of days alive without CV, renal, or pulmonary organ support
- # days free of treatment with vasopressors
- 28-day survival and all-cause mortality
- 60-day hospital mortality
- reduction rate of IL-6 serum concentration
- change in biomarkers indicative of endothelial activation and damage
- change in microvascular perfusion
- hemodynamic effects
- immune reconstitution of lymphocytopenic sepsis patients
- immunomodulatory effect (IL6/IL10 ratio)

- lymphocyte counts and percentage
- post-operative sepsis
- reduction in Sequential Organ Failure Assessment score (SOFA)

Four Phase 1 trials and three Phase 2 trials have been posted for interventional biologics with sepsis-related indications. Sponsors of the interventional biologic studies include Adrenomed AG, Biomedizinische Forschungs gmbH, Medical University of Vienna, Bristol-Myers Squibb, Central Hospital, Nancy, France, Diagnostica Stago; Hospices Civils de Lyon, Bioaster, BioMérieux, Sanofi, InflaRx GmbH, Intron Biotechnology, Inc., Revimmune, Washington University School of Medicine, University Hospital, Limoges, and George Clinical Pty Ltd.

Of the registered studies, one is not yet recruiting, one is currently recruiting, four have been completed, and one has been terminated. Primary outcomes of the investigational biologic trials include safety and pharmacokinetic/pharmacodynamic primary outcome measures such as adverse event rates, maximum tolerated dose, clearance rates, and distribution. Additional primary outcomes for these trials include:

- 90-day all-cause mortality
- 90-day mortality related to intervention
- clinical laboratory abnormalities
- ECG findings
- interruption of infusion due to intolerability
- lymphocyte reconstitution
- presence of antibodies to biologic intervention, and
- vital signs

Additionally, seven interventional device studies for sepsis-related indications have been registered since January 2013. Sponsors for these studies include ExThera Medical Corporation, Cheetah Medical Inc., Alteco Medical AB, TFS Trial Form Support, Uppsala University, Mespere Lifesciences Inc., Wayne State University, Magnolia Medical Technologies, Inc., PRo-IV, and Bait Balev Hospital. Of the interventional device studies, one if currently recruiting participants, two have been completed, two were terminated, and two are of unknown status. Primary outcomes of the interventional device studies include:

- safety/AEs
- fluid balance at 72 hours or ICU discharge

- 30-day readmission
- rate of blood culture contamination, and
- successful operation of device.

Severe sepsis and septic shock patients are among 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, Switzerland, Belgium, Luxembourg, Poland, Norway, Denmark, Sweden and the Netherlands, with our own direct sales force. In December 2016, we announced the achievement of a permanent, dedicated reimbursement procedure code for CytoSorb therapy in Germany, providing for specific and enhanced reimbursement in the largest medical device market in Europe. We have established strategic partnerships with Fresenius Medical Care, the world's largest dialysis company, for exclusive distribution of CytoSorb for critical care applications in France, Finland, the Czech Republic, Mexico, and Korea, and Terumo Cardiovascular, the largest cardiac surgery disposables company, for exclusive distribution of the CytoSorb Cardiopulmonary Bypass Kit in France, Denmark, Sweden, Norway, Finland, and Iceland. We are also partnered with Biocon Ltd, India's largest biopharmaceutical company, for exclusive distribution of CytoSorb in India, Sri Lanka, Malaysia, and other select emerging markets and Dr. Reddy's Laboratories, for exclusive distribution of CytoSorb in South Africa 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 55 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, 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 ICU 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 $4,300 per day in the ICU in the U.S.). 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 $6 billion 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 LVAD 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 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, barotrauma, 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 has been high (16-33%), 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 through tight junction disruption of respiratory endothelium, leading to capillary leak syndrome, and other factors. 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 ICU 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. However, techniques to improve ventilation and reduce ongoing lung injury are being used. For example low tidal volume ventilation has been demonstrated to improve mortality (31.0% as compared to 39.8% control) in this patient population in the ARDSNet Trial. Prone positioning, or placing a patient chest-side down, in severe ARDS patients in order to redistribute gravity-dependent pulmonary edema and allow ventilation of collapsed or atelectatic alveoli, is also used following studies that suggest benefit including the PROSEVA trial (16% vs 32.8% in the control). However, even with these interventions, 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 May 2018, the approved indications for use of CytoSorb in the EU were expanded to include the removal of myoglobin in trauma. 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.

Acute Liver Disease

Chronic liver disease afflicts an estimated 850 million people worldwide, or 11% of the world population, due to the prevalence of viral hepatitis infection, alcohol abuse, and non-alcoholic steatohepatitis (NASH or “fatty liver”). Chronic liver disease is blamed for nearly one million deaths a year, with another one million dying of hepatic cancer and acute hepatitis. In the U.S., liver disease is the second leading cause of death from digestive disease, and the 10th leading cause of death amongst men. Many patients with advanced chronic liver disease will develop an acute exacerbation or decompensation (“acute-on-chronic”) of their disease, with associated inflammation and cytokine elevation, often requiring hospitalization. Also, many patients will present with acute hepatitis triggered by viral infection or alcohol. A range of symptoms, depending on the severity of illness include jaundice (high bilirubin), variceal hemorrhage, cognitive dysfunction and hepatic encephalopathy, ascites, coagulopathy, renal failure, liver failure, and others. The extracorporeal blood purification of liver toxins such as bilirubin has been used to help treat patients and is often called “liver dialysis”. Current liver dialysis therapies include MARS (Molecular Adsorbent Recirculation System; Baxter), Prometheus (Fresenius), SPAD (single pass albumin dialysis), and others. However, none of these therapies can remove cytokines, key elements in acute-on-chronic exacerbations and cases of acute hepatitis. CytoSorb represents a potentially superior liver dialysis therapy, as it can remove both liver toxins such as bilirubin and bile salts, as well as cytokines. In May 2018, the approved indications for use of CytoSorb in the E.U. were expanded to include the removal of bilirubin in liver disease. The total addressable market for CytoSorb for the treatment of acute-on-chronic liver disease, acute hepatitis, and acute liver failure is estimated in excess of $15 billion

worldwide.

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, hyperlipidemia, 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, enteral 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.

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

In the CRS literature, researchers have drawn parallels to both macrophage activating syndrome and secondary hemophagocytic lymphohistiocytosis (HLH) which produce a similar clinical picture and cytokine storm profile. To date, CytoSorb has been used successfully in approximately a dozen cases of secondary HLH. In March 2017, the pioneer of CAR T-cell immunotherapy, Dr. Carl June at University of Pennsylvania, joined our scientific advisory board. In 2017, both Kymriah from University of Pennsylvania and Novartis, and Yescarta from Kite Pharma and Gilead Sciences, received FDA approval for the treatment of certain hematologic cancers.

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.

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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% to 40% 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. CytoSorbents has also received grant and contract funding to develop the HemoDefend platform to enable both universal plasma and fresh whole blood transfusions through the reduction of anti-A and anti-B blood group antibodies. Today, plasma and whole blood products must be carefully blood-type matched to prevent potentially fatal hemolytic transfusion reactions in the recipient, caused by the accidental administration of mismatched blood products. The reduction of anti-A and anti-B antibodies could potentially reduce or eliminate this risk, allowing for a broader range of available donors and simplifying the transfusion process. 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 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 $_2$ -microglobulin. Over time, $_2$ -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 14 sites in Germany of 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.

We manufacture the CytoSorb device at our facility located in Monmouth Junction, New Jersey. We purchase our raw materials from multiple vendors located primarily in the United States. We believe that our risk of an interruption in the supply of our raw materials is minimal due to the use of multiple vendors and the availability of alternate vendors. We do not have contractual minimum finished goods inventory requirements, however our practice is to maintain a minimum inventory level sufficient to provide a supply of products for the next three months.

The CytoSorb Device (Critical Care)

APPLICATION: Adjunctive Therapy in the Treatment of Sepsis

Sepsis is a potentially life-threatening disease defined as “life-threatening organ dysfunction caused by a dysregulated host response to an infection”. Sepsis is mediated by high levels of inflammatory mediators such as cytokines, which are released into the bloodstream 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 Global Sepsis Alliance, the worldwide incidence is estimated to be 30 million cases annually. The incidence of sepsis is also rising due to:

- an aging population;
- increased incidence of antibiotic resistance;
- increase in co-morbid conditions like cancer and diabetes; and
- 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 56,000 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, myoglobin, free hemoglobin, 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, Switzerland, Belgium, Luxembourg, Poland, Norway, Sweden, Denmark, and the Netherlands with a direct sales force. Based on its CE Mark approval, CytoSorb can also be sold throughout all 28 countries of the EU and countries outside the EU that will accept European regulatory approval with registration. Overall, we have established either direct sales or distribution (via distributors or strategic partners) of CytoSorb in 55 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 distributed in Turkey, India, Sri Lanka, Australia, New Zealand, Russia, South Africa, Serbia, Norway, Vietnam, Malaysia, Hong Kong, Chile, Iceland, Iran, Panama, Saudi Arabia and other Middle Eastern countries, Mexico and South Korea. 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. by 2021.

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 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. In addition, the expanded indications for use label now includes reduction of bilirubin and reduction of myoglobin, which further strengthens the on-label use of the technology for the treatment of liver disease and severe trauma, respectively. Our goal is to stimulate investigator-initiated clinical studies with our device for these applications. Currently, we have more than 50 investigator initiated or company-sponsored studies being planned, enrolling, or 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 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 hemoglobin, and other inflammatory mediators from accumulating in the bloodstream 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 ICUs; 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, cardiac perfusionists, and cardiothoracic ICU intensivists in Germany, Austria, and other countries have now used CytoSorb successfully intra-operatively and post-operatively in more than 18,000 treatments in 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 Hemoglobin) amongst 20 patients and three U.S. clinical sites. The FDA subsequently approved an amendment to the protocol, expanding the trial to a 40 patient randomized controlled study (20 treatment, 20 control) in eight clinical centers. REFRESH I represented 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 REFRESH I study was designed to evaluate the safety and feasibility of CytoSorb when used intra-operatively with a heart-lung machine to reduce plasma free hemoglobin (pfHb) and cytokines in patients undergoing complex cardiac surgery. The study was not powered to measure effect on clinical outcomes. 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 are correlated with the incidence of serious post-operative complications such as kidney injury, renal failure and other organ dysfunction. The goal of CytoSorb is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications. Enrollment was completed with 46 patients. A total of 38 patients were evaluable for pfHb and completed all aspects of the study.

The primary safety and efficacy endpoints of the study were the assessment of serious device related adverse events and the change in plasma free hemoglobin levels, respectively. On October 5, 2016, we announced positive top-line safety data. In addition, following a detailed review of all reported adverse events in a total of 46 enrolled patients, the DSMB found no serious device related adverse events with the CytoSorb device, achieving the primary safety endpoint of the trial. In addition, the therapy was well-tolerated and technically feasible, implementing easily into the cardiopulmonary bypass circuit without the need for an additional external blood pump. This study represents the first randomized controlled trial demonstrating the safety of intra-operative CytoSorb use in patients undergoing high risk cardiac operations.

Investigators of the REFRESH I trial submitted an abstract with data, including free hemoglobin data, from the REFRESH I trial which was selected for a podium presentation at the American Association of Thoracic Surgery conference on May 1, 2017. On May 5, 2017, we announced additional REFRESH I data, including data from the study on the reduction of pfHb and activated complement, and disclosed that investigators of the study have submitted a manuscript of the REFRESH I trial for publication.

In December 2017, the FDA approved our IDE application for our REFRESH 2-AKI study, permitting us to conduct this pivotal trial designed to provide the key safety and efficacy data needed to support United States regulatory approval for CytoSorb in cardiac surgery, which we plan to pursue via the premarket approval (PMA) pathway. The REFRESH 2-AKI trial is a randomized, controlled, multi-center, clinical trial designed to evaluate intraoperative CytoSorb use as a therapy to reduce the incidence and severity of AKI, as measured by Kidney Disease Improving Global Outcomes (KDIGO) criteria, following complex cardiac surgery. Postoperative AKI following cardiac surgery is common and is associated with 1-5 year mortality, and is a risk factor for developing chronic kidney disease requiring hemodialysis in the future. The trial will enroll up to 400 patients at increased risk of cardiovascular surgery-associated AKI, undergoing elective, non-emergent open-heart surgery for either valve replacement, or aortic reconstruction with hypothermic cardiac arrest. In April 2018, we announced the first patient enrollment into the pivotal U.S. REFRESH 2-AKI trial. Based on the recommendations of key clinical advisors, a protocol amendment was submitted to the FDA on July 18, 2018 to improve operational aspects of the patient screening process and expand the inclusion criteria. It was the preference of clinical trial sites to defer enrollment until the amendment was approved by the FDA, which occurred on August 17, 2018. Following the subsequent ethics committee approvals of the amended protocol at all trial sites, as of March 6, 2019, the trial had 21 initiated sites and another 8 sites that were undergoing approvals, contracting and initiation. As of March 6, 2019, the trial had enrolled 56 patients. We anticipate that patient enrollment in the REFRESH 2-AKI trial will be complete by 2020, but this could take longer if enrollment challenges or other factors causing delays are encountered. If the trial is successful, we plan to submit a PMA application in 2021.

The German government, via the German Federal Ministry of Education and Research, is funding a 250 patient, multi-center randomized, controlled study (“REMOVE”) using CytoSorb during valve replacement open heart surgery in patients with infective endocarditis. The study enrolled its first patient in January 2018. As of February 28, 2019, the trial had enrolled 130 patients at 13 sites. A planned interim analysis of the first 50 patients has been completed. On February 4, 2019 Prof. Dr. med. Frank Brunkhorst, Director of the Center for Clinical Studies at Jena University Hospital who is providing management and oversight to the REMOVE trial, and Prof. Dr. med. Torsten Doenst,

Director of the Clinic for Cardiac and Thoracic Surgery at the University of Jena, provided the following joint statement, “The Scientific Advisory Board (SAB) of the Center of Sepsis Control and Care (CSCC) and the Data Safety Monitoring Board (DSMB) of the REMOVE study recommended continuation of the study, based upon results of a pre-specified interim analysis that analyzed cytokine and vasoactive mediator levels as an indicator of the mechanistic mode of action of the device in 28 CytoSorb-treated patients and 22 control patients. There were no device-associated adverse events in the CytoSorb group.”

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

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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 VetResQ Device (Animal Health Critical Care)

APPLICATION: Adjunctive Therapy in the Treatment of Sepsis, Pancreatitis and Other Critical Illnesses in Animals

Potential Benefits and Rationale: In January 2017, the VetResQ device became commercially available for the United States veterinary market. VetResQ is a broad spectrum blood purification adsorber based upon similar underlying technology to CytoSorb and has been configured in 3 sizes (50, 150 and 300mL sized cartridges) to accommodate treatment of small, medium, and large animals such as cats, dogs, and high-value animals such as foals and horses. VetResQ is compatible with standard hemodialysis, continuous renal replacement therapy ("CRRT"), and hemoperfusion blood pumps. Like CytoSorb, VetResQ is designed to help treat (via hemoadsorption of cytokines, bacterial toxins and other inflammatory mediators) deadly inflammation and toxic injury in animals with critical illnesses such as septic shock, toxic shock syndrome, toxin-mediated diseases, pancreatitis, trauma, liver failure, drug intoxication, and lung injury. Critical illness in animals is similar to that in humans. Based upon cumulative studies, VetResQ is capable of reducing a broad range of excessive inflammatory mediators and toxins that could otherwise cause direct tissue injury or serious systemic inflammation that can rapidly lead to instability, organ failure, and death. VetResQ is available in the U.S. only for veterinary animal usage and is not for human use.

Projected Timeline : VetResQ is now available for commercial purchase for animal health applications in the United States. The FDA was notified of the launch in 2016 and we have provided the FDA with the related instructions for use and a marketing brochure.

The CytoSorb-XL Device (Critical Care)

APPLICATION: Adjunctive Therapy in the Treatment of Sepsis and other critical illnesses

Potential Benefits and Rationale: The CytoSorb-XL device is a next-generation porous polymer under advanced development and targets the same markets as CytoSorb. Through novel patent-pending chemistry, CytoSorb-XL adds the ability to reduce Gram negative bacterial endotoxin (lipopolysaccharide) to broad spectrum cytokine, exotoxin, and other inflammatory mediator removal. CytoSorb-XL removed comparable amounts of endotoxin when compared *in vitro* against the leading standalone endotoxin filter, Toraymyxin (Toray, Japan). This could potentially increase the effectiveness of CytoSorb in sepsis and septic shock caused by Gram negative bacteria.

Projected Timeline : CytoSorb-XL is in advanced pre-clinical development as a potential next generation polymer to CytoSorb. It is expected to follow a similar path to E.U. approval as CytoSorb, expected within 4-5 years.

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 (approximately 1% to 3%), 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 (completed) 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 TRANSFUSE Trial was a large scale RCT in Australia evaluating the impact of age of leukodepleted pRBCs (short-term storage: 11.8 days mean, N=2,457, mean 4.1 units transfused; long-term storage: 22.4 days mean, N=2,462, m) on 90-day mortality in critically-ill patients. There was no significant difference in 90-day mortality (24.8% mortality short-term storage vs 24.1% long-term storage) though there were statistically more febrile non-hemolytic transfusion reactions (n=123; 5% short-term storage vs n=88; 3.6% long-term storage). Also, patients who had short-term storage blood with APACHE III > 21.5% (median risk), demonstrated higher mortality (37.7% vs 34% long-term storage , p=0.05). The outcomes of these 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 NHLBI, a division of the National Institute of Health, under a Phase I SBIR, an awarded $1.5M Phase II SBIR contract (funded by NHLBI and U.S. Special Operation Command (USSOCOM)), and more recently under a $3M multi-year Phase IIB bridge contract funded by NHLBI. We expect to advance the in-line filter to human testing, expected in the second half of 2019. 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.

K⁺ontrol (Acute and Critical Care)

APPLICATION: Treatment of severe hyperkalemia that can occur in patients with life-threatening conditions such as trauma, burn injury, kidney failure, tumor lysis syndrome, and those with no access to dialysis

Potential Benefits: K⁺ontrol was developed to rapidly treat severe hyperkalemia by reducing potassium in the blood. Although hemodialysis remains the definitive treatment for severe hyperkalemia, K⁺ontrol represents a simpler, and more flexible alternative. The primary goals for this application are to:

- Enable the rapid treatment of deadly hyperkalemia without the need for hemodialysis
- Prevent potentially fatal cardiac arrhythmias following severe injury
- Improve survival in victims in remote areas and during prolonged field care in combat

Background and Rationale: Potassium is an important electrolyte in the body that is present inside cells at high concentrations, with the amount in blood tightly regulated. Following injury to cells by, for example, trauma, burn injury, ischemia, or cytotoxic drugs, such cells will continuously leak high levels of potassium into the blood, resulting in hyperkalemia. The kidneys normally excrete excess potassium from the blood, but when compromised, as in critically-ill patients suffering from kidney failure or in chronic dialysis patients with end-stage kidney disease, the levels of blood potassium can rapidly rise unabated. When the potassium level in the blood exceeds a concentration of 6.0 mmol/L (normal 3.6 - 5.2 mmol/L), the risk of heart arrhythmias and sudden cardiac death increases significantly. Orally administered potassium sorbents such as Kayexalate® (Sanofi-Aventis) and Veltassa® (Relypsa) are only recommended for the non-emergent lowering of mild to moderate hyperkalemia, while the use of insulin and glucose to drive potassium into cells in severe hyperkalemia is only a temporary strategy. Dialysis has been the definitive treatment of severe hyperkalemia, but requires a large dialysis machine, electricity, bags of dialysate, a skilled technician, and prolonged treatment times that are not practical in certain situations such as in remote locations, during

prolonged field care in combat, in areas that lack modern medical facilities, or in situations where the numbers of victims outstrip available dialysis equipment and supplies. Because of this, there is a major need for simple, but effective ways to rapidly treat severe hyperkalemia.

Hyperkalemia is a common problem and has been reported to occur in 1.7-5.2% of hospitalized patients in a number of studies. It has also been recognized as a serious complication of combat injury since World War II, when hyperkalemia and acute kidney injury was associated with a mortality rate of 90%, and was a leading cause of post-traumatic death in the Korean War, until the advent of dialysis therapy. In the wars in Iraq and Afghanistan, an estimated 5.8% of all combat casualties developed hyperkalemia within 48 hours of injury. Even in non-crush traumatic injury, severe hyperkalemia (>6 mmol/L) occurred in approximately 20% of patients. Hyperkalemia was also observed in approximately 16% of victims of natural disasters such as earthquakes, where crush injury is common.

Projected Timeline: K^+ontrol has demonstrated the ability to reduce potassium in several animal models of hyperkalemia and is currently being optimized with funding support from the US Army and Defense Health Agency under two separate SBIR contracts. We plan to move forward with clinical development of this product, pending the successful outcome of these animal studies.

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 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 distribution agreement with Biocon Ltd. (“Biocon”), India’s largest biopharmaceuticals company, under which Biocon was granted exclusive commercialization rights to the CytoSorb therapy in India and select emerging markets, initially focused on sepsis. Biocon committed to annual minimum purchases to maintain exclusivity. In October 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 December 2017, the Biocon partnership was further expanded to include exclusive distribution of CytoSorb in Malaysia. Under the terms of the expanded partnership, Biocon has committed to minimum annual purchases in Malaysia to maintain exclusivity this territory and the term of the distribution agreement was extended to December 2022.

Fresenius Medical Care AG

In December 2014, we entered into a multi-country strategic partnership with Fresenius Medical Care AG & Co KGaA (together with its affiliates, as appropriate, "Fresenius") to commercialize the CytoSorb therapy. Under the agreement reflecting the terms of the partnership, Fresenius was granted exclusive rights to distribute CytoSorb for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership allows Fresenius to offer an innovative and easy way to use blood purification therapy for removing cytokines in patients that are treated in the ICU. To promote the success of CytoSorb, Fresenius agreed to 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. In May 2016, Fresenius launched the product in the six countries for which it was granted exclusive distribution rights. In January 2017, the Fresenius partnership was expanded pursuant to a revised three-year agreement. The terms of the revised agreement extended Fresenius' exclusive distributorship of CytoSorb for all critical care applications in their existing territories through 2019 and include guaranteed minimum quarterly orders and payments, evaluable every one and a half years.

At the same time, we entered into a comprehensive co-marketing agreement with Fresenius. Under the terms of the co-marketing agreement, CytoSorbents and Fresenius agreed to jointly market CytoSorb to Fresenius' critical care customer base in all countries where CytoSorb is being actively commercialized. CytoSorb continues to be sold by our direct sales force or through our international network of distributors and partners, while Fresenius sells all ancillary products to their customers. Fresenius further provides written endorsements of CytoSorb for use with their multiFiltrate and multiFiltratePRO acute care dialysis machines that can be used by us and our distribution partners to promote CytoSorb worldwide. Training and preparation for this co-marketing program began in five initial countries in 2017 and is continuing, with implementation of the co-marketing program in additional countries planned for the future.

In December 2018, the Fresenius agreement signed in December 2014 was amended, to grant Fresenius exclusive distribution rights for the Czech Republic and Finland and all critical care medicine and ICU applications on dialysis or ECMO machines for France. In addition, starting in 2019, Poland, Sweden, Denmark, and Norway will be transitioned into the co-marketing program. Finally, the guaranteed minimum quarterly purchases and payments requirements were removed for 2019.

In addition, also in December 2018, we entered into agreements to expand the partnership with Fresenius into Korea and Mexico. Under the terms of these agreements, Fresenius has exclusive rights to distribute CytoSorb for acute care and other hospital applications in South Korea and Mexico. Commercial sales of CytoSorb are expected to commence after securing market registration clearance from the South Korean and Mexican health authorities. These multi-year agreements include an initial stocking order and are subject to annual minimum purchases of CytoSorb to maintain exclusivity.

Aferetica s.r.l.

In 2015, we entered into a distribution agreement with Aferetica s.r.l., a distributor based in Bologna, Italy that specializes in the sale of certain medical products and devices, specifically extracorporeal therapies, in the critical care, cardiac surgery and liver disease markets ("Aferetica"). Under the terms of the agreement, we granted Aferetica the exclusive right to distribute CytoSorb in Italy, San Marino and the Vatican for application in CRRT (Continuous Renal Replacement Therapies), dialysis and hemoperfusion machine run treatments, as described in the agreement. In connection with the grant of distribution rights, Aferetica agreed to certain minimum purchase and inventory requirements. Aferetica further agreed not to market or sell products competitive with CytoSorb in Italy, San Marino and the Vatican.

The agreement expires by its terms on December 31, 2021, subject to renewal for up to two additional 12 month terms upon mutual agreement of the parties. The agreement may be terminated by either party prior to expiration (i) in the event of a material breach thereof by the other party, provided that the breaching party shall have thirty (30) days to cure the breach, or (ii) upon the bankruptcy or insolvency of the other party. In addition, either party may terminate the agreement in the event of a change of control of the other party that is reasonably expected to result in a material adverse effect on the terminating party, subject to the non-terminating party's right to design a remedy to cure the material adverse effect.

In addition, in September 2017, we announced a partnership with Aferetica to provide dedicated, branded sorbent cartridges for use with Aferetica's proprietary PerLife™ ex-vivo organ perfusion system, with the goal of rehabilitating or preserving the function solid organs destined for eventual transplant. In July 2018, Aferetica and CytoSorbents debuted the PerLife™ system for organ preservation at the 27th International Congress of the Transplantation Society. Aferetica is currently seeking CE Mark registration of the system.

Terumo Cardiovascular Group

In September 2016, we entered into a multi-country strategic partnership with Terumo Cardiovascular Group ("Terumo") to commercialize CytoSorb for cardiac surgery applications. Under the terms of the agreement, Terumo has exclusive rights to distribute the CytoSorb CPB procedure pack for intra-operative use during cardiac surgery in France, Sweden, Denmark, Norway, Finland and Iceland. Terumo launched CytoSorb in its six exclusive countries in December 2016.

Dr. Reddy's Laboratories Ltd.

In March 2017, we entered into a partnership with Dr. Reddy's Laboratories Ltd. ("Dr. Reddy's") for the South African market. Under the terms of the agreement, Dr. Reddy's has the exclusive right to distribute CytoSorb for intensive

care, cardiac surgery, and other hospital applications in South Africa. This is a multi-year agreement and is subject to annual minimum purchases of CytoSorb to maintain exclusivity.

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 were 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 developed polymers for use in these studies.

A grant of $1 million was awarded to the University of Pittsburgh Medical Center in 2003. The project sought 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, was planned to involve viable donors. However, we are not currently focusing our efforts on the commercialization of CytoSorb for application in organ donors.

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 Sepsis 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 and has authored more than 400 publications and has received numerous research grants from foundations and industry.

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 six 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 member of RenalTech International, LLC at the time, to make a $4 million investment in RenalTech International, LLC, Ms. Montiel was granted 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 RenalTech International, LLC. Such membership units ultimately were converted into and became 7,420 shares of our common stock following our June 30, 2006 merger. For the year ended December 31, 2018 we have recorded royalty costs of approximately $600,000.

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 or, in certain cases, in direct contact with a physiological fluid other than blood. The royalty payments provided for under the Settlement Agreement would apply to our currently envisioned CytoSorb, VetResQ, and BetaSorb products. For the year ended December 31, 2018 per the terms of the license agreement we have recorded royalty costs of approximately $1,002,000.

Following the expiration of the 18-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

Germany

Effective January 1, 2017, we achieved a permanent dedicated reimbursement code in Germany that will provide for specific and enhanced reimbursement for our CytoSorb device. We believe that this dedicated reimbursement code will provide our customers with a path to negotiate higher reimbursement that not only covers the cost of the device, but the procedural costs as well. 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.

Switzerland

We have been assigned a specific procedure code for cytokine removal from the Swiss Federal Statistical Office, a division of the Federal Department of Home Affairs in Switzerland for our CytoSorb device that became effective January 1, 2019. This code will facilitate the collection of cost data related to use of the CytoSorb device, a prerequisite for receiving reimbursement from the Swiss DRG system.

Europe (excluding Germany and Switzerland)

Payment for our CytoSorb device for the removal of cytokines in patients with life-threatening illnesses is country dependent in Europe. We are pursuing 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. There can be no assurances that reimbursement will be granted or that additional clinical data may not be required to establish reimbursement.

United States

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.

CytoSorb is not yet approved in the U.S., and we have not fully accessed the potential for reimbursement for the device. Payment for our CytoSorb device in the U.S. for the treatment and prevention of sepsis and other related acute care applications is anticipated to fall under the DRG prospective repayment system, which is currently the predominant inpatient hospital reimbursement methodology in the U.S. Under this system, hospital reimbursement is generally based upon pre-determined amounts payable for specific diagnoses (e.g. septic shock with respiratory failure), regardless of the number of services provided during the patient's stay. If CytoSorb can improve outcomes and reduce the costs of ICU treatment and hospital length of stay, it could potentially save hospitals a significant amount of money.

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, VetResQ, CytoSorb XL, 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 many experimental therapies has been discontinued, including Eritoran from Eisai, CytoFab from BTG/Astra Zeneca, Talactoferrin from Agennix, tranexemic acid from Leading Biosciences, selective cytapheresis from CytoPheryx, and others.

Since January 1, 2013, there have been three Phase 1, one Phase 1/2, nine Phase 2, four Phase 2/3, three Phase 3, and five Phase 4 interventional drug trials posted on clinicaltrials.gov for sepsis-related indications (sepsis, late-onset sepsis, severe sepsis, septic shock, systemic inflammatory response). Of these studies, three are not yet recruiting, nine are currently recruiting, five have been completed, and five have been terminated. Three additional studies were scheduled to be completed at this time, but their current status is unknown.

The sponsors for these studies include the following industry and academic organizations:

- Asahi Kasei Pharma America Corporation
- Baxter Healthcare Corporation
- Bristol-Myers Squibb
- Exponential Biotherapies Inc.
- Ferring Pharmaceuticals
- Fresenius Kabi
- Hamad Medical Corporation
- HK Surgical, Inc.
- Jafron
- Inotrem
- Kaneka Pharma America LLC
- Leading BioSciences, Inc
- Merck Sharp & Dohme Corp.
- Octapharma
- Pfizer
- PRA Health Sciences
- Revimmune
- Sanofi
- SciClone Pharmaceuticals
- Shionogi, Shionogi Inc.
- Techpool Bio-Pharma Co., Ltd.
- Tianjin Chasesun Pharmaceutical Co., LTD
- Yuria-Pharm

Primary outcomes of the investigational drug trials include safety and pharmacokinetic/pharmacodynamic primary outcome measures such as adverse event rates, maximum tolerated dose, clearance rates, and distribution. Additional primary outcomes for these trials include:

- # of days alive without CV, renal, or pulmonary organ support
- # days free of treatment with vasopressors
- 28-day survival and all-cause mortality
- 60-day hospital mortality
- reduction rate of IL-6 serum concentration
- change in biomarkers indicative of endothelial activation and damage
- change in microvascular perfusion
- hemodynamic effects
- immune reconstitution of lymphocytopenic sepsis patients
- immunomodulatory effect (IL6/IL10 ratio)
- lymphocyte counts and percentage
- post-operative sepsis
- reduction in Sequential Organ Failure Assessment score (SOFA)

Notable active Phase III trials in sepsis include the following:

Initiated in November 2012, the 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 DSMB recommended that the trial continue. The primary completion date of the trial was expected to be March 2015, however, according to clinicaltrials.gov, the trial is still enrolling patients and is expected complete in July 2019. 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 in earlier studies (~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. The 800 patient Phase III SCARLET-2 randomized, controlled trial will begin in July 2019 with an estimated study completion date of May 2023 and will measure 28-day all-cause mortality; 3-month, 6-month, and 12-month all-cause mortality; and resolution of organ dysfunction at 28 days.

Another study is being conducted by Atox Bio, 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 or Reltecimod, binds CD28 co-stimulatory receptor to attempt to restore the host's appropriate immune response to severe infections and is being evaluated in the ACCUTE Trial, a Phase 3 randomized controlled trial in 60 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. According to clinicaltrials.gov, the estimated study completion date is December 2019.

Spectral Medical, Inc. collaborated 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 completed enrollment in June 2016. 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. Spectral announced in June 2016 that they had completed enrollment for the EUPHRATES trial. In October 2016, Spectral announced top-line results that the trial did not meet the main goal of absolute reduction in 28-day all-cause mortality, but reiterated safety of treatment and potential benefit in the sickest group of patients (multiple organ dysfunction score > 9). A secondary analysis of the sub-population of patients with septic shock and high circulating endotoxin activity also failed to demonstrate a beneficial effect of Toraymyxin on 28-day mortality in sepsis, however, an exploratory post-hoc analysis of the suggested trends toward improvements in changes in mean arterial pressure and ventilator-free days. In February 2019, Spectral announced an amendment of the original EUPHRATES trial to enroll an additional 150 septic shock patients under the TIGRIS expansion, in patients with a MODS score > 9 and an EAA level between 0.60 and 0.90, and will analyze the combined data from these two trials using a Bayesian statistical approach.

In 2017, a single center, retrospective, non-randomized, unblinded before-after clinical study evaluating the effect of hydrocortisone, intravenous Vitamin C, and thiamine in a total of 94 patients with severe sepsis and septic shock was published suggesting a significant decrease in hospital mortality of 8.5% (4 of 47 treated) versus mortality of 40.4% (19 of 47 control), $p<0.001$. Mechanistically, Vitamin C is an antioxidant that scavenges free oxygen radicals, and plays a role in preserving endothelial function and microcirculatory flow. Thiamine is a co-factor of pyruvate dehydrogenase that is a key step in the conversion of lactate to pyruvate to acetyl-CoA, then to the Krebs cycle, leading to a consumption of lactate. Steroids are anti-inflammatory. Vitamin C or steroids alone have not demonstrated a significant benefit in patients with severe sepsis and septic shock in large scale clinical trials. Observational studies in septic patients have demonstrated a deficiency in Vitamin C and thiamine. Critics of this study cite weaknesses in the study design, and confounders such as the significantly higher incidence of renal replacement therapy in the control arm (33% vs 10% treatment, $p=0.02$), that is an independent and significant risk

factor for mortality in sepsis. Many compare it to another well-known single center trial in 2001 in 263 patients that suggested a significant reduction in hospital mortality (30.5%, N=130 treatment versus 46.5%, N=133 control) due to early goal directed therapy (EGDT), which protocolized resuscitation, oxygenation, and hemodynamic targets in the emergency room for patients with severe sepsis or septic shock prior to being admitted to the ICU. Three subsequent large scale randomized controlled trials failed to demonstrate any benefit. Regardless, the results of the Vitamin C, thiamine and steroid single center trial have spawned a number of randomized controlled clinical trials evaluating this therapeutic strategy, including VICTAS, VITAMINS, ACTS, and others. The largest of these studies is VICTAS, a 2,000 patient U.S. multi-center randomized controlled trial that started in August 2018 comparing intravenous Vitamin C, thiamine, and hydrocortisone for 4 days or until ICU discharge versus placebo and standard of care in patients with suspected or confirmed infection and either respiratory dysfunction requiring mechanical support or shock of less than 24 hours from enrollment. The primary outcome is vasopressor and ventilator-free days at 30 days. The trial is expected to conclude in 2021. The ACTS trial is a 200 patient U.S. multicenter study that started in February 2018 comparing 4 days of treatment with intravenous Vitamin C (6g/d), thiamine (400 mg/d), and hydrocortisone (50 mg every 6 hours) versus saline placebo in patients having suspected or confirmed infection, requiring vasopressors. The primary endpoint is change in SOFA score in 72 hours. Expected study completion is September 2019. The VITAMINS RCT began in Australia and New Zealand in November 2017, comparing the effect of Vitamin C (6g/d), thiamine (400 mg/d) and hydrocortisone (50mg every 6 hours) versus hydrocortisone (50mg every 6 hours) alone, in 216 patients with septic shock and a blood lactate > 2 mmol/L, with a primary endpoint of time alive and free of vasopressors at day 7 after randomization, and is expected to complete in mid-2019.

Four Phase 1 trials and three Phase 2 trials have been posted for interventional biologics with sepsis-related indications. Sponsors of the interventional biologic studies include Adrenomed AG, Biomedizinische Forschungs gmbH, Medical University of Vienna, Bristol-Myers Squibb, Central Hospital, Nancy, France, Diagnostica Stago; Hospices Civils de Lyon, Bioaster, BioMérieux, Sanofi, InflaRx GmbH, Intron Biotechnology, Inc., Revimmune, Washington University School of Medicine, University Hospital, Limoges, and George Clinical Pty Ltd.

Of the registered studies, one is not yet recruiting, one is currently recruiting, four have been completed, and one has been terminated. Primary outcomes of the investigational biologic trials include safety and pharmacokinetic/pharmacodynamic primary outcome measures such as adverse event rates, maximum tolerated dose, clearance rates, and distribution. Additional primary outcomes for these trials include:

- 90-day all-cause mortality
- 90-day mortality related to intervention
- clinical laboratory abnormalities
- ECG findings
- interruption of infusion due to intolerability
- lymphocyte reconstitution
- presence of antibodies to biologic intervention, and
- vital signs

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 collaborated with Toray on the EUPHRATES trial, combining an endotoxin assay with extracorporeal endotoxin removal by Toraymyxin, a polymyxin-B immobilized polystyrene fiber cartridge. As noted above, the EUPHRATES trial failed to demonstrate its primary endpoint. Spectral is now pursuing an amendment to EUPHRATES trial called TIGRIS. There have been now several large scale studies failing to demonstrate a benefit of Toraymyxin on 28-day mortality in sepsis. Toraymyxin represents a competitive, although potentially complementary, therapeutic approach to CytoSorb.

In September 2017, Baxter re-launched oXiris in the E.U., a hollow-fiber acrylonitrile and methalylsulfonate (AN69) membrane hemofilter coated with polyethyleneimine (PEI) that was originally launched by Gambro in 2009 for use in hemodialysis as a strategy to treat acute kidney injury and gram negative septic shock while reducing endotoxin. The filter itself has not changed. However, Baxter has expanded the label to now include reduction of cytokines based on a set of *in vitro* experiments evaluating cytokine reduction from recirculating plasma over two hours. In December 2018, Baxter began a 40 patient randomized, controlled trial, called ECRO, evaluating the effect of endotoxin and cytokine (IL-6) removal during continuous hemofiltration with oXiris in patients with septic shock due to peritonitis, as compared to a standard polysulfone filter. In addition, Baxter also launched the Theranova mid-molecular weight cutoff or high retention onset (HRO) hemodialysis membrane to improve the efficiency of hemodialysis, claiming improved mid-molecular weight substance removal. Neither oXiris nor Theranova are approved in the U.S.

Each of the following technologies claims to remove inflammatory mediators such as cytokines, or to treat sepsis, and represents a potential competitive alternative to CytoSorb. However, to our knowledge, none of these technologies are approved in the U.S. and, with the exception of oXiris, none are approved in the European Union to reduce cytokines.

Toray 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 AN69 CRRT membrane, to bind endotoxin. To our knowledge, neither are specifically approved for the treatment of sepsis. Fresenius had launched a high molecular weight cut off filter in response to SepteX 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, acquired by Medtronic in February 2016, 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. In 2018, Hemolife Medical filed for Chapter 11 bankruptcy. 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 obtained U.S. humanitarian device exemption for Lixelle in March 2015, but is restricted to treating amyloidosis in chronic dialysis patients. 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. To our knowledge, none of the following technologies are approved in the U.S. and none are approved for cytokine reduction or as a therapy to treat sepsis in the EU. Jafron Biomedical is an integrated dialysis public company in China selling dialysis machines and hemodialysis and hemoperfusion cartridges containing a neutral microporous adsorption resin to purify blood of toxins in liver failure, critical illness, poisoning, and autoimmune diseases. Jafron is currently recruiting a 144 patient efficacy and safety study in China using its CA330 cartridge to reduce IL-6 in septic patients. Foshan Biosun Medical Technology Co, Ltd, and Baihe Medical Technology Co, market hemoperfusion cartridges under the BioSky brand name, including the MG series claiming cytokine reduction, and the DX series for bilirubin reduction. 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 polyurethane 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 has completed a 15 patient CE Mark registration trial in Germany evaluating the safety and efficiency of bacterial removal from blood and planned to file for EU approval in Q4 2018. In addition, in 2013, it has partnered with BioBridge Global to apply its technology to pathogen reduction in transfused blood products. Seraph was recently designated by FDA for inclusion into the Expedited Access Pathway (EAP) Program for the specific application of removing drug resistant pathogens from whole blood. Other potential competitors include the now defunct Arbios Systems, Inc. and Hemocleanse Technologies, LLC. We believe our CytoSorb cartridge has significant competitive, technological, and/or economic advantages over systems by these other companies.

Acute Respiratory Distress Syndrome

Treatment of ARDS is predominantly supportive care using supplemental oxygen, careful fluid management, multiple modes of ventilation incorporating the concepts of low tidal volume, high frequency oscillation, and prone ventilation, and extracorporeal membrane oxygenation ("ECMO"). 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, mechanical ventilation, and ECMO 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. CytoSorb reduces myoglobin, and other polymers under development, reduces myoglobin, some without significant losses of albumin.

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. Other than blood compatible sorbent technologies, 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 patients undergoing cardiopulmonary bypass during cardiac surgery. To our knowledge, CytoSorb is the leading 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. Cell saver machines that collect and wash pericardial shed blood is one potential alternative, but is typically done in batches and not a real-time filter during surgery. 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., now Renalguard Solutions, 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. The administration of lipid emulsions, such as Intralipid have been used with some success to create a depot for lipophilic drugs. 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-microglobulin, a complication

of chronic dialysis. HDE approval applies to the treatment of diseases with an incidence of less than 8,000 cases a year in the U.S. annually. Other than blood compatible sorbents, 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 instrument 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 process, in 2011 we completed our randomized, controlled, European Sepsis Trial amongst 14 trial sites in Germany, 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 and published in PLOS ONE. In the European Sepsis Trial, the treatment was

well-tolerated with no serious device related adverse events reported. The trial also demonstrated the ability of CytoSorb to reduce cytokines such as IL-6 from the blood of septic patients. The trial was not powered to demonstrate significant reduction in other clinical endpoints such as mortality.

Cardiac Surgery

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 Hemoglobin) amongst 20 patients and three U.S. clinical sites. The FDA subsequently approved an amendment to the protocol, expanding the trial to a 40 patient randomized controlled study (20 treatment, 20 control) in eight clinical centers. REFRESH I represented 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 REFRESH I study was designed to evaluate the safety and feasibility of CytoSorb when used intra-operatively with a heart-lung machine to reduce plasma free hemoglobin (pfHb) and cytokines in patients undergoing complex cardiac surgery. The study was not powered to measure effect on clinical outcomes. 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 are correlated with the incidence of serious post-operative complications such as kidney injury, renal failure and other organ dysfunction. The goal of CytoSorb is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications. Enrollment was completed with 46 patients. A total of 38 patients were evaluable for pfHb and completed all aspects of the study.

The primary safety and efficacy endpoints of the study were the assessment of serious device related adverse events and the change in plasma free hemoglobin levels, respectively. On October 5, 2016, we announced positive top-line safety data. In addition, following a detailed review of all reported adverse events in a total of 46 enrolled patients, the DSMB found no serious device related adverse events with the CytoSorb device, achieving the primary safety endpoint of the trial. In addition, the therapy was well-tolerated and technically feasible, implementing easily into the cardiopulmonary bypass circuit without the need for an additional external blood pump. This study represents the first randomized controlled trial demonstrating the safety of intra-operative CytoSorb use in patients undergoing high risk cardiac operations.

Investigators of the REFRESH I trial submitted an abstract with data, including free hemoglobin data, from the REFRESH I trial which was selected for a podium presentation at the American Association of Thoracic Surgery conference on May 1, 2017. On May 5, 2017, we announced additional REFRESH I data, including data from the study on the reduction of pfHb and activated complement, and disclosed that investigators of the study have submitted a manuscript of the REFRESH I trial for publication.

In December 2017, the FDA approved our IDE application for our REFRESH 2-AKI study, permitting us to conduct this pivotal trial designed to provide the key safety and efficacy data needed to support United States regulatory approval for CytoSorb in cardiac surgery, which we plan to pursue via the premarket approval (PMA) pathway. The REFRESH 2-AKI trial is a randomized, controlled, multi-center, clinical trial designed to evaluate intraoperative CytoSorb use as a therapy to reduce the incidence and severity of AKI, as measured by Kidney Disease Improving Global Outcomes (KDIGO) criteria, following complex cardiac surgery. Postoperative AKI following cardiac surgery is common and is associated with 1-5 year mortality, and is a risk factor for developing chronic kidney disease requiring hemodialysis in the future. The trial will enroll up to 400 patients at increased risk of cardiovascular surgery-associated AKI, undergoing elective, non-emergent open-heart surgery for either valve replacement, or aortic reconstruction with hypothermic cardiac arrest. In April 2018, we announced the first patient enrollment into the pivotal U.S. REFRESH 2-AKI trial. Based on the recommendations of key clinical advisors, a protocol amendment was submitted to the FDA on July 18, 2018 to improve operational aspects of the patient screening process and expand the inclusion criteria. It was the preference of clinical trial sites to defer enrollment until the amendment was approved by the FDA, which occurred on August 17, 2018. Following the subsequent ethics committee approvals of the amended protocol at all trial sites, as of March 6, 2019, the trial had 21 initiated sites and another 8 sites that were undergoing approvals, contracting and initiation. As of March 6, 2019, the trial had enrolled 56 patients. We anticipate that patient enrollment in the REFRESH 2-AKI trial will be complete by 2020, but this could take longer if enrollment challenges or other factors causing delays are encountered. If the trial is successful, we plan to submit a PMA application in 2021.

The German government, via the German Federal Ministry of Education and Research, is funding a 250 patient, multi-center randomized, controlled study (“REMOVE”) using CytoSorb during valve replacement open heart surgery in patients with infective endocarditis. The study enrolled its first patient in January 2018. As of February 28, 2019, the trial had enrolled 130 patients at 13 sites. A planned interim analysis of the first 50 patients has been completed. On February 4, 2019 Prof. Dr. med. Frank Brunkhorst, Director of the Center for Clinical Studies at Jena University Hospital, who is providing management and oversight to the REMOVE trial, and Prof. Dr. med. Torsten Doenst,

Director of the Clinic for Cardiac and Thoracic Surgery at the University of Jena, provided the following joint statement, “The Scientific Advisory Board (SAB) of the Center of Sepsis Control and Care (CSCC) and the Data Safety Monitoring Board (DSMB) of the REMOVE study recommended continuation of the study, based upon results of a pre-specified interim analysis that analyzed cytokine and vasoactive mediator levels as an indicator of the mechanistic mode of action of the device in 28 CytoSorb-treated patients and 22 control patients. There were no device-associated adverse events in the CytoSorb group.”

Government Research Grants

Two government research grants by the NIH and the U.S. Department of Health and Human Services were 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 developed polymers for use in these studies.

A grant of $1 million was awarded to the University of Pittsburgh Medical Center in 2003. The project sought 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, was completed. Although the next phase of this study, the treatment phase, would have involved 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 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 sought to develop a therapeutic blood purification device that was 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 was for advanced technology development of our hemocompatible porous polymer technologies to remove cytokines and a number of pathogen and biowarfare toxins from blood. We have completed our work under the contract with DARPA and SSC Pacific under Contract No.

N66001-12-C-4199, that provided for maximum funding of approximately $3,825,000. As of December 31, 2018, we received approximately $3,825,000 in funding under this contract and no funding remains.

In September 2012, we were awarded a Phase II SBIR contract by the U.S. Army Medical Research and Material 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 $803,000 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. In June 2016, this contract was further amended to increase the maximum funding by $443,000 to approximately $1,246,000. As of December 31, 2018, we received approximately $1,246,000 in funding under this contract. Our performance under this contract has been completed.

In September 2013, the NHLBI awarded us a Phase I SBIR contract, (contract number HHSN-268201-300044C), valued at $203,351, 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 was to reduce the risk of potential side effects of blood transfusions, and help to extend the useful life of pRBCs. Our performance under this contract has been completed.

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" (contract number HHSN-268201-600006C), provided for maximum funding of approximately $1,524,000 over a two year period. As of December 31, 2018, we received approximately $1,524,000 under this contract. Our performance under this contract has been completed.

In March 2016, we were awarded a Phase I SBIR contract for a development program entitled "Mycotoxin Absorption with Hemocompatible Porous Polymer Beads." The purpose of this contract was to develop effective blood purification countermeasures for weaponized mycotoxins that can be easily disseminated in water, food and air. This work was funded by the U.S. Joint Program Executive Office for Chemical and Biological Defense, or JPEO-CBD, under contract number W911QY-16-P-0048 and provided for maximum funding of $150,000. We received approximately $150,000 and no funding remains under this contract.

In June 2016, we were awarded a Phase I Small Business Technology Transfer ("STTR") contract for a development program entitled "Use of Highly Porous Polymer Beads to Remove Anti-A and Anti-B antibodies from Plasma for Transfusion". The purpose of this contract was to develop our HemoDefend blood purification technology to potentially enable universal plasma. This work is being funded by the USAMRAA under contract W81XWH-16-C-0025 and provided for maximum funding of $150,000. We received approximately $150,000 and no funding remaining under this contract.

In July 2016, we were awarded a Phase I Small Business Innovation Research ("SBIR") contract for a development program entitled "Investigation of a sorbent-based potassium adsorber for the treatment of hyperkalemia induced by traumatic injury and acute kidney injury in austere conditions". The objective of this Phase I project was to develop two novel and distinct treatment options for life-threatening hyperkalemia. This work was funded by the U.S. Army Medical Research Acquisition Activity ("USAMRAA") under contract W81XWH-16-C-0080 and provided for maximum funding of approximately $150,000. We received approximately $150,000 and no funding remains under this contract.

In January 2017, the Company was awarded a Phase II contract to continue development of CytoSorb for fungal mycotoxin blood purification. This program focuses on demonstrating the ability of CytoSorb to adsorb mycotoxins *in vivo* and improve survival in animals. This contract, W911QY-17-C-0007, provides for maximum funding of $999,996 over two years. This program is funded by the Chemical and Biological Defense ("CBD") SBIR program. As of December 31, 2018, we received approximately $884,000 in funding under this contract and have approximately $116,000 remaining under this contract.

In May 2017, the Company was awarded a Phase II STTR contract Titled "Use of Highly Porous Polymer Beads to Remove Anti-A and Anti-B Antibiotics from Plasma Transfusion". The purpose of this contract is to continue

development of our HemoDefend blood purification technology to potentially enable universal plasma. We will collaborate with researchers at Penn State University on this project. This contract provides for maximum funding of $999,070 over two years. This work is being funded by the USAMRAA under contract number W81XWH-17-C-0053. As of December 31, 2018, we received approximately $759,000 and have approximately $240,000 remaining under this contract.

In May 2017, the Company was awarded a Congressionally Directed Medical Research Program (“CDMRP”) Phase I contract to improve delayed evacuation and prolonged field care for severe burn injury via novel hemoadsorptive and hydration therapies. This work is being funded by the USAMRAA under contract number W81WH-17-2-0013. This contract provides for maximum funding of $719,000 over four years. As of December 31, 2018, we received approximately $300,000 and have approximately $419,000 remaining under this contract.

In September 2017, the Company was awarded a Phase II SBIR contract for its development program entitled “Investigation of a sorbent-based potassium adsorber for the treatment of hyperkalemia induced by traumatic injury and acute kidney injury”. The purpose of this contract is to continue development of two novel and distinct treatment options for life-threatening hyperkalemia. This work is being funded by the USAMRAA under contract W81XWH-17-C-0142 and provides for maximum funding of $999,871. As of December 31, 2018, we received approximately $348,000 and have approximately $652,000 remaining under this contract.

In August 2018, we were awarded a Phase IIB Bridge SBIR contract by the NHLBI to facilitate and accelerate the commercialization of our HemoDefend blood purification technology for the purification of pRBC transfusions. The contract, entitled “pRBCs Contaminant Removal with Hemocompatible Porous Polymer Beads” (award number 2R44HL141928-03), provides for maximum funding of approximately $2,971,000 over a three year period. As of December 31, 2018, we received approximately $300,000 in funding under this contract and have approximately $2,671,000 remaining under this contract. Under the terms of this contract, we must make a matching contribution equal to the funds awarded thereunder.

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. 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.

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

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 June 2016, we successfully completed an ISO 13485:2003 annual surveillance audit maintaining our good standing with our notified body. In September 2016, we were granted a two-year renewal for the CytoSorb CE Mark. In June 2018, we received clearance from our notified body to begin production in our new manufacturing facility. In July 2018, we successfully completed an audit upgrade from an ISO 13485:2003 certification to an ISO 13485:2016 certification.

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 *denovo* presents another path to market, but we do not currently anticipate that it will be utilized for our product candidates). 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. The FDA's 510(k) review process usually takes from three to six months, but may take longer. The FDA may require additional information, including clinical data, to make a determination regarding substantial equivalence. 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 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 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, an applicant will submit a PMA with required data. Within 45 days after a PMA is received by the FDA, the agency will notify the applicant whether the application has been "filed" (a threshold determination that the application is sufficiently complete to begin an in-depth review), then a substantive review period begins on the date of filing. Although the stated regulatory timeframe for the FDA's review of PMAs is 180 days, FDA does not meet this goal for all applications; review often takes at least one year and may take significantly longer. During this review period, the FDA may request additional information or clarification of information already provided. Also during the review period, an advisory panel of experts from outside the FDA may be convened to review and evaluate the application and provide recommendations to the FDA. In addition, the FDA generally will conduct a pre-approval inspection of the manufacturing facility to evaluate compliance with Quality System Regulation, which requires manufacturers to implement and follow design, testing, control, documentation and other quality assurance procedures.

Following review 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. Alternatively the agency may issue an “approvable letter” or “not approvable letter” identifying deficiencies of varying degrees, or issue an order denying approval. The PMA 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 sepsis, 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 and some state laws apply regardless of payor (i.e., even in self-pay scenarios). These and other laws (including, for example, the Physician Payment Sunshine Act and state transparency and compliance laws) will become increasingly important as we progress toward commercialization in the U.S. 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.

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.

Pertaining to our VetResQ™ device (offered for veterinary use only), in the U.S., the FDA does not require submission of a 510(k), PMA, or any pre-market approval for devices used in veterinary medicine. Device manufacturers who exclusively manufacture or distribute veterinary devices are not required to register their establishments and list veterinary devices and are exempt from post-marketing reporting. FDA does have regulatory oversight over veterinary devices and can take appropriate regulatory action if a veterinary device is misbranded or adulterated. It is the responsibility of the manufacturer and/or distributor of these articles to assure that these animal devices are safe, effective, and properly labeled.

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. 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. In March 2016, we established CytoSorbents Switzerland GmbH, a wholly-owned subsidiary of CytoSorbents Europe GmbH, to conduct marketing and direct sales in Switzerland. This subsidiary began operations during the second quarter of 2016. In 2017 we began direct sales in Belgium and Luxembourg. On March 5, 2019, the Company announced the expansion of direct sales of CytoSorb for all applications to Poland and the Netherlands, and critical care applications to Sweden, Denmark and Norway. As part of this effort, the Company established CytoSorbents Poland Sp. z.o.o., a wholly-owned subsidiary of CytoSorbents Europe GmbH. From the beginning of the controlled market release in the fourth quarter of 2011 through December 31, 2018, we achieved cumulative sales of CytoSorb of approximately $49,934,000. During this time period, the CytoSorb device represented substantially all of our product sales. At the end of 2018, we had hundreds of KOLs worldwide who are either using CytoSorb or supporting its use in clinical practice and/or in clinical studies. These relationships with KOLs 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, including Germany, United Kingdom, Italy, France and Spain, and currently have either direct sales or distributor or strategic partnership in 55 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.

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, 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 s.r.l. 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. In June 2016, we announced an exclusive distribution agreement with Palex Medical SA to distribute CytoSorb in Spain and Portugal. In September 2016, we announced an exclusive agreement with Armaghan Salamat Kish Group (Arsak) to distribute CytoSorb in Iran. In April 2017, we entered into a distribution agreement with KRA Technical Services to distribute CytoSorb in Qatar. In

July 2017, we announced an exclusive agreement with Droguería, Ramón, González, Revilla (DRGR) S.A. to distribute CytoSorb in Panama. In April 2018, we entered into exclusive agreements with Pharmaworld and Chong Lap (H.K.) Co. Ltd. to distribute CytoSorb in Lebanon and Hong Kong, respectively. As of the third quarter of 2018, we had expanded distribution to include Bosnia, Herzegovina, and Croatia with Medis, d.o.o.; Estonia, Latvia, and Lithuania with SIA Scanmed; and Montenegro and Serbia with Mar Medica, d.o.o. and Cardiotec Vascular Ltda., in Chile. CytoSorb is also distributed in the United Kingdom by Chalice Medical, Ltd., which focuses its efforts in England and Ireland.

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 biopharmaceuticals 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 October 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 December 2017, the Biocon partnership was further expanded to include exclusive distribution of CytoSorb in Malaysia. Under the terms of the agreement, Biocon has committed to minimum annual purchases in Malaysia to maintain exclusivity this territory. In addition, the term of the original agreement was extended to December 2022.

In December 2014, we entered into a multi-country strategic partnership with Fresenius Medical Care AG & Co KGaA (together with its affiliates, as appropriate, "Fresenius") to commercialize the CytoSorb therapy. Under the agreement reflecting the terms of the partnership, Fresenius was granted exclusive rights to distribute CytoSorb for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership allows Fresenius to offer an innovative and easy way to use blood purification therapy for removing cytokines in patients that are treated in the ICU. To promote the success of CytoSorb, Fresenius agreed to 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. In May 2016, Fresenius launched the product in the six countries for which it was granted exclusive distribution rights. In January 2017, the Fresenius partnership was expanded pursuant to a revised three year agreement. The terms of the revised agreement extended Fresenius' exclusive distributorship of CytoSorb for all critical care applications in their existing territories through 2019 and include guaranteed minimum quarterly orders and payments, evaluable every one and a half years.

At the same time, we entered into a comprehensive co-marketing agreement with Fresenius. Under the terms of the co-marketing agreement, CytoSorbents and Fresenius agreed to jointly market CytoSorb to Fresenius' critical care customer base in all countries where CytoSorb is being actively commercialized. CytoSorb continues to be sold by our direct sales force or through our international network of distributors and partners, while Fresenius sells all ancillary products to their customers. Fresenius further provides written endorsements of CytoSorb for use with their multiFiltrate and multiFiltratePRO acute care dialysis machines that can be used by us and our distribution partners to promote CytoSorb worldwide. Training and preparation for this co-marketing program began in five initial countries in 2017 and is continuing, with implementation of the co-marketing program in additional countries planned for the future.

In December 2018, the Fresenius agreement signed in December 2014 was amended to grant Fresenius exclusive distribution rights for the Czech Republic and Finland and all critical care medicine and ICU applications on dialysis or ECMO machines for France. In addition, starting in 2019, Poland, Sweden, Denmark, and Norway will be transitioned into the co-marketing program. Finally, the guaranteed minimum quarterly purchases and payments requirements were removed for 2019.

In addition, also in December 2018, we entered into agreements to expand the partnership with Fresenius into South Korea and Mexico. Under the terms of these agreements, Fresenius has exclusive rights to distribute CytoSorb for acute care and other hospital applications in Korea and Mexico. Commercial sales of CytoSorb are expected to commence after securing market registration clearance from the South Korean and Mexican health authorities. These multi-year agreements include an initial stocking order and are subject to annual minimum purchases of CytoSorb to maintain exclusivity.

In September 2016, we entered into a multi-country strategic partnership with Terumo Cardiovascular Group to commercialize CytoSorb for cardiac surgery applications. Under the terms of the agreement, Terumo has exclusive rights to distribute the CytoSorb cardiopulmonary bypass (“CPB”) procedure pack for intra-operative use during cardiac surgery in France, Sweden, Denmark, Norway, Finland and Iceland. Terumo launched the product in these six countries in December 2016.

In March 2017, we entered into a partnership with Dr. Reddy’s Laboratories Ltd. for the South African market. Under the terms of the agreement, Dr. Reddy’s has the exclusive right to distribute CytoSorb for intensive care, cardiac surgery, and other hospital applications in South Africa. This is a multi-year agreement and is subject to annual minimum purchases of CytoSorb to maintain exclusivity.

A significant portion of our revenues are from product sales in Germany. Substantially all of our grant and other income are from grant agencies in the United States.

In 2018 and 2017, no agency, distributor or direct customer represented more than 10 percent of the Company's total revenue. In 2016, one direct customer, HDZ Herz and Diabeteszentrum NRW, accounted for approximately 11 percent of total revenue.

Orders received for product from both direct customers and distributors are fulfilled upon receipt. Accordingly, we have no significant sales backlog.

We maintain a small amount of property and equipment in Germany. These assets were approximately one percent of total assets for the years ending December 31, 2018, 2017 and 2016, respectively.

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. As of February 28, 2019, our patent portfolio includes 19 issued United States patents as well as multiple issued foreign patents and pending patent applications both in the U.S. and internationally, directed to various compositions and methods of use related to our blood purification technologies, which are expected to expire between 2020 and 2035, absent any patent term extensions. Management believes that any expiring patents will not have a significant impact on our ongoing business. 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	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	1/15/2021	Standard
CytoSorb	Method of Introducing Fluids into a Patient’s Body	20 Years	2/17/2021	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	7/6/2023	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
CytoSorb	Size-Selective Hemoperfusion Polymeric Adsorbents	20 Years	11/20/2026	Standard
CytoSorb	Method of Treating Inflammation	20 Years	4/30/2031	Standard
CytoSorb	Polymer Modification	20 Years	12/31/2031	Standard
CytoSorb	Method of Treating Acute Radiation Syndrome	20 Years	10/22/2035	Standard
CytoSorb	Method of Treating Inflammation	20 Years	3/31/2031	Standard
CytoSorb	Method of Removal of Impurities from Whole Blood	20 Years	1/6/2032	Standard

In addition to the above, we have received notice from the U.S. Patent Office that two of our patent applications have been allowed and we are awaiting the issuance of the formal patent number.

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. Certain of these patents also have foreign counterparts.

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.

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.

We currently hold multiple trademarks including CytoSorb®, HemoDefend™, BetaSorb™, Krol™, and VetResQ™. We have spent considerable resources registering the trademark and building brand awareness and equity of the CytoSorb® tradename, which has been used in commerce since 2006. We expect to maintain and defend our various trademarks to the fullest extent possible.

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 $187,000 for the year ended December 31, 2018.

Employees

As of February 11, 2019, we had 125 full-time and part-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.

Financial Information

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 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, 2018, we had an accumulated deficit of approximately $169,524,000, which included net losses of approximately $17,211,000, $8,797,000 and $11,763,000 for the years ended December 31, 2018, 2017 and 2016, respectively. Due in part 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, clinical studies 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 net 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 continued adoption and usage of our products in the market, obtaining additional regulatory approvals in markets not covered by the CE mark, establishing sales and marketing arrangements with third parties, satisfactory reimbursement in key territories, 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 reimbursement will be available or satisfactory, 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 these 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, 2018, we had current assets of approximately $28,264,000, including cash on hand of approximately $22,369,000 and current liabilities of approximately $6,538,000. For the year ended December 31, 2018, our cash burn was approximately $9,080,000. 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. The amount of long-term capital needed is expected to depend on many factors, including:

- rate of sales growth and adoption of our products in the marketplace;
- product gross margin;
- 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.

We have an effective shelf registration statement with the SEC which enables us to raise up to $150 million in one or more offerings, through the issuance and sale of any combination of equity securities, debt securities, warrants and units.

In addition, we are party to that certain Controlled Equity Offering℠ Sales Agreement, as amended (the "Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor"), pursuant to which we may offer to sell, from time to time through Cantor, shares of the Company's common stock. During the year ended December 31, 2018, we sold a total of 1,515,260 shares of our common stock at an average price of $9.61 per share, under the terms of the Sales Agreement, generating net proceeds of approximately $14,127,000.

On March 29, 2018, we entered into an Amended and Restated Loan and Security Agreement with Bridge Bank, a division of Western Alliance Bank (the "Bank"), pursuant to which the Bank agreed to loan us up to an aggregate of $15,000,000, to be disbursed in two tranches of $10 million and $5 million, respectively. The proceeds from the first tranche of $10 million were used to refinance our existing indebtedness with the Bank. The second tranche of $5 million is available to us through March 31, 2019, subject to certain conditions as outlined in the Amended and Restated Loan and Security Agreement.

Despite the foregoing, we expect we will require additional financing in the future. Should the financing we require be unavailable to us, or on terms unacceptable to us when we require it, the consequences could have 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 non-dilutive 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. Such events may have a material adverse effect on our business, operating results, financial condition and prospects.

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 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.

If users of our products are unable to obtain adequate reimbursement from third-party payers, or if reimbursement is not available in specific countries, 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, 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.

Outside of the United States, reimbursement systems vary significantly by country. Many foreign markets often have a combination of government-managed and privately-managed healthcare systems that govern reimbursement for medical devices and related procedures. Socialized medicine is common in the EU, and reimbursement and the pricing of medical devices is often subject to governmental control. Application for reimbursement, subsequent approvals, if any, and pricing negotiations with governmental authorities can take considerable time after a device has been CE marked. Private insurance has similar challenges. CytoSorb is currently reimbursed in Germany under government-funded insurance, and in other countries may be covered under the DRG, or "lump sum payment" reimbursement, or other generalized reimbursement for acute care medical products. We are continuously working to obtain or improve upon the type and amount of reimbursement available to us in countries where CytoSorb is available, and as we attempt to move from an existing reimbursement platform to a new reimbursement platform, we may experience interruptions and/or reductions in the amount available for reimbursement. Because of this, there can be no assurance that new reimbursement will be obtained or that existing reimbursement will continue or that such reimbursement will be sufficient to adequately cover the cost of the device or treatment. As a result, our future revenues, profitability and access to capital may be negatively affected by any interruption or reduction in amounts of reimbursement. 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.

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

As of February 11, 2019, we had 125 full-time and part-time employees as well as several consultants and 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. Eric R. Mortensen, our Chief Medical Officer. The employment agreements for Dr. Chan, Mr. Capponi, and Ms. Bloch expired on December 31, 2018. The Company is currently negotiating new employment agreements with Dr. Chan, Mr. Capponi and Ms. Bloch, however, 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.

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;
- the development by our competitors of products or product candidates that are similar or identical to ours;
- 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 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. In addition, certain of our existing patents expire between 2020 and 2035. 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 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.

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 expire between 2020 and 2035. 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 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 marketing authorization in the EU under the CE marking process 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 EU, as well as in the U.S. and in other 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 may pursue various indications for our product candidates, and they may be subject to different FDA regulatory pathways for marketing authorization, and under the jurisdiction of different FDA review divisions within the FDA's Office of Device Evaluation.

As we seek to determine commercially viable indications for our product candidates, we may consider pursuing a variety of indications that may be approved through one of several different FDA regulatory clearance or approval pathways, and under the jurisdiction of different FDA review divisions within the FDA's Office of Device Evaluation. We expect the pathways available to us will be impacted by the FDA regulatory history of the category of "sorbent hemoperfusion systems" and our options may also be impacted by the FDA's interpretations and application of these

and other regulatory standards to our product candidates. The regulatory pathways available to us may impact the level and type of data necessary to support our applications, and the post-marketing requirements to which we and our products will be subject.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner, affect whether government agencies promptly pay amounts awarded under grants from such agencies, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new drugs and medical devices can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs and medical devices to be reviewed and/or approved by necessary government agencies as well as affect whether we receive timely payment of amounts awarded to us under grants and contracts with government agencies, including DARPA, which would adversely affect our business. For example, over the last several years, including from December 22, 2018 until January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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, 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. At the same time, relationships with these individuals and entities are the subject of heightened scrutiny and may present the potential for future healthcare enforcement risk.

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. In addition, our interactions, communications, and financial relationships with these individuals and

entities present future healthcare enforcement risks.

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 EU. 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.

In the second quarter of 2018, we commissioned our expanded CytoSorb manufacturing facility in New Jersey that quadruples manufacturing capacity. While we currently believe we have established sufficient production capacity to supply potential near term demand for the CytoSorb device, we will likely 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.

Our business could be harmed by adverse economic conditions in Germany, our primary geographical market, or by economic and/or political instability in the EU caused by Brexit, or other factors.

For the year ended December 31, 2018, we derived a majority of our net product sales from sales in Germany. Despite modest European and global growth, there are many economic and political issues that could negatively impact the health of Germany's economy, the broader EU economy, and the world economy overall. Examples include the uncertainty over the United Kingdom's intended exit from the EU, also known as "Brexit," economic instability in a number of EU member countries, and changes in the political leadership in the EU and United States. Germany and other European countries face additional risks to their local economies, some of which include the impact of foreign exchange fluctuations, unemployment, tightening of monetary policy, the economic burden of immigration, diminished liquidity and reliance on debt, the rising cost of healthcare, and other factors. In addition, the German government, insurance companies, health maintenance organizations and other payers of healthcare costs continue to focus on healthcare reform and containment of healthcare costs. We cannot predict whether Germany's economy will continue to grow or decline consistent with the overall global economy, which decline would negatively impact the demand for medical devices and healthcare technologies generally and lead to reduced spending on the products we provide. In addition, continued healthcare cost containment efforts may result in lower prices and a reduction or elimination of reimbursement for our products. Due to the concentration of our product sales in this country, any of the foregoing may have a negative impact on our revenues, business operations and financial condition.

Our business may be negatively affected if the United States and/or the countries in which we sell our products participate in wars, military actions or are otherwise the target of international terrorism.

Involvement in a war or other military action or international acts of terrorism may cause significant disruption to commerce throughout the world. To the extent that such disruptions result in (i) delays or cancellations of customer orders, (ii) a general decrease in consumer spending on healthcare technology, (iii) our inability to effectively market and distribute our products globally or (iv) our inability to access capital markets, our business and results of operations could be materially and adversely affected. We are unable to predict whether acts of international terrorism or the involvement in a war or other military actions by the United States and/or the countries in which we sell our products will result in any long-term commercial disruptions or if such involvement or responses will have any long-term material adverse effect on our business, results of operations, or financial condition.

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 (the "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.

We are subject to governmental export and import controls that could impair our ability to compete in international markets due to licensing requirements and subject us to liability if we are not in compliance with applicable laws.

Our products are subject to export control and import laws, tariffs, and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations

administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Exports of our products must be made in compliance with these laws, tariffs, and regulations. If we fail to comply with these laws, tariffs, and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us and responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers.

In addition, changes in our products or changes in applicable export or import laws, tariffs, and regulations may create delays in the introduction and sale of our products in international markets or, in some cases, prevent the export or import of our products to certain countries, governments or persons altogether. Any change in export or import laws and regulations, shift in the enforcement or scope of existing laws, tariffs, and regulations, or change in the countries, governments, persons, products, or technologies targeted by such laws, tariffs, and regulations, could also result in decreased use of our products, or in our decreased ability to export or sell our products to existing or potential customers. Any decreased use of our products or limitation on our ability to export or sell our products would likely adversely affect our business, financial condition and results of operations.

Cyberattacks and other security breaches could compromise our proprietary and confidential information which could harm our business and reputation.

In the ordinary course of our business, we generate, collect and store proprietary information, including intellectual property and business information. The secure storage, maintenance, and transmission of and access to this information is important to our operations and reputation. Computer hackers may attempt to penetrate our computer systems and, if successful, misappropriate our proprietary and confidential information including e-mails and other electronic communications. In addition, an employee, contractor, or other third-party with whom we do business may attempt to obtain such information, and may purposefully or inadvertently cause a breach involving such information. While we have certain safeguards in place to reduce the risk of and detect cyber-attacks, our information technology networks and infrastructure may be vulnerable to unpermitted access by hackers or other breaches, or employee error or malfeasance. Any such compromise of our data security and access to, or public disclosure or loss of, confidential business or proprietary information could disrupt our operations, damage our reputation, provide our competitors with valuable information, and subject us to additional costs which could adversely affect our business.

The recently passed Tax Cuts and Jobs Act (the "TCJA") could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the TCJA, which significantly reforms the Internal Revenue Code. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses generated after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks, immediate deductions for certain new investments instead of deductions for depreciation expense over time and modifying or repealing many business deductions and credits. Federal net operating losses arising in taxable years ending after December 31, 2017 will be carried forward indefinitely pursuant to the TCJA. We continue to examine the impact this tax reform legislation may have on our business. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the TCJA is uncertain and our business and financial condition could be adversely affected. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our common stock.

Our failure to comply with data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

European Union member states and other foreign jurisdictions, including Switzerland, have adopted data protection laws and regulations which impose significant compliance obligations. Moreover, the collection and use of personal

health data in the European Union, which was formerly governed by the provisions of the European Union Data Protection Directive, was replaced with the European Union General Data Protection Regulation, or the GDPR, in May 2018. The GDPR, which is wide-ranging in scope, imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and the use of third party processors in connection with the processing of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States, provides an enforcement authority and imposes large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. The recent implementation of the GDPR has increased our responsibility and liability in relation to personal data that we process, including in clinical trials, and we may in the future be required to put in place additional mechanisms to ensure compliance with the GDPR, which could divert management's attention and increase our cost of doing business. In addition, new regulation or legislative actions regarding data privacy and security (together with applicable industry standards) may increase our costs of doing business. In this regard, we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the United States, the European Union and other jurisdictions, and we cannot determine the impact such future laws, regulations and standards may have on our business.

In the U.S., even for companies that are not “covered entities” or business associates” under HIPAA, the U.S. Federal Trade Commission, or the FTC, failing to take appropriate steps to keep consumers’ personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 U.S.C § 45(a). The FTC expects a company’s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Medical data is considered sensitive data that merits stronger safeguards. The FTC’s guidance for appropriately securing consumers’ personal information is similar to what is required by the HIPAA Security Rule. Some state privacy and security laws apply more broadly than HIPAA and associated regulations. For example, California recently enacted legislation – the California Consumer Privacy Act, or CCPA – which goes into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Legislators have stated that they intend to propose amendments to the CCPA before it goes into effect, and the California Attorney General will issue clarifying regulations. Although the law includes limited exceptions, including for certain information collected as part of clinical trials as specified in the law, it may regulate or impact our processing of personal information depending on the context. It remains unclear what, if any, modifications will be made to this legislation or how it will be interpreted.

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, 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 Nasdaq and our common stock began trading on Nasdaq on December 23, 2014 under the symbol "CTSO." Our common stock closed as high as $14.80 and as low as $6.55 per share between January 1, 2018 and December 31, 2018 on Nasdaq. On March 5, 2019, the closing price of our common stock, as reported on Nasdaq, was $7.97. 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 and our competitors; and
- general market conditions.

There is no assurance that the price of our common stock will not continue to be volatile.

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. As of December 31, 2018, one shareholder holds 7.6% of our shares and our directors and officers hold 4.5% of our shares on a fully diluted basis.

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, 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 18,226,000 shares remain available for issuance as of December 31, 2018 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 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 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 may cause our share price to fall.

We are party to a Controlled Equity Offering[SM] Sales Agreement, as amended, with Cantor Fitzgerald & Co. pursuant to which we may offer shares of our common stock from time to time through "at-the-market" offerings. We are not obligated to make or continue to make any sale of shares of our common stock under the "at-the-market" offerings. Although any sale of securities pursuant to the "at-the-market" offerings will result in a concomitant increase in cash for each share sold, it may result in shareholder dilution and may 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 19,920 sq. ft., housing research laboratories, manufacturing operations and clinical and administrative offices, under a lease agreement which expires in May 2020. 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 February 2019 is approximately $32,400 and additionally we reimburse the landlord for monthly operating expenses of approximately $28,600.

We also operate a facility in Berlin, Germany housing our sales and administrative offices and warehouse space. We entered into a lease for this office on September 1, 2016. The lease expires on August 31, 2021. We rent this space for $9,003 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 under the symbol "CTSO." Previously, the Company's common stock traded in the over-the counter-market on the OTC Bulletin Board.

Approximate Number of Equity Security Holders

As of February 15, 2019, there were approximately 7,300 stockholders of record. 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 of record.

Stock Performance Graph

The following graph shows the value of an investment of $100 on December 31, 2013 in each of CytoSorbents Corporation common stock, the Russell 2000 Index and the Nasdaq Biotech Index. All values assume reinvestment of the pretax value of dividends and are calculated as of December 31 st of each year. The historical stock price performance of the Company's common stock shown in the performance graph is not necessarily indicative of future stock price performance.

CytoSorbents Corporation vs. Russell 2000 Index and Nasdaq Biotech Index

Comparison of 5 Year Total Cumulative Return

Value of a $100 Investment on December 31, 2013

Issuer Purchases of Securities

There were no repurchases of the Company's securities during the year ended December 31, 2018.

Recent Sales of Unregistered Securities

We had no sales of unregistered securities in 2018 that have not been previously disclosed in a Current Report on Form 8-K or Quarterly Report on Form 10-Q.

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,				
	2018	2017	2016	2015	2014
Revenue:					
Sales	$20,252,383	$13,381,853	$8,206,036	$4,043,819	$3,135,387
Grant income	2,251,525	1,768,901	1,321,807	735,863	978,271
Other revenue	—	—	—	11,934	9,167
Total revenue	22,503,908	15,150,754	9,527,843	4,791,616	4,122,825
Cost of revenue	7,489,400	5,518,360	3,953,725	2,212,546	2,133,888
Gross margin	15,014,508	9,632,394	5,574,118	2,579,070	1,988,937
Operating expenses:					
Research and development	7,723,028	3,221,233	4,073,093	3,744,803	2,288,101
Legal, financial and other consulting	2,002,032	1,339,493	1,184,788	1,089,145	896,847
Selling general and administrative	20,874,376	14,914,266	11,808,362	7,048,781	5,696,825
Total operating expenses	30,599,436	19,474,992	17,066,243	11,882,729	8,881,773
Loss from Operations	(15,584,928)	(9,842,598)	(11,492,125)	(9,303,659)	(6,892,836)
Other income (expense):					
Interest income/(expense), net	(1,461,045)	(749,076)	(231,804)	(9,301)	(310,024)
Foreign currency transaction gain (loss)	(784,752)	1,454,136	(358,077)	(507,276)	(385,956)
Total other income (expense), net	(2,245,797)	705,060	(589,881)	(497,975)	(695,980)
Loss before benefit from income taxes	(17,830,725)	(9,137,538)	(12,082,006)	(9,801,634)	(7,588,816)
Benefit from income taxes	619,546	676,739	318,550	324,606	385,642
Net loss	(17,211,179)	(8,460,799)	(11,763,456)	(9,477,028)	(7,203,174)
Dividends	—	335,731	—	—	9,266,673
Net loss available to common stockholders, basic and diluted	(17,211,179)	(8,796,530)	(11,763,456)	(9,477,208)	(16,469,847)
Weighted average common shares outstanding, basic and diluted	30,719,176	27,613,911	25,433,719	24,885,809	14,382,813
Net loss per share, basic and diluted	$(0.56)	$(0.32)	$(0.46)	$(0.38)	$(1.15)

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	As of December 31,				
	2018	2017	2016	2015	2014
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$22,368,837	$17,321,862	$5,245,178	$5,316,851	$3,605,280
Short term investments	—	—	—	2,192,000	1,944,547
Working capital	21,725,888	12,891,009	3,550,353	8,452,677	6,082,982
Total assets	32,747,326	24,103,307	9,693,844	11,254,366	8,468,625
Preferred stock	—	—	—	—	—
Accumulated deficit	(169,523,815)	(152,312,636)	(143,516,106)	(131,752,650)	(122,275,622)
Total stockholders' equity	16,934,600	10,262,835	1,337,459	9,846,715	6,944,601

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, 2018, 2017 and 2016 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 using blood purification technology to treat deadly inflammation in hospitalized patients around the world. 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 19 issued U.S. patents, multiple issued foreign patents and 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 17 years.

In March 2011, we received EU regulatory approval under the CE Mark and Medical Devices Directive for our flagship product, CytoSorb, as an extracorporeal cytokine filter indicated for use in clinical situations where cytokines are elevated. 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 ICU, and remains a major unmet medical need, with little more than supportive care therapy (e.g., mechanical ventilation, dialysis, vasopressors, fluid support, ECMO, etc.) as treatment options. By potentially preventing or treating organ failure, CytoSorb may improve clinical outcome, including survival, while reducing the need for costly ICU treatment, thereby potentially saving significant healthcare costs. 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 January 2018, the Company received approval for the first CytoSorb label extension increasing treatment time from six hours to 24 hours. In May 2018, the Company received the second label extension for CytoSorb covering use of the device for the removal of bilirubin and myoglobin in the treatment of liver failure and trauma, respectively.

Our CE Mark enables CytoSorb to be sold throughout all 28 countries of the EU. 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 predominately septic shock 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 13485:2016 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 and for additional clinical studies. We also established general reimbursement for CytoSorb in Germany. We have also been assigned a specific procedure code for cytokine removal in Switzerland for our CytoSorb device that became effective January 1, 2019 and is pending reimbursement valuation assignment.

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. 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.

In March 2016, we established CytoSorbents Switzerland GmbH, a wholly-owned subsidiary of CytoSorbents Europe GmbH, to conduct marketing and direct sales in Switzerland. This subsidiary began operations during the second quarter of 2016. In 2017, we further expanded our direct sales efforts into Belgium and Luxemburg.

On March 5, 2019, the Company announced the expansion of direct sales of CytoSorb for all applications to Poland and the Netherlands, and critical care applications to Sweden, Denmark and Norway. As part of this effort, the Company established CytoSorbents Poland Sp. z.o.o., a wholly-owned subsidiary of CytoSorbents Europe GmbH.

At the end of 2018, 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 February 11, 2019, our European sales, marketing and clinical support team includes 29 direct sales people, one contract sales person and 22 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, Bahrain, and Oman (the GCC) and Yemen, Iraq, and Jordan through an exclusive agreement with Techno Orbits. 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 s.r.l. 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. In June 2016, we announced an exclusive distribution agreement with Palex Medical SA to distribute CytoSorb in Spain and Portugal. In September 2016, we announced an exclusive agreement with Armaghan Salamat Kish Group (Arsak) to distribute CytoSorb in Iran. In April 2017, we entered into a distribution agreement with KRA Technical Services to distribute CytoSorb in Qatar. In July 2017, we announced an exclusive agreement with Droguería, Ramón, González, Revilla (DRGR) S.A. to distribute CytoSorb in Panama. In April 2018, we entered into exclusive agreements with Pharmaworld and Chong Lap (H.K.) Co. Ltd. to distribute CytoSorb in Lebanon and Hong Kong, respectively. In July 2018, we disclosed an expansion to 53 countries, including Bosnia, Herzegovina, and Croatia with Medis, d.o.o.; Estonia, Latvia, and Lithuania with SIA Scanmed; and

Montenegro and Serbia with Mar Medica, d.o.o. We also disclosed a change in our distributor in the United Kingdom, focused on England and Ireland, with Chalice Medical, Ltd. In July 2018, we entered into a distribution agreement with Cardiotec Vascular Ltda., to distribute CytoSorb in Chile.

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 biopharmaceuticals 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 October 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 December 2017, the Biocon partnership was further expanded to include exclusive distribution of CytoSorb in Malaysia. Under the terms of the agreement, Biocon has committed to minimum annual purchases in Malaysia to maintain exclusivity this territory. In addition, the term of the original agreement was extended to December 2022.

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 agreement reflecting the terms of the partnership, Fresenius was granted exclusive rights to distribute CytoSorb for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership allows Fresenius to offer an innovative and easy way to use blood purification therapy for removing cytokines in patients that are treated in the ICU. To promote the success of CytoSorb, Fresenius agreed to 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. In May 2016, Fresenius launched the product in the six countries for which it was granted exclusive distribution rights. In January 2017, the Fresenius partnership was expanded pursuant to a revised three year agreement. The terms of the revised three-year agreement extended Fresenius' exclusive distributorship of CytoSorb for all critical care applications in their existing territories through 2019 and include guaranteed minimum quarterly orders and payments, evaluable every one and a half years. At the same time, we entered into a new comprehensive co-marketing agreement with Fresenius. Under the terms of the co-marketing agreement, CytoSorbents and Fresenius agreed to jointly market CytoSorb to Fresenius' critical care customer base in all countries where CytoSorb is being actively commercialized. CytoSorb will continue to be sold by our direct sales force or through our international network of distributors and partners, while Fresenius sells all ancillary products to their customers. Fresenius further agreed to provide written endorsements of CytoSorb for use with their multiFiltrate and multiFiltratePRO acute care dialysis machines that can be used by us and our distribution partners to promote CytoSorb worldwide. Training and preparation for this co-marketing program began in five initial countries in 2017 and is continuing, with implementation of the co-marketing program in additional countries planned for the future.

In December 2018, the Fresenius agreement originally signed in 2014 was amended, thereby modifying the territory to include exclusive distribution rights for Czech Republic and Finland and all critical care medicine and intensive care unit (ICU) applications on dialysis or ECMO machines for France. In addition, starting in 2019, Poland, Sweden, Denmark, and Norway will be transitioned into the co-marketing program. Finally, the guaranteed minimum quarterly purchases and payments requirements were removed for 2019.

In addition, in this December 2018 reconfiguration of territories, the Fresenius partnership was expanded to include South Korea and Mexico. Under the terms of these agreements, Fresenius Medical Care has the exclusive rights to distribute CytoSorb for acute care and other hospital applications in Korea and Mexico. Commercial sales of CytoSorb are expected to commence after securing market registration clearance from Korean and Mexican health authorities. These multi-year agreements include an initial stocking order and are subject to annual minimum purchases of CytoSorb to maintain exclusivity.

In September 2016, we entered into a multi-country strategic partnership with Terumo Cardiovascular Group to commercialize CytoSorb for cardiac surgery applications. Under the terms of the agreement, Terumo has exclusive rights to distribute the CytoSorb cardiopulmonary bypass (“CPB”) procedure pack for intra-operative use during cardiac surgery in France, Sweden, Denmark, Norway, Finland and Iceland. Terumo launched the product in these six countries in December 2016.

In March 2017, we entered into a partnership with Dr. Reddy’s Laboratories Ltd. for the South African market. Under the terms of the agreement, Dr. Reddy’s has the exclusive right to distribute CytoSorb for intensive care, cardiac surgery, and other hospital applications in South Africa. This is a multi-year agreement and is subject to annual minimum purchases of CytoSorb to maintain exclusivity.

We continuously evaluate other potential distributor and strategic partner networks in other 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. The publication for this study is currently under preparation.

In addition, we now have more than 50 investigator-initiated studies planned, enrolling or completed in Germany, Austria, Switzerland, the Netherlands, Hungary, the United Kingdom, India, and the U.S. Approximately 20 of these studies are currently enrolling patients. Others have been completed. These trials, which are funded and supported by well-known university hospitals and KOLs, are the equivalent of Phase II clinical studies. They have provided and will continue to provide invaluable information regarding the success of the device in the treatment of sepsis, cardiac 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 U.S. Food and Drug Administration (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 Hemoglobin) amongst 20 patients and three U.S. clinical sites. The FDA subsequently approved an amendment to the protocol, expanding the trial to a 40 patient randomized controlled study (20 treatment, 20 control) in eight clinical centers. REFRESH I represented 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 REFRESH I study was designed to evaluate the safety and feasibility of CytoSorb when used intra-operatively with a heart-lung machine to reduce plasma free hemoglobin (pfHb) and cytokines in patients undergoing complex cardiac surgery. The study was not powered to measure effect on clinical outcomes. 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 are correlated with the incidence of serious post-operative complications such as kidney injury, renal failure and other organ dysfunction. The goal of CytoSorb is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications. Enrollment was completed with 46 patients. A total of 38 patients were evaluable for pfHb and completed all aspects of the study.

The primary safety and efficacy endpoints of the study were the assessment of serious device related adverse events and the change in plasma free hemoglobin levels, respectively. On October 5, 2016, we announced positive top-line safety data. In addition, following a detailed review of all reported adverse events in a total of 46 enrolled patients, the DSMB found no serious device related adverse events with the CytoSorb device, achieving the primary safety endpoint of the trial. In addition, the therapy was well-tolerated and technically feasible, implementing easily into the cardiopulmonary bypass circuit without the need for an additional external blood pump. This study represents the first randomized controlled trial demonstrating the safety of intra-operative CytoSorb use in patients undergoing high risk cardiac operations.

Investigators of the REFRESH I trial submitted an abstract with data, including free hemoglobin data, from the REFRESH I trial which was selected for a podium presentation at the American Association of Thoracic Surgery conference on May 1, 2017. On May 5, 2017, we announced additional REFRESH I data, including data from the study on the reduction of pfHb and activated complement, and disclosed that investigators of the study have submitted a manuscript of the REFRESH I trial for publication.

In December 2017, the FDA approved our IDE application for our REFRESH 2-AKI study, permitting us to conduct this pivotal trial designed to provide the key safety and efficacy data needed to support United States regulatory approval for CytoSorb in cardiac surgery, which we plan to pursue via the premarket approval (PMA) pathway. The REFRESH 2-AKI trial is a randomized, controlled, multi-center, clinical trial designed to evaluate intraoperative CytoSorb use as a therapy to reduce the incidence and severity of AKI, as measured by Kidney Disease Improving Global Outcomes (KDIGO) criteria, following complex cardiac surgery. Postoperative AKI following cardiac surgery is common and is associated with 1-5 year mortality, and is a risk factor for developing chronic kidney disease requiring hemodialysis in the future. The trial will enroll up to 400 patients at increased risk of cardiovascular surgery-associated AKI, undergoing elective, non-emergent open-heart surgery for either valve replacement, or aortic reconstruction with hypothermic cardiac arrest. In April 2018, we announced the first patient enrollment into the pivotal U.S. REFRESH 2-AKI trial. Based on the recommendations of key clinical advisors, a protocol amendment was submitted to the FDA on July 18, 2018 to improve operational aspects of the patient screening process and expand the inclusion criteria. It was the preference of clinical trial sites to defer enrollment until the amendment was approved by the FDA, which occurred on August 17, 2018. Following the subsequent ethics committee approvals of the amended protocol at all trial sites, as of March 6, 2019, the trial had 21 initiated sites and another 8 sites that were undergoing approvals, contracting and initiation. As of March 6, 2019, the trial had enrolled 56 patients. We anticipate that patient enrollment in the REFRESH 2-AKI trial will be complete by 2020, but this could take longer if enrollment challenges or other factors causing delays are encountered. If the trial is successful, we plan to submit a PMA application in 2021.

The German government, via the German Federal Ministry of Education and Research, is funding a 250 patient, multi-center randomized, controlled study ("REMOVE") using CytoSorb during valve replacement open heart surgery in patients with infective endocarditis. The study enrolled its first patient in January 2018. As of February 28, 2019, the trial has enrolled 130 patients at 13 sites. A planned interim analysis of the first 50 patients has been completed. On February 4, 2019 Prof. Dr. med. Frank Brunkhorst, Director of the Center for Clinical Studies at Jena University Hospital who is providing management and oversight to the REMOVE trial, and Prof. Dr. med. Torsten Doenst, Director of the Clinic for Cardiac and Thoracic Surgery at the University of Jena, provided the following joint statement, "The Scientific Advisory Board (SAB) of the Center of Sepsis Control and Care (CSCC) and the DSMB of the REMOVE study recommended continuation of the study, based upon results of a pre-specified interim analysis that analyzed cytokine and vasoactive mediator levels as an indicator of the mechanistic mode of action of the device in 28 CytoSorb-treated patients and 22 control patients. There were no device-associated adverse events in the CytoSorb group."

The market focus of CytoSorb is prevention or treatment of organ failure in life-threatening conditions, including commonly seen illnesses in the ICU 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 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 SIRS response and either prevent or treat organ failure.

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 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.

- CytoSorb XL – an intended next generation successor to CytoSorb currently in advanced pre-clinical testing designed to reduce a broad range of cytokines and inflammatory mediators, including lipopolysaccharide (LPS) endotoxin,

from blood.

- VetResQ - a broad spectrum blood purification adsorber designed to help treat deadly inflammation and toxic injury in animals with critical illnesses such as septic shock, toxic shock syndrome, severe systemic inflammation, toxin-mediated diseases, pancreatitis, trauma, liver failure, and drug intoxication. VetResQ is being commercialized in the United States.

- HemoDefend – a development-stage blood purification technology designed to remove non-infectious contaminants in blood transfusion products, with the goal of reducing transfusion reactions and improving the quality and safety of blood. With the support of NHLBI, we plan to initiate a U.S. pivotal trial designed to support U.S. FDA approval, expected to begin in the second half of 2019.

- K^+ontrol – a development-stage blood purification technology designed to reduce excessive levels of potassium in the blood in severe hyperkalemia.

- 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 b2-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 governmental agencies such as the National Institutes of Health and the U.S. Department of Defense, including the Defense Advanced Research Projects Agency, or DARPA, the U.S. Army, U.S. Special Operations Command, and others.

Results of Operations

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

Comparison of the year ended December 31, 2018 and 2017

Revenues:

For the year ended December 31, 2018, we generated total revenue, which includes product revenue and grant income, of approximately $22,504,000 as compared to revenues of approximately $15,151,000 for the year ended December 31, 2017, an increase of approximately $7,353,000, or 49%. Revenue from product sales was approximately $20,252,000 for the year ended December 31, 2018, as compared to approximately $13,382,000 in the year ended December 31, 2017, an increase of approximately $6,870,000 or 51%. This increase was primarily driven by increases in both direct and distributor sales from both new customers and repeat orders from existing customers. In addition, approximately $792,000 of this increase was due to the increase in the average Euro to U.S. dollar exchange rate for the year ended December 31, 2018 as compared to the year ended December 31, 2017.

Grant income increased by approximately $483,000, or 27%, to approximately $2,251,000 in 2018 from $1,768,000 in 2017 as a result of increased revenue received from existing grants and revenue received from a new grant awarded in 2018.

Cost of Revenue:

For the years ended December 31, 2018 and 2017, cost of revenue was approximately $7,489,000 and $5,518,000, respectively, an increase of approximately $1,971,000, or 36%. This increase is related to an increase in product cost of revenue of approximately $1,482,000 attributable to increased sales in 2018. Product gross margins were approximately 74% for the year ended December 31, 2018, as compared to approximately 71% for the year ended December 31, 2017, due to a reduction in the cost of devices manufactured as a result of production efficiencies achieved and, to a lesser extent, the impact of the increase in the exchange rate of the Euro. Grant income related expenses increased by approximately $489,000 during the year ended December 31, 2018 as compared to the year ended December 31, 2017 due to an increase in direct labor and other costs being deployed toward grant-funded activities during the year ended December 31, 2018 as compared to the year ended December 31, 2017.

Gross Profit:

Gross profit was approximately $15,015,000 for the year ended December 31, 2018, an increase of approximately $5,383,000 or 56%, over gross profit of $9,632,000 in 2017. This increase is primarily attributed to an increase in CytoSorb product sales during 2018, and, to a lesser extent, a result of the increase in product gross margins.

Research and Development Expenses:

Our research and development costs were approximately $7,723,000 and $3,221,000 for the years ended December 31, 2018 and 2017, respectively, an increase of approximately $4,502,000, or 140%. This increase in research and development expenditures was due to an increase in our clinical trial costs of approximately $4,179,000, which is primarily related to our REFRESH 2-AKI trial, an increase in non-clinical research and development salary related costs of approximately $329,000 and an increase in new product development costs of approximately $164,000 and increase in other non-grant related research and development costs of approximately $319,000. These increases were offset by an increase in direct labor and other costs being deployed toward grant-funded activities of approximately $489,000, which had the effect of decreasing the amount of our non-reimbursable research and development costs.

Legal, Financial and Other Consulting Expenses:

Our legal, financial and other consulting costs were approximately $2,002,000 and $1,339,000 for the years ended December 31, 2018 and 2017, respectively, an increase of approximately $663,000, or 50%. This increase was due to an increase in employment agency fees of approximately $271,000 related to the recruitment of senior level personnel, an increase in legal fees of approximately $254,000 related to certain corporate initiatives, an increase in accounting fees of approximately $39,000 related to fees in Germany and an increase in other professional fees of approximately $99,000.

Selling, General and Administrative Expenses:

Our selling, general and administrative expenses were approximately $20,874,000 and $14,914,000 for the years ended December 31, 2018 and 2017, respectively, an increase of approximately $5,960,000, or 40%. The increase in selling, general, and administrative expenses was due to an increase in non-cash stock compensation expense of approximately $1,379,000 primarily based upon achievement of the 2018 operating milestones, increases in salaries, commissions and related costs of approximately $2,831,000 due to headcount additions, an increase in royalty

expenses of approximately $555,000 due to the increase in product sales, additional sales and marketing costs, which include advertising and conferences of approximately $343,000, an increase in travel and entertainment costs and other expenses of approximately $453,000, an increase in occupancy cost of approximately $237,000 related to our manufacturing facility expansion, an increase in public relations expense of approximately $98,000 and an increase in other G&A expenses of approximately $64,000.

Interest Expense, Net:

For the year ended December 31, 2018, interest expense, net was approximately $1,461,000, as compared to interest expense, net of approximately $749,000 for the year ended December 31, 2017. This increase in net interest expense of approximately $712,000 is directly related to the settlement of the Success Fee with Bridge Bank in the amount of $637,000 that became due in May 2018 in accordance with the terms of the 2016 Success Fee Letter with Bridge Bank and the additional interest related to the drawdown of the Term B Loan (as defined in the Loan and Security Agreement dated June 30, 2016 with Bridge Bank) on June 30, 2017 in the amount of $5,000,000.

Gain (Loss) on Foreign Currency Transactions:

For the year ended December 31, 2018, the loss on foreign currency transactions was approximately $785,000, as compared to a gain on foreign currency transactions of approximately $1,454,000 for the year ended December 31, 2017. The 2018 loss is directly related to the decrease in the exchange rate of the Euro at December 31, 2018, as compared to December 31, 2017. The exchange rate of the Euro to the U.S. dollar was $1.15 per Euro at December 31, 2018 as compared to $1.20 per Euro at December 31, 2017. The 2017 income is directly related to the increase in the exchange rate of the Euro at December 31, 2017, as compared to December 31, 2016. The exchange rate of the Euro to the U.S. dollar was $1.20 per Euro at December 31, 2017 as compared to $1.05 per Euro at December 31, 2016.

Benefit from Income Taxes:

Our benefit from income taxes was approximately $620,000 and $677,000 for the years ended December 31, 2018 and 2017, respectively. These benefits were realized by utilizing the New Jersey Technology Business Tax Certificate Transfer Program whereby the State of New Jersey allows us to sell a portion of our state net operating losses to a third party.

Comparison of the year ended December 31, 2017 and 2016

Revenues:

For the year ended December 31, 2017, we generated total revenue, which includes product revenue and grant income, of approximately $15,151,000 as compared to revenues of approximately $9,528,000 for the year ended December 31, 2016, an increase of approximately $5,623,000, or 59%. Revenue from product sales was approximately $13,382,000 for the year ended December 31, 2017, as compared to approximately $8,206,000 in the year ended December 31, 2016, an increase of approximately $5,176,000 or 63%. This increase was largely driven by an increase in direct sales from both new customers and repeat orders from existing customers, along with an increase in distributor sales.

Grant income increased by approximately $447,000, or 34%, to approximately $1,769,000 in 2017 from $1,322,000 in 2016 as a result of revenue received from new grants awarded during 2017.

Cost of Revenue:

For the years ended December 31, 2017 and 2016, cost of revenue was approximately $5,518,000 and $3,954,000, respectively, an increase of approximately $1,564,000, or 40%. This increase is related to an increase in product cost of revenue of approximately $1,117,000 attributable to increased sales in 2017. Product gross margins were approximately 71% for the year ended December 31, 2017, as compared to approximately 67% for the year ended December 31, 2016 due to a reduction in our product costs and a change the mix of direct and distributor sales. Grant income related expenses increased by approximately $447,000 during the year ended December 31, 2017 as compared to the year ended December 31, 2016 due to an increase in direct labor and other costs being deployed toward grant-funded activities during the year ended December 31, 2017 as compared to the year ended December 31, 2016.

Gross Profit:

Gross profit was approximately $9,632,000 for the year ended 2017, an increase of approximately $4,058,000 or 73%, over gross profit of $5,574,000 in 2016. This increase is entirely attributed to an increase in CytoSorb product sales during 2017.

Research and Development Expenses:

Our research and development costs were approximately $3,221,000 and $4,073,000 for the years ended December 31, 2017 and 2016, respectively, a decrease of approximately $852,000, or 21%. This decrease in research and development expenditures is related to an increase in direct labor and other costs being deployed toward grant-funded activities of approximately $447,000, which had the effect of decreasing the amount of our non-reimbursable research and development costs, and a decrease in costs related to our various clinical studies and trials of approximately $580,000. These decreases were offset an increase in salaries related to non-clinical research and development activities of approximately $36,000 and an increase in supplies and other research and development expenses of approximately $161,000.

Legal, Financial and Other Consulting Expenses:

Our legal, financial and other consulting costs were approximately $1,339,000 and $1,185,000 for the years ended December 31, 2017 and 2016, respectively, an increase of approximately $154,000, or 13%. This increase was due to an increase in employment agency fees of approximately $123,000 related to the hiring of senior level personnel in 2017, an increase in legal fees of approximately $17,000 related to various corporate initiatives and an increase in accounting and consulting fees of approximately $14,000.

Selling, General and Administrative Expenses:

Our selling, general and administrative expenses were approximately $14,914,000 and $11,808,000 for the years ended December 31, 2017 and 2016, respectively, an increase of approximately $3,106,000, or 27%. The increase in selling, general, and administrative expenses was due to an increase in non-cash stock compensation expense of approximately $894,000 primarily based upon achievement of the 2017 operating milestones, increases in salaries, commissions and related costs of approximately $834,000 due to headcount additions, an increase in royalty expenses of approximately $480,000 due to the increase in product sales, additional sales and marketing costs, which include advertising and conferences of approximately $299,000, an increase in travel and entertainment costs and other expenses of approximately $213,000, an increase in occupancy cost of approximately $90,000 related to facility expansion, an increase in public relations expense of approximately $105,000, an increase in office supplies and related expenses of approximately $148,000 and other general and administrative cost increases of approximately $60,000. These increases were offset by a decrease in bad debt expense of approximately $66,000.

Interest Income (Expense), Net:

For the year ended December 31, 2017, interest expense, net was approximately $749,000, as compared to interest expense, net of approximately $232,000 for the year ended December 31, 2016. This increase in net interest expense of approximately $517,000 is directly related to interest expense incurred and amortization of loan acquisition costs related to the Company’s financing facility with Bridge Bank on which $5,000,000 was drawn on June 30, 2016 and outstanding for the year ended December 31, 2017 and $5,000,000 was drawn on June 30, 2017 and was outstanding during the six months ended December 31, 2017.

Gain (Loss) on Foreign Currency Transactions:

For the year ended December 31, 2017, the gain on foreign currency transactions was approximately $1,454,000, as compared to a loss on foreign currency transactions of approximately $358,000 for the year ended December 31, 2016. The 2017 gain is directly related to the increase in the exchange rate of the Euro at December 31, 2017, as compared to December 31, 2016. The exchange rate of the Euro to the U.S. dollar was $1.20 per Euro at December 31, 2017 as compared to $1.05 per Euro at December 31, 2016. The 2016 loss is directly related to the decrease in the exchange rate of the Euro at December 31, 2016, as compared to December 31, 2015. The exchange rate of the Euro to the U.S. dollar was $1.05 per Euro at December 31, 2016 as compared to $1.08 per Euro at December 31, 2015.

Benefit from Income Taxes:

Our benefit from income taxes was approximately $677,000 and $319,000 for the years ended December 31, 2017 and 2016, respectively. These benefits were realized by utilizing the New Jersey Technology Business Tax Certificate Transfer Program whereby the State of New Jersey allows us to sell a portion of our state net operating losses to a third party.

History of Operating Losses

We have experienced substantial operating losses since inception. As of December 31, 2018, we had an accumulated deficit of approximately $169,524,000, which included losses of approximately $17,211,000, $8,461,000 and $11,763,000 for years ended December 31, 2018, 2017 and 2016, respectively. Historically, our losses have resulted principally from costs incurred in the research and development of our polymer technology, our legal, financial and consulting expenses, and selling, general and administrative expenses, which together were approximately $30,599,000, $19,475,000 and $17,066,000 for the years ended December 31, 2018, 2017 and 2016, 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, 2018, we had current assets of approximately $28,264,000 including cash on hand of approximately $22,369,000 and had current liabilities of approximately $6,538,000. In January 2019, we received approximately $620,000 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 into 2020. We will need to raise additional capital 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 in Europe.

Loan and Security Agreement:

On June 30, 2016, the Company and its wholly-owned subsidiary, CytoSorbents Medical, Inc. (together, the "Borrower"), entered into a Loan and Security Agreement with Bridge Bank, a division of Western Alliance Bank, (the "Bank"), pursuant to which the Company borrowed $10 million in two equal tranches of $5 million (the "Original Term Loans"). On March 29, 2018 (the "Closing Date"), the Original Term Loans were refinanced with the Bank pursuant to an Amended and Restated Loan and Security Agreement by and between the Bank and the Borrower (the "Amended and Restated Loan and Security Agreement"), under which the Bank agreed to loan the Borrower up to an aggregate of $15 million to be disbursed in two tranches (1) one tranche of $10 million (the "Term A Loan"), which was funded on the Closing Date and used to refinance the Original Term Loans, and (2) a second tranche of $5 million which may be disbursed at the Borrower's sole request prior to March 31, 2019 provided certain conditions are met (the "Term B Loan" and together with the Term A Loan, the "Term Loans"). The proceeds of the Term Loans will be used for general business requirements in accordance with the Amended and Restated Loan and Security Agreement. Outstanding balances on the Term Loans bear interest at the prime rate reported in the Wall Street Journal plus 3.66%. This rate was 9.16% at December 31, 2018.

On the Closing Date, the Company was required to pay a non-refundable closing fee of $25,000, expenses incurred by the Bank related to the Amended and Restated Loan and Security Agreement of $11,000 and a portion of the final fee for the period the Original Term Loans were outstanding of $85,938. In addition, the Company incurred legal expenses related to the Amended and Restated Loan and Security Agreement of $20,050. As of the Closing Date, the total unamortized loan costs related to the Term Loans amounted to $130,060. These costs have been presented as a direct deduction from the proceeds of the loan on the consolidated balance sheet in accordance with the provisions of ASC 850. These costs are being amortized over the loan period as a charge to interest expense. For the years ended December 31, 2018, 2017 and 2016, the Company recorded interest expense amounting to $31,946, $29,971 and $14,855, respectively, related to these costs. After accounting for the various costs outlined above, the effective interest rate on the Term A Loan was 9.1% as of March 29, 2018. Commencing on the first calendar day of the calendar month after a Term Loan is made, the Company shall make monthly payments of interest only during the term of each Term Loan. Commencing on November 1, 2019, if the Term B Loan is not made, the Company shall make equal monthly payments of principal of $333,333, together with accrued and unpaid interest. Commencing on May 1, 2020, subject to certain conditions as outlined in the Amended and Restated Loan and Security Agreement, if the Term B Loan is made, which is at the Company’s sole discretion, the Company shall make equal monthly payments of principal of $625,000, together with accrued and unpaid interest. In either event, all unpaid principal and accrued and unpaid interest shall be due and payable in full on April 1, 2022. In addition, the Amended and Restated Loan and Security Agreement requires the Company to pay a non-refundable final fee equal to 2.5% of the principal amount of each Term Loan funded upon the earlier of the (i) April 1, 2022 maturity date or (ii) termination of the Term Loan via acceleration or prepayment. This final fee is being accrued and charged to interest expense over the term of the loan. For the years ended December 31, 2018, 2017 and 2016, the Company recorded interest expense of $65,104, $52,083 and $15,625, respectively, related to the final fee. The Term Loans shall be evidenced by one or more secured promissory notes issued to the Bank by the Company. If the Company elects to prepay the Term Loan(s) pursuant to the terms of the Amended and Restated Loan and Security Agreement, it will owe a prepayment fee to the Bank, as follows: (1) for a prepayment made on or after the funding date of a Term Loan through and including the first anniversary of such funding date, an amount equal to 2.0% of the principal amount of such Term Loan prepaid; (2) for a prepayment made after the first anniversary of the funding date of a Term Loan through and including the second anniversary of such funding date, an amount equal to 1.5% of the principal amount of such Term Loan prepaid; and (3) for a prepayment made after the second anniversary of the funding date of a Term Loan through April 1, 2022, an amount equal to 1.0% of the principal amount of such Term Loan prepaid.

Events of default which may cause repayment of the Term Loans to be accelerated include, among other customary events of default, (1) non-payment of any obligation when due, (2) the failure to perform any obligation required under the Amended and Restated Loan and Security Agreement and to cure such default within a reasonable time frame, (3) the occurrence of a Material Adverse Event (as defined in the Amended and Restated Loan and Security Agreement), (4) the attachment or seizure of a material portion of the Borrower's assets if such attachment or seizure is not released, discharged or rescinded within 10 days, and (5) if the Borrower becomes insolvent or starts an insolvency proceeding or if an insolvency proceeding is brought by a third party against the Borrower and such proceeding is not dismissed or stayed within 30 days. The Amended and Restated Loan and Security Agreement includes customary loan conditions, Borrower representations and warranties, Borrower affirmative covenants and Borrower negative covenants for secured transactions of this type.

The Company's and CytoSorbents Medical, Inc.'s obligations under the Amended and Restated Loan and Security Agreement are joint and severable and are secured by a first priority security interest in favor of the Bank with respect to the Company's Shares (as defined in the Amended and Restated Loan and Security Agreement) and the Borrower's Collateral (as defined in the Amended and Restated Loan and Security Agreement, which definition excludes the Borrower's intellectual property and other customary exceptions).

Success Fee Letters:

Pursuant to that certain Success Fee Letter (the "2016 Letter") entered into between the Borrower and the Bank in connection with the Original Term Loans, the Borrower agreed to pay to the Bank a success fee in the amount equal to 6.37% of the funded amount of the Original Term Loans (the "2016 Letter Success Fee") upon the first occurrence of any of the following events: (a) a sale or other disposition by the Borrower of all or substantially all of its assets; (b) a merger or consolidation of the Borrower into or with another person or entity, where the holders of the Borrower's outstanding voting equity securities as of immediately prior to such merger or consolidation hold less than a majority of the issued and outstanding voting equity securities of the successor or surviving person or entity as of immediately following the consummation of such merger or consolidation; (c) a transaction or a series of related transactions in which any "person" or "group" (within the meaning of Section 13(d) and 14(d)(2) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") becomes the "beneficial owner" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of a sufficient number of shares of all classes of stock then outstanding of the Borrower ordinarily entitled to vote in the election of directors, empowering such "person" or "group" to elect a majority of the Board of Directors of the Borrower, who did not have such power before such transaction; or (d) the closing price per share for the Company's common stock on Nasdaq being $8.00 (after giving effect to any stock splits or consolidations effected after the date thereof) or more for five successive business days. On May 18, 2018, the 2016 Letter Success Fee became due to the Bank as result of an occurrence of the event described in clause (d) above. The Company elected to satisfy the 2016 Letter Success Fee by issuing shares of its common stock, which was permitted under the terms of the 2016 Letter. On May 23, 2018, the Company issued 68,791 shares of its common stock in full satisfaction of the 2016 Letter Success Fee, and the obligations of the Borrower under the 2016 Letter. The 2016 Letter Success Fee was valued at $637,000 and was charged to interest expense in the accompanying Statement of Operations and Comprehensive Loss.

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In connection with the Amended and Restated Loan and Security Agreement, the Borrower entered into an additional Success Fee Letter (the "2018 Letter"), which will only be effective if the Term B Loan is drawn. Pursuant to the 2018 Letter, the Borrower shall pay to the Bank a success fee in the amount equal to 6.37% of the funded amount of the Term B Loan (the "2018 Letter Success Fee") upon the first occurrence of any of the following events: (a) a sale or other disposition by the Borrower of all or substantially all of its assets; (b) a merger or consolidation of the Borrower into or with another person or entity, where the holders of the Borrower's outstanding voting equity securities as of immediately prior to such merger or consolidation hold less than a majority of the issued and outstanding voting equity securities of the successor or surviving person or entity as of immediately following the consummation of such merger or consolidation; (c) a transaction or a series of related transactions in which any "person" or "group" (within the meaning of Section 13(d) and 14(d)(2) of the Exchange Act")) becomes the "beneficial owner" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of a sufficient number of shares of all classes of stock then outstanding of the Borrower ordinarily entitled to vote in the election of directors, empowering such "person" or "group" to elect a majority of the Board of Directors of the Borrower, who did not have such power before such transaction; or (d) the closing price per share for the Company's common stock on Nasdaq being the greater of (i) 70% or more over $7.05, the closing price of the Company's common stock on March 29, 2018 (after giving effect to any stock splits or consolidations effected after the date thereof) for five successive business days, or (ii) at least 26.13% more than the closing price of the Company's common stock on the date of the funding of the Term B Loan.

If the 2018 Letter Success Fee is due pursuant an event described in clause (d) of the two preceding paragraphs, the Company may elect, in lieu of paying the 2018 Letter Success Fee in cash, to issue and sell to the Bank, in exchange for the 2018 Letter Success Fee, such number of shares of the Company's common stock as would be equal to the quotient (calculated by rounding up the nearest whole number) obtained by dividing (a) the 2018 Letter Success Fee by (b) the volume weighted average price per share of the Company's common stock for the same five successive business days on which the closing price per share of the Company's common stock caused the 2016 Letter Success Fee to become payable.

The Bank's right to receive the 2018 Letter Success Fee and the Borrower's obligation to pay such 2018 Letter Success Fee terminate on the fifth anniversary of the funding of the Term B Loan and shall survive the termination of the Amended and Restated Loan and Security Agreement and any prepayment of the Term Loans.

Contractual Obligations

The following table summarizes our obligations with regard to our contractual obligations as of December 31, 2018, 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.

1-3 Years 3-5 Years

	Less than 1 Year			More than 5 Years
Operating Lease Obligations	$495,870	$342,271	$–	$ –
Long-term debt	$666,667	$8,000,000	$1,333,333	$ –

Effects of Recent Accounting Pronouncements

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 updated guidance is effective for public entities for fiscal years beginning after December 31, 2018. The Company has evaluated the impact of the updated guidance and has determined that the adoption of ASU 2016-02 will result in the recognition of a right-of-use asset and corresponding lease liability of approximately $1,449,000 as of December 31, 2018 based on the present value of the remaining minimum lease payments over the remaining terms of the leases. In addition, certain disclosures related to these leases will be enhanced as required by Topic 842.

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 to both direct and distributor/strategic partner customers are recognized at the time when control passes to the customer, in accordance with the terms of their respective contracts. Recognition of revenue occurs as each performance obligation is completed.

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 the associated performance obligation is fulfilled. Costs are recorded as incurred. Costs subject to reimbursement by these grants have been reflected as costs of revenue.

Research and Development

All research and development costs, payments to laboratories, research consultants and costs related to clinical trials and studies are expensed when incurred.

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.

Off-Balance Sheet Arrangements

We currently operate a facility near Princeton, New Jersey with approximately 19,920 sq. ft., housing research laboratories, clinical manufacturing operations and administrative offices, under a lease agreement which expires in May 2020. We expect to secure additional square footage to support increased manufacturing capacity in the future. Our monthly base rent as of February 2019 is approximately $32,400 and, additionally, we reimburse the landlord for monthly operating expenses of approximately $29,000.

We also operate a facility in Berlin, Germany housing our sales and administrative offices and warehouse space. We entered into a lease for this office on September 1, 2016. The lease expires on August 31, 2021. We rent this space for $9,000 per month.

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

We are exposed to certain market risks in the ordinary course of business. These risks result primarily from changes in foreign currency exchange rates and interest rates. In addition, international operations are subject to risks related to differing economic conditions, changes in political climate, differing tax structures and other regulations and restrictions.

To date we have not utilized derivative financial instruments or derivative commodity instruments. We do not expect to employ these or other strategies to hedge market risk in the foreseeable future. Cash is held in checking, savings, and money market funds, which are subject to minimal credit and market risk. We generate sales in both dollars and euros most significantly, the majority of our sales are in Euros and changes in the exchange rate of the Euro to the U.S. dollar may positively or negatively impact our revenue. On the other hand, should sales decline due to a devaluation of the Euro relative to the U.S. dollar, expenses related to our European subsidiary would also decline. This produces a natural currency hedge. We believe that the market risks associated with these financial instruments are immaterial, although there can be no guarantee that these market risks will be immaterial to us in the future.

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

In accordance with Rules 13a-15 and 15d-15, under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), we carried out an evaluation, under the supervision and with the participation of management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of our disclosure controls and procedures as of the end of the period covered by this report. Based upon that evaluation, our Chief Executive Officer and Chief

Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2018, to ensure that information required to be disclosed in our reports filed or submitted under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure.

Management's Annual 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.

Attestation Report of the Registered Public Accounting Firm

WithumSmith+Brown, PC, the independent registered public accounting firm that audited the financial statements of included in Item 8 of this Annual Report on Form 10-K, has issued an attestation report on the effectiveness of our internal control over financial reporting as of December 31, 2018. This report is included with the financial statements included in Item 8 of this Annual Report on Form 10-K and 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, 2018 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.

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 2019 annual meeting of stockholders scheduled to be held on June 4, 2019, 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 2019 annual meeting of stockholders scheduled to be held on June 4, 2019, 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 2019 annual meeting of stockholders scheduled to be held on June 4, 2019, 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 2019 annual meeting of stockholders scheduled to be held on June 4, 2019, 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 2019 annual meeting of stockholders scheduled to be held on June 4, 2019, 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 2019 annual meeting of stockholders scheduled to be held on June 4, 2019, 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.

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 2019 annual meeting of stockholders scheduled to be held on June 4, 2019, 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 2019 annual meeting of stockholders scheduled to be held on June 4, 2019, 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 as of 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 as of 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).+
10.3	Employment Agreement with Kathleen P. Bloch Effective as of 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).+
10.4	Consulting Agreement with Dr. Robert Bartlett Effective as of 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	Fourteenth Amendment to Lease Agreement by and between the Registrant and Princeton Corporate Plaza, LLC, dated April 1, 2016 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed on May 9, 2016).
10.8	Amended and Restated Fourteenth Amendment to Lease Agreement by and between the Registrant and Princeton Corporate Plaza LLC, dated August 5, 2016 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed on May 9, 2016).
10.9	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).

10.10	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).
10.11	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).†

10.12	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).†
10.13	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).
10.14	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).+
10.15	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).+
10.16	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).+
10.17	Loan and Security Agreement, dated as of June 30, 2016, by and among CytoSorbents Corporation, CytoSorbents Medical, Inc. and Western Alliance Bank (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on July 1, 2016).
10.18	Success Fee Letter, dated as of June 30, 2016, by and among CytoSorbents Corporation, CytoSorbents Medical, Inc. and Western Alliance Bank (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on July 1, 2016).
10.19	Underwriting Agreement, dated as of March 30, 2017, by and among CytoSorbents Corporation and Cowen and Company, LLC, as representative of the several underwriters (incorporated by reference to Exhibit 1.1 to the Registrant's Current Report on Form 8-K filed on April 3, 2017).
10.20	Amended and Restated Loan and Security Agreement, dated as of March 29, 2018, by and among CytoSorbents Corporation, CytoSorbents Medical, Inc. and Western Alliance Bank (incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K filed on April 4, 2018).
10.21	Success Fee Letter, dated as of March 29, 2018, by and among CytoSorbents Corporation, CytoSorbents Medical, Inc. and Western Alliance Bank (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on April 2, 2018).
10.22	Amendment No. 1 to Sales Agreement, dated as of July 26, 2018, by and between CytoSorbents Corporation and Cantor Fitzgerald & Co. (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on July 26, 2018).
10.23	Exclusive Distribution Agreement, dated as of December 15, 2014, by and between CytoSorbents Europe GmbH and Aferetica s.r.l.*†
10.24	Amendment to Exclusive Distribution Agreement, dated December 15, 2015, by and between CytoSorbents Europe GmbH and Aferetica s.r.l.*†

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, 2018, formatted in Extensible Business Reporting Language (XBRL): (1) Consolidated Balance Sheets at December 31, 2018 and December 31, 2017, (iii) Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2018, 2017 and 2016, (iii) Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Equity/(Deficit) for the years ended December 31, 2018, 2017 and 2016, (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2018, 2017 and 2016, and (v) Notes to the Consolidated Financial Statements.

* 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.

Item 16. Form 10-K Summary.

None.

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 7th day of March, 2019.

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 7, 2019
/s/ Kathleen P. Bloch Kathleen P. Bloch	Chief Financial Officer (Principal Financial and Accounting Officer)	March 7, 2019
/s/ Al Kraus Al Kraus	Chairman of the Board	March 7, 2019
/s/ Alan D. Sobel Alan D. Sobel	Director	March 7, 2019
/s/ Edward R. Jones Edward R. Jones	Director	March 7, 2019
/s/Michael G. Bator Michael G. Bator	Director	March 7, 2019

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, 2018.

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, was engaged to audit our Internal Control. Their report appears on page F-3.

/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 7, 2019

Report of Independent Registered Public Accounting Firm

Board of Directors and Stockholders

Cytosorbents Corporation:

Opinion on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Cytosorbents Corporation (the "Company") as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2018, based on the criteria established in *Internal Control—Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in Internal *Control-Integrated Framework* (2013) issued by the COSO.

Substantial Doubt Regarding Going Concern

As disclosed in Note 1 to the consolidated financial statements, the Company sustained net losses for the years ended December 31, 2018, 2017 and 2016 of approximately $17.2 million, $8.5 million and $11.8 million, respectively. Further, the Company believes it will have to raise additional capital to fund its planned operations for the twelve month period through March 2020. These matters raise substantial doubt regarding the Company's ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1 to the consolidated financial statements. The consolidated financial statements do not include any adjustments related to the outcome of this uncertainty.

Basis for Opinion

The Company's management is responsible for these consolidated financial statements, 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 Company's consolidated financial statements and an opinion on the Company’s internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. 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 audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

A company'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. A company'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 company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with accounting principles generally accepted in the United States of America, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) 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. 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.

/s/ WithumSmith+Brown, PC
WithumSmith+Brown, PC

We have served as the Company's auditor since 2004.

East Brunswick, New Jersey

March 7, 2019

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CYTOSORBENTS CORPORATION

CONSOLIDATED BALANCE SHEETS

December 31,	2018	2017
ASSETS		
Current Assets:		
Cash and cash equivalents	$22,368,837	$17,321,862
Grants and accounts receivable, net of allowance for doubtful accounts of $83,726 and $72,697 at December 31, 2018 and 2017, respectively	3,943,119	2,205,859
Inventories	833,133	795,657
Prepaid expenses and other current assets	1,118,998	415,962
Total current assets	28,264,087	20,739,340
Property and equipment – net	1,729,860	1,402,782
Other assets	2,753,379	1,961,185
Total Assets	$32,747,326	$24,103,307
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$1,485,812	$1,244,411
Accrued expenses and other current liabilities	4,385,720	2,603,920
Current maturities of long-term debt	666,667	4,000,000
Total current liabilities	6,538,199	7,848,331
Long-term debt, net of current maturities and debt issuance costs	9,274,527	5,992,141
Total liabilities	15,812,726	13,840,472
Commitments and contingencies (Note 9)		
Stockholders’ Equity:		
Common Stock, Par Value $0.001, 50,000,000 shares authorized; 31,774,139 and 28,973,679 shares issued and outstanding at December 31, 2018 and 2017, respectively	31,774	28,974
Additional paid-in capital	186,138,466	162,907,482
Accumulated other comprehensive income	288,175	(360,985)
Accumulated deficit	(169,523,815)	(152,312,636)
Total stockholders’ equity	16,934,600	10,262,835
Total Liabilities and Stockholders' Equity	$32,747,326	$24,103,307

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, 2018	Year ended December 31, 2017	Year ended December 31, 2016
Revenue:			
CytoSorb sales	$20,143,354	$13,254,953	$8,206,036
Other sales	109,029	126,900	—
Total product sales	20,252,383	13,381,853	8,206,036
Grant income	2,251,525	1,768,901	1,321,807
Total revenue	22,503,908	15,150,754	9,527,843
Cost of revenue	7,489,400	5,518,360	3,953,725
Gross profit	15,014,508	9,632,394	5,574,118
Operating expenses:			
Research and development	7,723,028	3,221,233	4,073,093
Legal, financial and other consulting	2,002,032	1,339,493	1,184,788
Selling, general and administrative	20,874,376	14,914,266	11,808,362
Total operating expenses	30,599,436	19,474,992	17,066,243
Loss from operations	(15,584,928)	(9,842,598)	(11,492,125)
Other income (expense):			
Interest expense, net	(1,461,045)	(749,076)	(231,804)
Gain/(loss) on foreign currency transactions	(784,752)	1,454,136	(358,077)
Total other income (expense), net	(2,245,797)	705,060	(589,881)
Loss before benefit from income taxes	(17,830,725)	(9,137,538)	(12,082,006)
Benefit from income taxes	619,546	676,739	318,550
Net loss	(17,211,179)	(8,460,799)	(11,763,456)
Dividend, warrant exercise price adjustment	—	335,731	—
Net loss attributable to common shareholders	$(17,211,179)	$(8,796,530)	$(11,763,456)
Basic and diluted net loss per common share	$(0.56)	$(0.32)	$(0.46)
Weighted average number of shares of common stock outstanding	30,719,176	27,613,911	25,433,719
Comprehensive loss:			
Net loss	$(17,211,179)	$(8,460,799)	$(11,763,456)
Other comprehensive income (loss):			

Currency translation adjustment	649,160	(1,259,669)	314,367
Comprehensive loss	$(16,562,019)	$(9,720,468)	$(11,449,089)

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

CYTOSORBENTS CORPORATION

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY

FOR THE YEARS ENDED DECEMBER 31, 2018, 2017 and 2016

	Common Stock Shares	Par value	Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Stockholders' Equity (Deficit)
Balance at December 31, 2015	25,397,056	$25,397	$140,989,651	$584,317	$(131,752,650)	$9,846,715
Stock based compensation - employees, consultants and directors	—	—	2,631,734	—	—	2,631,734
Issuance of restricted stock units	26,665	27	125,032	—	—	125,059
Proceeds from exercise of warrants	20,000	20	64,980	—	—	65,000
Cashless exercise of warrants	4,045	4	(4)	—	—	—
Proceeds from exercise of stock options	36,200	36	118,004	—	—	118,040
Other comprehensive income, foreign translation adjustment	—	—	—	314,367	—	314,367
Net loss	—	—	—	—	(11,763,456)	(11,763,456)
Balance at December 31, 2016	25,483,966	25,484	143,929,397	898,684	(143,516,106)	1,337,459
Stock based compensation - employees, consultants and directors	—	—	3,313,603	—	—	3,313,603
Issuance of common stock - offerings, net of fees incurred	3,105,555	3,106	13,676,624	—	—	13,679,730
Issuance of restricted stock options	41,390	41	207,567	—	—	207,608
Proceeds from exercise of warrants	192,001	192	852,812	—	—	853,004
Cashless exercise of warrants	1,516	2	(2)	—	—	—
Proceeds from exercise of stock options	145,848	146	591,753	—	—	591,899

Cashless exercise of stock options	3,403	3	(3)	—	—	—
Dividend, warrant exercise price adjustment	—	—	335,731	—	(335,731)	—
Other comprehensive income foreign translation adjustment	—	—	—	(1,259,669)	—	(1,259,669)
Net loss	—	—	—	—	(8,460,799)	(8,460,799)
Balance at December 31, 2017	28,973,679	28,974	162,907,482	(360,985)	(152,312,636)	10,262,835
Stock based compensation - employees, consultants and directors	—	—	4,437,250	—	—	4,437,250
Issuance of common stock - offerings, net of fees incurred	1,515,260	1,515	14,125,010	—	—	14,126,525
Issuance of restricted stock options	62,406	62	545,631			545,693
Proceeds from exercise of warrants	313,802	314	1,280,142	—	—	1,280,456
Cashless exercise of warrants	89,556	89	(89)	—	—	—
Proceeds from exercise of stock options	683,673	684	2,206,176	—	—	2,206,860
Cashless exercise of stock options	66,972	67	(67)	—	—	—
Success fee – Bridge Bank	68,791	69	636,931	—	—	637,000
Other comprehensive income foreign translation adjustment	—	—	—	649,160	—	649,160
Net loss	—	—	—	—	(17,211,179)	(17,211,179)
Balance at December 31, 2018	31,774,139	$31,774	$186,138,466	$288,175	$(169,523,815)	$16,934,600

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

CYTOSORBENTS CORPORATION

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016
Cash flows from operating activities:			
Net loss	$(17,211,179)	$(8,460,799)	$(11,763,456)
Adjustments to reconcile net loss to net cash used by operating activities:			
Non-cash interest expense	637,000	–	–
Non-cash compensation	947,910	691,480	431,352
Depreciation and amortization	390,551	218,271	161,613
Bad debt expense	14,762	904	65,378
Foreign currency transaction (gains) losses	784,752	(1,454,136)	358,077
Stock-based compensation	4,437,250	3,313,603	2,756,793
Amortization of loan acquisition costs	97,041	82,054	30,480
Changes in operating assets and liabilities:			
Grants and accounts receivable	(1,847,848)	(649,318)	(889,715)
Inventories	(56,751)	57,320	340,392
Prepaid expenses and other current assets	(731,672)	(76,981)	187,099
Other assets	(6,345)	(15,000)	(41,112)
Accounts payable and accrued expenses	1,704,845	(168,103)	1,632,132
Net cash used by operating activities	(10,839,684)	(6,460,705)	(6,730,967)
Cash flows from investing activities:			
Purchases of property and equipment	(671,970)	(990,673)	(140,724)
Patent costs	(848,294)	(687,446)	(454,807)
Proceeds from sale of short-term investments	–	–	2,192,000
Net cash provided/(used) by investing activities	(1,520,264)	(1,678,119)	1,596,469
Cash flows from financing activities:			
Proceeds from long-term debt	666,667	5,000,000	5,000,000
Repayment of long-term debt	(666,667)	–	–
Payment of loan acquisition costs	(147,988)	(1,560)	(118,833)
Equity contributions - net of fees incurred	14,126,525	13,679,730	–
Proceeds from exercise of stock options	2,206,860	591,899	118,040
Proceeds from exercise of warrants	1,280,456	853,004	65,000
Net cash provided by financing activities	17,465,853	20,123,073	5,064,207
Effect of exchange rates on cash	(58,930)	92,435	(1,382)
Net change in cash and cash equivalents	5,046,975	12,076,684	(71,673)
Cash and cash equivalents at beginning of year	17,321,862	5,245,178	5,316,851
Cash and cash equivalents at end of year	$22,368,837	$17,321,862	$5,245,178
Supplemental disclosure of cash flow information:			
Cash paid during the year for interest	$891,386	$634,608	$175,897

Supplemental disclosure of non-cash financing activities:			
Settlement of accrued bonuses with restricted stock units	$545,693	$207,608	$–
Dividend, warrant exercise price adjustment	$–	$335,731	$–

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

CYTOSORBENTS CORPORATION

Notes to Consolidated Financial 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"). In addition, the financial statements include CytoSorbents Switzerland GmbH and CytoSorbents Poland Sp. z.o.o., wholly-owned subsidiaries of CytoSorbents Europe GmbH. These entities are 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 will have to raise additional capital to fund its planned operations over the next twelve-month period.

As of December 31, 2018, the Company had an accumulated deficit of $169,523,815, which included net losses of $17,211,179 for the year ended December 31, 2018, $8,460,799 for the year ended December 31, 2017 and $11,763,456 for the year ended December 31, 2016. The Company's losses have resulted principally from costs incurred in the research and development of the Company's 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. The Company's 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 previously received for the Company's CytoSorb product 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 the Company's activities. No assurance can be given that the Company's product development efforts will be successful, that the Company's 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 using blood purification technology to treat deadly inflammation in critically-ill and cardiac surgery patients around the world. 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 wholly owned European subsidiary, CytoSorbents Europe GmbH, conducts sales and marketing related operations for the CytoSorb device. In March 2016, the Company formed CytoSorbents Switzerland GmbH, a wholly-owned subsidiary of CytoSorbents Europe GmbH. This subsidiary, which began operations during the second quarter of 2016, provides marketing and direct sales services in Switzerland. In November 2018, the Company formed CytoSorbents Poland Sp. z.o.o., a wholly-owned subsidiary of CytoSorbents Europe GmbH. This subsidiary, which began operations during the first quarter of 2019, provides marketing and direct sales services in Poland. CytoSorb, the Company’s flagship product, was approved in the European Union (“EU”) in March 2011, and is currently being marketed in and distributed in fifty-five 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. In May 2018, the Company received a label extension for CytoSorb covering use of the device for the removal of bilirubin and myoglobin which allows for the use of the device in the treatment of liver failure and trauma, respectively. 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.

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 19 issued U.S. patents and multiple international patents, with applications pending both in the U.S. and internationally, including HemoDefend, ContrastSorb, DrugSorb, and others. These patents and patent applications are directed to various compositions and methods of use related to our blood purification technologies and are expected to expire between 2020 and 2035, absent any patent term extensions. Management believes that any near term expiring patents will not have a significant impact on our ongoing business.

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. In addition, the financial statements include CytoSorbents Switzerland GmbH and CytoSorbents Poland Sp. z.o.o., wholly owned subsidiaries of 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 gain (loss) included in net loss amounted to approximately $(785,000), $1,454,000 and $(358,000) for the years ended December 31, 2018, 2017 and 2016, 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 accumulated other comprehensive income (loss) as a component of stockholder's equity.

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.

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 both specific, where applicable, and general accruals for estimated bad debts which amounted to approximately $84,000 and $73,000 at December 31, 2018 and December 31, 2017, respectively.

Inventories

Inventories are valued at the lower of cost or net realizable value. Cost is determined using a first-in first-out ("FIFO") basis. At December 31, 2018 and 2017, the Company's inventory was comprised of finished goods, which amounted to $213,839 and $151,872, respectively, work in process which amounted to $415,265 and $528,039, respectively and raw materials which amounted to $204,029 and $115,746, 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.

Revenue Recognition

Product Sales: Revenues from sales of products to both direct and distributor/strategic partner customers are recognized at the time when control passes to the customer, in accordance with the terms of their respective contracts. Recognition of revenue occurs as each performance obligation is completed.

*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 the associated performance obligation is fulfilled. Costs are recorded as incurred. Costs subject to reimbursement by these grants have been reflected as costs of revenue.

Research and Development

All research and development costs, payments to laboratories, research consultants and costs related to clinical trials and studies are expensed when incurred.

Advertising Expenses

Advertising costs are charged to activities when incurred. Advertising expense amounted to approximately $212,000, $162,000 and $173,000 in 2018, 2017 and 2016, 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 Tax Cuts and Jobs Act (the “Act”) was enacted on December 22, 2017. The Act reduces the U.S. federal corporate tax rate from 35% to 21%. See Note 8 for the impact of the tax rate change on deferred tax assets and liabilities.

The Company follows the accounting standards associated with uncertain tax provisions. The Company had no unrecognized tax benefits at December 31, 2018 or 2017. The Company files tax returns in the U.S. federal and state jurisdictions.

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.

CytoSorbents Europe GmbH, CytoSorbents Switzerland GmbH and CytoSorbents Poland Sp. z.o.o. files an annual corporate tax return, a VAT return and a trade tax return in Germany, Switzerland and Poland, respectively.

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 and valuation methods used to determine the change in fair value of the down round feature related to certain of the Company's outstanding warrants.

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.

A significant portion of our revenues are from product sales in Germany. Substantially all of our grant and other income are from grant agencies in the United States. (See Note 3 for further information relating to the Company's revenue.)

As of December 31, 2018, two distributors/strategic partners accounted for 29 percent of the outstanding grants and accounts receivables. As of December 31, 2017, two distributors/strategic partners accounted for 28 percent of outstanding grants and accounts receivables. As of December 31, 2016, one distributor/strategic partners and one government agency accounted for approximately 22 percent of grants and accounts receivable. For the years ended December 31, 2018 and 2017, no agency, distributor/strategic partners or direct customer represented more than 10% of the Company's total revenue. For the year ended December 31, 2016, one direct customer accounted for approximately 11 percent of total revenue.

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 loss attributable 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 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 updated guidance is effective for public entities for fiscal years beginning after December 31, 2018. The Company has evaluated the impact of the updated guidance and has determined that the adoption of ASU 2016-02 will result in the recognition of a right-of-use asset and corresponding lease liability of approximately $1,449,000 as of December 31, 2018 based on the present value of the remaining minimum lease payments over the remaining terms of the leases. In addition, certain disclosures related to these leases will be enhanced as required by Topic 842.

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 cost of revenue. Total freight costs amounted to approximately $424,000, $257,000 and $167,000 for the years ended December 31, 2018, 2017 and 2016, respectively.

Reclassifications

Certain reclassifications have been made to the December 31, 2018, 2017 and 2016 financial statements in order to conform to the 2018 financial statement presentation. There was no change in the reported amount of the accumulated deficit as a result of these reclassifications.

3. REVENUE

On January 1, 2018, the Company adopted the new accounting standard ASC 606, Revenue from Contracts with Customers and all related amendments (the "new revenue standard") to all contracts with customers using the modified retrospective method. The adoption of the new revenue standard had no impact on retained earnings as of December 31, 2017 and, accordingly, no cumulative adjustment was required. We do not expect the new revenue standard to have a significant impact on our net income on an ongoing basis.

The following table disaggregates the Company's revenue by customer type and geographic area for the year ended December 31, 2018:

	Direct	Distributors/ Strategic Partners	United States Government Agencies	Total
Product sales:				
United States	$95,500	$ –	$ –	$95,500
Germany	11,771,645	–	–	11,771,645
All other countries	2,702,689	5,682,549	–	8,385,238
Total product revenue	14,569,834	5,682,549	–	20,252,383
Grant and other income:				
United States	–	–	2,251,525	2,251,525
Total revenue	$14,569,834	$ 5,682,549	$ 2,251,525	$22,503,908

The following table disaggregates the Company's revenue by customer type and geographic area for the year ended December 31, 2017:

	Direct	Distributors/ Strategic Partners	United States Government Agencies	Total
Product sales:				
United States	$126,900	$ –	$ –	$126,900
Germany	7,906,851	–	–	7,906,851
All other countries	1,771,144	3,576,958	–	5,348,102
Total product revenue	9,804,895	3,576,958	–	13,381,853
Grant and other income:				
United States	–	–	1,768,901	1,768,901

Total revenue	$9,804,895	$ 3,576,958	$ 1,768,901	$15,150,754

The following table disaggregates the Company's revenue by customer type and geographic area for the year ended December 31, 2016:

	Direct	Distributors/ Strategic Partners	United States Government Agencies	Total
Product sales:				
Germany	$4,892,613	$ –	$ –	$4,892,613
All other countries	784,265	2,529,158	–	3,313,423
Total product revenue	5,676,878	2,529,158	–	8,206,036
Grant and other income:				
United States	–	–	1,321,807	1,321,807
Total revenue	$5,676,878	$ 2,529,158	$ 1,321,807	$9,527,843

The Company has two primary revenue streams: (1) sales of the CytoSorb device and related device accessories and (2) grant income from contracts with various agencies of the United States government. Both of these revenue streams are within the scope of this accounting pronouncement. The following is a brief description of each revenue stream.

CytoSorb Sales

The Company sells its CytoSorb device using both its own sales force (direct sales) and through the use of distributors and/or strategic partners. All sales of the device are outside the United States, as CytoSorb is not yet approved in the United States. Direct sales are fulfilled from the Company's office in Berlin, Germany. Direct sales relate to sales to hospitals located in Germany, Switzerland, Austria, Belgium and Luxembourg. There are no formal sales contracts with any direct customers relating to product price or minimum purchase requirements. However, there are agreements in place with certain direct customers that provide for either free of charge product or rebate credits based upon achieving minimum purchase levels. The Company records the value of these items as earned as a reduction of revenue. These customers submit purchase orders and the order is fulfilled and shipped directly to the customer. Prices to all direct customers are based on a standard price list based on the packaged quantity (6 packs vs 12 packs).

Distributor and strategic partner sales make up the remaining product sales. These distributors are located in various countries throughout the world. The Company has a formal written contract with each distributor/strategic partner. These contracts have terms ranging from 1-5 years in length, with three years being the typical term.

Each distributor's/strategic partner's contract has minimum annual purchase requirements in order to maintain exclusivity in their respective territories.

There is no additional consideration or monetary penalty that would be required to be paid to CytoSorbents if a distributor does not meet the minimum purchase commitments included in the contract, however, at the discretion of the Company, the distributor may lose its exclusive rights in the territory if such commitments are not met. In addition, certain distributors are eligible for volume discount pricing if their unit sales are in excess of the base amount in the contract.

Government Grants

The Company has been the recipient of various grant contracts from various agencies of the United States government, primarily the Department of Defense, to perform various research and development activities. These contacts fall into one of the following categories:

1. Fixed price – the Company invoices the contract amount in equal installments over the term of the contract without regard to the timing of the costs incurred related to this contract.
2. Cost reimbursement – the Company submits monthly invoices during the term of the contract for the amount of direct costs incurred during that month plus an agreed percentage that relates to allowable overhead and general and administrative expenses. Cumulative amounts invoiced may not exceed the maximum amount of funding stipulated in the contract.

3. Cost plus – this type of contract is similar to a cost reimbursement contract but this type also allows for the Company to additionally invoice for a fee amount that is included in the contract.

In summary, the contracts the Company has with customers are the distributor/strategic partner contracts related to CytoSorb product sales, agreements with direct customers related to free-of-charge product and credit rebates based upon achieving minimum purchase levels, and contracts with various government agencies related to the Company's grants. The Company does not currently incur any outside/third party incremental costs to obtain any of these contracts. The Company does incur internal costs, primarily salary related costs, to obtain the contracts related to the grants. Company employees spend time reviewing the program requirements and developing the budget and related proposal to submit to the grantor agency. There may additionally be travel expenditures involved with meeting with government agency officials during the negotiation of the contract. These internal costs are expensed as incurred.

The following table provides information about receivables and contract liabilities from contracts with customers:

	December 31, 2018	December 31, 2017
Receivables, which are included in grants and accounts receivable	$ 2,399,662	$ 1,267,459
Contract liabilities	$ 42,219	$ 30,380

Contract liabilities represent the value of free of charge goods and credit rebates earned in accordance with the terms of certain direct customer agreements during the years ended December 31, 2018 and December 31, 2017.

4. PROPERTY AND EQUIPMENT, NET:

Property and equipment - net, consists of the following:

December 31,	2018	2017	Depreciation/ Amortization Period
Furniture and fixtures	$621,702	$469,329	7 years
Equipment and computers	3,340,282	2,938,137	3 to 7 years
Leasehold improvements	942,228	850,744	Lesser of term of lease or estimated useful life
	4,904,212	4,258,210	
	3,174,352	2,855,428	

Less accumulated depreciation and amortization		
Property and Equipment, Net	$1,729,860	$1,402,782

Depreciation expense for the years ended December 31, 2018, 2017 and 2016 amounted to $329,469, $177,776 and $126,112 respectively.

5. OTHER ASSETS:

Other assets consist of the following:

December 31,	2018	2017
Patents	$2,929,517	$2,081,222
Less accumulated amortization	(304,252)	(243,170)
Patents, net	2,625,265	1,838,052
Security deposits	128,114	123,133
Total	$2,753,379	$1,961,185

Amortization expense amounted to $61,082, $40,495 and $35,501 for the years ended December 31, 2018, 2017 and 2016, respectively.

Amortization expense for the next five years will be approximately $78,900 for the year ended December 31, 2019; approximately $78,000 for the year ended December 31, 2020; approximately $76,400 for the year ended December 31, 2021; approximately $73,100 for the year ended December 31, 2022; and approximately $69,800 for the year ended December 31, 2023.

6. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES:

Accrued expenses and other current liabilities consist of the following:

December 31,	2018	2017
Accrued salaries and commissions	$1,840,457	$1,009,913
Clinical studies	822,085	111,394
Accrued accounts payable	479,783	310,227
Accrued royalties	433,589	334,335
Professional fees	280,381	300,351
Travel and entertainment	187,047	164,985
Sales, payroll and income taxes payable	182,753	178,592
Interest	76,726	78,585
Congresses	51,549	72,291
Board of director fees	31,350	28,500
Customer Deposits	-	14,747
	$4,385,720	$2,603,920

7. LONG-TERM DEBT

On June 30, 2016, the Company and its wholly-owned subsidiary, CytoSorbents Medical, Inc. (together, the "Borrower"), entered into a Loan and Security Agreement with Bridge Bank, a division of Western Alliance Bank, (the "Bank"), pursuant to which the Company borrowed $10 million in two equal tranches of $5 million (the "Original Term Loans"). On March 29, 2018 (the "Closing Date"), the Original Term Loans were refinanced with the Bank pursuant to an Amended and Restated Loan and Security Agreement by and between the Bank and the Borrower (the "Amended and Restated Loan and Security Agreement"), under which the Bank agreed to loan the Borrower up to an aggregate of $15 million to be disbursed in two tranches (1) one tranche of $10 million (the "Term A Loan"), which was funded on the Closing Date and used to refinance the Original Term Loans, and (2) a second tranche of $5 million which may be disbursed at the Borrower's sole request prior to March 31, 2019 provided certain conditions are met (the "Term B Loan" and together with the Term A Loan, the "Term Loans"). The proceeds of the Term Loans will be used for general business requirements in accordance with the Amended and Restated Loan and Security Agreement. Outstanding balances on the Term Loans bear interest at the prime rate reported in the Wall Street Journal plus 3.66%. This rate was 9.16% at December 31, 2018.

On the Closing Date, the Company was required to pay a non-refundable closing fee of $25,000, expenses incurred by the Bank related to the Amended and Restated Loan and Security Agreement of $11,000 and a portion of the final fee for the period the Original Term Loans were outstanding of $85,938. In addition, the Company incurred legal expenses related to the Amended and Restated Loan and Security Agreement of $20,050. As of the Closing Date, the total unamortized loan costs related to the Term Loans amounted to $130,060. These costs have been presented as a direct deduction from the proceeds of the loan on the consolidated balance sheet in accordance with the provisions of ASC 850. These costs are being amortized over the loan period as a charge to interest expense. For the years ended December 31, 2018, 2017 and 2016, the Company recorded interest expense amounting to $31,946, $29,971 and $14,855, respectively, related to these costs. After accounting for the various costs outlined above, the effective interest rate on the Term A Loan was 9.1% as of March 29, 2018. Commencing on the first calendar day of the calendar month after a Term Loan is made, the Company shall make monthly payments of interest only during the term of each Term Loan. Commencing on November 1, 2019, if the Term B Loan is not made, the Company shall make equal monthly payments of principal of $333,333, together with accrued and unpaid interest. Commencing on May 1, 2020, subject to certain conditions as outlined in the Amended and Restated Loan and Security Agreement, if the Term B Loan is made, which is at the Company's sole discretion, the Company shall make equal monthly payments of principal of $625,000, together with accrued and unpaid interest. In either event, all unpaid principal and accrued and unpaid interest shall be due and payable in full on April 1, 2022. In addition, the Amended and Restated Loan and Security Agreement requires the Company to pay a non-refundable final fee equal to 2.5% of the principal amount of each Term Loan funded upon the earlier of the (i) April 1, 2022 maturity date or (ii) termination of the Term Loan via acceleration or prepayment. This final fee is being accrued and charged to interest expense over the term of the loan. For the years ended December 31, 2018, 2017 and 2016, the Company recorded interest expense of $65,104, $52,083 and $15,625, respectively, related to the final fee. The Term Loans shall be evidenced by one or more secured promissory notes issued to the Bank by the Company. If the Company elects to prepay the Term Loan(s) pursuant to the terms of the Amended and Restated Loan and Security Agreement, it will owe a prepayment fee to the Bank, as follows: (1) for a prepayment made on or after the funding date of a Term Loan through and including the first anniversary of such funding date, an amount equal to 2.0% of the principal amount of such Term Loan prepaid; (2) for a prepayment made after the first anniversary of the funding date of a Term Loan through and including the second anniversary of such funding date, an amount equal to 1.5% of the principal amount of such Term Loan prepaid; and (3) for a prepayment made after the second anniversary of the funding date of a Term Loan through April 1, 2022, an amount equal to 1.0% of the principal amount of such Term Loan prepaid.

Events of default which may cause repayment of the Term Loans to be accelerated include, among other customary events of default, (1) non-payment of any obligation when due, (2) the failure to perform any obligation required under the Amended and Restated Loan and Security Agreement and to cure such default within a reasonable time frame, (3) the occurrence of a Material Adverse Event (as defined in the Amended and Restated Loan and Security Agreement), (4) the attachment or seizure of a material portion of the Borrower's assets if such attachment or seizure is not released, discharged or rescinded within 10 days, and (5) if the Borrower becomes insolvent or starts an insolvency proceeding or if an insolvency proceeding is brought by a third party against the Borrower and such proceeding is not dismissed or stayed within 30 days. The Amended and Restated Loan and Security Agreement includes customary loan conditions, Borrower representations and warranties, Borrower affirmative covenants and Borrower negative covenants for secured transactions of this type.

The Company's and CytoSorbents Medical, Inc.'s obligations under the Amended and Restated Loan and Security Agreement are joint and severable and are secured by a first priority security interest in favor of the Bank with respect to the Company's Shares (as defined in the Amended and Restated Loan and Security Agreement) and the Borrower's Collateral (as defined in the Amended and Restated Loan and Security Agreement, which definition excludes the Borrower's intellectual property and other customary exceptions).

Success Fee Letters:

Pursuant to that certain Success Fee Letter (the "2016 Letter") entered into between the Borrower and the Bank in connection with the Original Term Loans, the Borrower agreed to pay to the Bank a success fee in the amount equal to 6.37% of the funded amount of the Original Term Loans (the "2016 Letter Success Fee") upon the first occurrence of any of the following events: (a) a sale or other disposition by the Borrower of all or substantially all of its assets; (b) a merger or consolidation of the Borrower into or with another person or entity, where the holders of the Borrower's outstanding voting equity securities as of immediately prior to such merger or consolidation hold less than a majority of the issued and outstanding voting equity securities of the successor or surviving person or entity as of immediately following the consummation of such merger or consolidation; (c) a transaction or a series of related transactions in which any "person" or "group" (within the meaning of Section 13(d) and 14(d)(2) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") becomes the "beneficial owner" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of a sufficient number of shares of all classes of stock then outstanding of the Borrower ordinarily entitled to vote in the election of directors, empowering such "person" or "group" to elect a majority of the Board of Directors of the Borrower, who did not have such power before such transaction; or (d) the closing price per share for the Company's common stock on Nasdaq being $8.00 (after giving effect to any stock splits or consolidations effected after the date thereof) or more for five successive business days. On May 18, 2018, the 2016 Letter Success Fee became due to the Bank as result of an occurrence of the event described in clause (d) above. The Company elected to satisfy the 2016 Letter Success Fee by issuing shares of its common stock, which was permitted under the terms of the 2016 Letter. On May 23, 2018, the Company issued 68,791 shares of its common stock in full satisfaction of the 2016 Letter Success Fee, and the obligations of the Borrower under the 2016 Letter. The 2016 Letter Success Fee was valued at $637,000 and was charged to interest expense in the accompanying Statement of Operations and Comprehensive Loss.

In connection with the Amended and Restated Loan and Security Agreement, the Borrower entered into an additional Success Fee Letter (the "2018 Letter"), which will only be effective if the Term B Loan is drawn. Pursuant to the 2018 Letter, the Borrower shall pay to the Bank a success fee in the amount equal to 6.37% of the funded amount of the Term B Loan (the "2018 Letter Success Fee") upon the first occurrence of any of the following events: (a) a sale or other disposition by the Borrower of all or substantially all of its assets; (b) a merger or consolidation of the Borrower into or with another person or entity, where the holders of the Borrower's outstanding voting equity securities as of immediately prior to such merger or consolidation hold less than a majority of the issued and outstanding voting equity securities of the successor or surviving person or entity as of immediately following the consummation of such merger or consolidation; (c) a transaction or a series of related transactions in which any "person" or "group" (within the meaning of Section 13(d) and 14(d)(2) of the Exchange Act) becomes the "beneficial owner" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of a sufficient number of shares of all classes of stock then outstanding of the Borrower ordinarily entitled to vote in the election of directors, empowering such "person" or "group" to elect a majority of the Board of Directors of the Borrower, who did not have such power before such transaction; or (d) the closing price per share for the Company's common stock on Nasdaq being the greater of (i) 70% or more over $7.05, the closing price of the Company's common stock on March 29, 2018 (after giving effect to any stock splits or consolidations effected after the date thereof) for five successive business days, or (ii) at least 26.13% more than the closing price of the Company's common stock on the date of the funding of the Term B Loan.

If the 2018 Letter Success Fee is due pursuant an event described in clause (d) of the two preceding paragraphs, the Company may elect, in lieu of paying the 2018 Letter Success Fee in cash, to issue and sell to the Bank, in exchange for the 2018 Letter Success Fee, such number of shares of the Company's common stock as would be equal to the quotient (calculated by rounding up the nearest whole number) obtained by dividing (a) the 2018 Letter Success Fee by (b) the volume weighted average price per share of the Company's common stock for the same five successive business days on which the closing price per share of the Company's common stock caused the 2016 Letter Success Fee to become payable.

The Bank's right to receive the 2018 Letter Success Fee and the Borrower's obligation to pay such 2018 Letter Success Fee terminate on the fifth anniversary of the funding of the Term B Loan, and shall survive the termination of the Amended and Restated Loan and Security Agreement and any prepayment of the Term Loans.

Long-term debt consists of the following at December 31, 2018, 2017 as follows:

	Year Ended December 31,	
	2018	2017
Principal amount	$10,000,000	$10,000,000
Less unamortized debt acquisition costs	(105,681)	(75,567)
Plus accrued final fee	46,875	67,708
Subtotal	9,941,194	9,992,141
Less Current maturities	666,667	4,000,000
Long-term debt net of current maturities	$9,274,527	$5,992,141

Principal payments of long-term debt are due as follows at December 31, 2018:

2019	$666,667
2020	4,000,000
2021	4,000,000
2022	1,333,333
Total	$10,000,000

8. 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 for the years ended December 31, 2018, 2017 and 2016 is as follows:

	Year Ended December 31 ,		
	2018	2017	2016
Domestic	$(14,105,664)	$(6,071,009)	$(9,300,042)
Foreign	(3,725,061)	(3,066,529)	(2,781,964)
Total	$(17,830,725)	$(9,137,538)	$(12,082,006)

The benefit from income taxes consists of the following:

	Year Ended December 31,		
	2018	2017	2016
State Tax, including sale of New Jersey losses & credits	$619,546	$676,739	$318,550
Foreign tax provision	—	—	—
	$619,546	$676,739	$318,550

As of December 31, 2018, the Company had federal net operating loss ("NOL") carry forwards of approximately $53.2 million, state NOL carry forwards of approximately $11.8 million, and foreign NOL carry forwards of approximately $15.7 million, which may be available to offset future taxable income, if any. The federal net operating loss carryforwards of $41.4 million, if not utilized, will expire between 2021 and 2037. The federal net operating loss carryforwards of $11.8 million generated in 2018 are subject to an 80% limitation on taxable income, do not expire and will carry forward indefinitely. The state net operating loss carryforwards of $11.8 million, if not utilized, will begin to expire in 2038. As of December 31, 2018, the Company had Federal and state research and development tax credit carryforwards of approximately $1,210,000 and $55,000, 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. In addition to the new provisions enacted under the Tax Cuts and Jobs Act, 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.

U.S. Tax Reform

On December 22, 2017, the United States enacted the Tax Cuts and Jobs Act ("Tax Reform Legislation"), which made significant changes to U.S. federal income tax law. The Company expects that certain aspects of the Tax Reform Legislation will positively impact the Company's future after-tax earnings in the U.S., primarily due to the lower federal statutory tax rate. Set forth below is a discussion of certain provisions of the Tax Reform Legislation and our preliminary assessment of the effect of such provisions on the Company's results of operations, cash flows and consolidated financial statements.

Beginning January 1, 2018, the Company's U.S. income, if any, will be taxed at a 21 percent federal corporate rate. Further, the Company is required to recognize the effect of this rate change on our deferred tax assets and liabilities, and deferred tax asset valuation allowances in the period the tax rate change is enacted. The Company does not expect any material non-cash impact from this rate change, with adjustments to deferred tax balances offset by adjustments to deferred tax valuation allowances.

Further, the Tax Reform Legislation provides for a one-time "deemed repatriation" of accumulated foreign earnings for the year ended December 31, 2017. The Company did not pay U.S. federal cash taxes on the deemed repatriation due to an accumulated deficit in foreign earnings for tax purposes. The Company does not expect that our future foreign earnings will be subject to U.S. federal income tax.

The Global Intangible Low-Taxed Income ("GILTI") provisions of the Tax Reform Act, enacted on December 22, 2017, require the Company to include in its U.S. income tax return foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. An accounting policy election is available to either account for the tax effects of GILTI in the period that is subject to such taxes or to provide deferred taxes for book and tax basis differences that upon reversal may be subject to such taxes. The Company has elected to account for the tax effects of this provision in the period that is subject to such tax. The Company concluded it was not subject to GILTI in 2018 and as such there was no impact from GILTI included in its 2018 provision. The Company does not expect to be subject to GILTI. However, in accordance with FASB guidance, the Company's policy will be to recognize GILTI in the period it arises and it will not recognize a deferred charge with regard to GILTI.

In addition, the Tax Reform Legislation provides for 100 percent bonus depreciation on tangible property expenditures through 2022. The bonus depreciation percentage is phased down from 100 percent beginning in 2023 through 2026. We do not expect this to have a material impact to the Company.

Sale of Net Operating Losses (NOLs)

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

In February 2019, the Company received a net cash amount of $619,546 from the sale of the 2017 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,		
	2018	2017	2016
Current and long term deferred tax assets:			
Net operating loss carry forward	$16,722,801	$12,517,356	$15,227,562
Stock Options	349,810	479,033	498,287
Warrants	—	—	108,594
Research and development credit carryforward	1,210,153	1,096,308	1,121,722
Accruals and others	(27,098)	74,477	213,791
Gross deferred tax assets	18,255,666	14,167,174	17,169,956
Less valuation allowance	(18,233,810)	(14,147,354)	(17,152,066)
	21,856	19,820	17,890
Deferred tax liability:			
Fixed Assets	(21,856)	(19,820)	(17,890)
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 (decreases) in valuation allowance for the years ended December 31, 2018, 2017 and 2016 were $3,904,803, $(3,004,712) and 2,405,975 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,		
	2018	2017	2016
Federal statutory rate	21.0 %	34.0 %	34.0 %
State taxes, net of federal benefit	(2.2)	(2.6)	(4.1)
Foreign rate differential	1.9	(1.4)	(1.0)
Permanent items	(2.9)	(5.1)	(8.4)
Rate change and true-up	7.6	(62.7)	(6.0)
Timing differences	—	—	—
Change in valuation allowance	(22.9)	44.3	(13.7)
R&D credit	0.7	0.8	1.8
Effective income tax rate	3.2 %	7.3 %	2.6 %

9. COMMITMENTS AND CONTINGENCIES:

The Company is obligated under non-cancelable operating leases for office space expiring at various dates through August 2021. The aggregate minimum future payments under these leases are approximately as follows:

Year ending December 31,	
2019	$ 495,870
2020	270,249
2021	72,022

Total	$ 838,141

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, 2018, 2017 and 2016 amounted to approximately $805,000, $676,000 and $473,000, 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. After 2017, these employment agreements automatically renew for one year, unless terminated by the Company or the employee. The Company is currently negotiating new employment agreements with Dr. Chan, Mr. Capponi, and Ms. Bloch. On May 30, 2017, CytoSorbents Corporation announced the appointment of Dr. Eric R. Mortensen as the Company’s Chief Medical Officer, pursuant to the terms of an employment agreement dated May 23, 2017. Dr. Mortensen’s employment agreement provides for an initial term commencing on June 1, 2017 and ending on December 31, 2019. These employment agreements each 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, 2018, 2017 and 2016, the Company recorded royalty expenses of approximately $600,000, $393,000 and $243,000 respectively. These expenses are included in selling, general and administrative expenses in the consolidated statement of operations.

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 license fees 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, 2018, 2017 and 2016 per the terms of the license agreement, the Company recorded licensing expenses of approximately $1,002,000, $655,000 and $324,000 respectively. These expenses are included in selling, general and administrative expenses in the consolidated statement of operations.

10. STOCKHOLDERS' EQUITY:

Preferred Stock

In December 2014, the Company amended and restated its articles of incorporation to reduce the total number of authorized shares of preferred stock. The amended and restated 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.

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 (the “2015 Shelf”), was declared effective using a “shelf” registration process. On July 26, 2018, in anticipation of the expiration of the 2015 Shelf, the Company filed a new registration statement on Form S-3 with the SEC (as amended, the “2018 Shelf”). The 2018 Shelf, which was declared effective on August 7, 2018, enables the Company to offer and sell, in one or more offerings, any combination of common stock, preferred stock, senior or subordinated debt securities, warrants and units, up to a total dollar amount of $150 million.

April 5, 2017 Equity Offering

On April 5, 2017, the Company closed on the sale of an aggregate of 2,222,222 shares of common stock pursuant to the Company's 2015 Shelf. The Company received gross proceeds of approximately $10,000,000, from the sale of such shares based on a public offering price of $4.50 per share. On April 11, 2017, the Company closed the sale of an additional 333,333 shares of the Company's common stock, pursuant to the underwriters' full exercise of an over-allotment option. The Company received gross proceeds of approximately $1,500,000 from the exercise of the option. As a result, the Company received total gross proceeds of $11,500,000 from the offering, and, after deducting the underwriting discounts and commissions and related expenses, the Company received total net proceeds of approximately $10,300,000.

As a result of this offering, the exercise price of the warrants issued in connection with the Company's March 11, 2014 public offering was reduced to $4.50 in accordance with the pricing provisions of those warrants. There was no change in the number of warrants which were repriced. As a result of the repricing of the warrants which occurred in connection with the April 2017 equity offering, the Company recorded a dividend of $335,731 during the year ended December 31, 2017.

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 & 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 (the "Shares"). Any Shares hereafter offered and sold will be issued pursuant to the Company's 2018 Shelf, and the related prospectus which the Company filed with the SEC pursuant to Rule 424(b)(5) under the Securities Act.

On July 26, 2018, the Company entered into that certain Amendment No. 1 to the Sales Agreement (the "Sales Agreement Amendment") to extend the term of the Sales Agreement until the expiration of the 2018 Shelf. The other provisions of the Sales Agreement remain unchanged. References herein to "Sales Agreement" shall refer to the Sales Agreement, as amended by the Sales Agreement Amendment.

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, including sales made directly on Nasdaq, 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 expiration of the 2018 Shelf or (b) the termination of the Sales Agreement by Cantor or the Company, as permitted therein. From November 4, 2015 through December 31, 2015, the Company sold 28,880 shares, generating net proceeds of approximately $225,000 under the Sales Agreement. There were no sales during the year ended December 31, 2016. During the year ended December 31, 2017, the Company sold 550,000 shares at an average price of $6.31 per share, generating net proceeds of approximately $3,367,000. During the year ended December 31, 2018, the Company sold 1,515,260 shares at an average cost of $9.61 per share, generating net proceeds of approximately $14,127,000. In the aggregate, the Company has sold 2,094,140 shares at an average selling price of $8.72 per share, generating net proceeds of approximately $17,718,000 under the terms of 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. In 2015, the Company reimbursed Cantor $50,000 for certain specified expenses in connection with the execution of the Sales Agreement.

The Company intends to use the net proceeds raised through “at the market” sales to fund clinical studies in the United States and abroad, expand production capacity, support its sales and marketing efforts, further develop its products, and for general working capital purposes.

Stock Option Plans

As of December 31, 2018, 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 7,400,000 and 2,400,000 shares of common stock are reserved for issuance under the 2014 Plan and the 2006 Plan, respectively. As of December 31, 2018, there were outstanding options to purchase approximately 3,185,000 and 954,000 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 Compensation Committee of the Board of Directors (the “Compensation Committee”).

The Compensation Committee 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 Compensation Committee 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 Compensation Committee.

The 2014 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, 2018, 2017 and 2016 amounted to approximately $4,437,000, $3,314,000 and $2,757,000, respectively. These amounts are included in selling, general, and administrative expenses on the consolidated statement of operations.

The summary of the stock option activity for the years ended December 31, 2018, 2017 and 2016 is as follows:

	Shares	Weighted Average Exercise per Share	Weighted Average Remaining Contractual Life (Years)
Outstanding January 1, 2016	2,477,279	$ 6.56	6.2
Granted	1,044,219	$ 4.68	-
Forfeited	(695,770)	$ 7.12	-
Expired	(27,351)	$ 114.33	-
Exercised	(36,200)	$ 3.26	2.5
Outstanding, December 31, 2016	2,762,177	$ 4.69	6.0
Granted	1,204,950	$ 5.46	9.2
Forfeited	(165,720)	$ 5.50	-
Expired	(34,020)	$ 34.61	-
Exercised	(188,849)	$ 4.40	-
Outstanding, December 31, 2017	3,578,538	$ 4.64	6.3
Granted	1,481,675	$ 8.01	9.2
Forfeited	(544,671)	$ 7.49	-
Expired	(800)	$ 2.88	-
Exercised	(856,280)	$ 3.65	-
Outstanding, December 31, 2018	3,658,462	$ 5.82	7.0

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 $6.85 to $14.80 per share in 2018) and expected life of the stock option (10 years in 2018), the current price of the underlying stock and its expected volatility (ranging from 61.6 to 66.4 percent in 2018), expected dividends (-0- percent) on the stock and the risk free interest rate (2.09 to 3.11 percent) for the term of the stock option. In addition, the Company recognizes forfeitures as they occur.

The intrinsic value is calculated at the difference between the market value as of December 31, 2018 of $8.08 and the exercise price of the shares.

Options Exercisable		
Number Exercisable at December 31, 2018	Weighted Average Exercise Price	Aggregate Intrinsic Value

2,406,845	$ 4.96	$7,517,438

Options Outstanding

Range of Exercise Price	Number Outstanding at December 31, 2018	Weighted Average Exercise Price	Weighted Average Remaining Life (Years)	Aggregate Intrinsic Value
$2.23 - $14.80	3,658,462	$ 5.82	7.0	$8,651,547

The summary of the status of the Company's non-vested options for the year ended December 31, 2018 is as follows:

	Shares	Weighted Average Grant Date Fair Value
Non-vested, January 1, 2018	1,070,959	$ 3.31
Granted	1,481,675	4.88
Forfeited	(524,674)	4.53
Vested	(776,343)	3.62
Non-vested, December 31, 2018	1,251,617	$ 4.56

As of December 31, 2018, the Company had approximately $943,000 of total unrecognized compensation cost related to stock options which will, on average, be amortized over seven months.

In 2019, the Board of Directors intends to grant a pool of options to purchase shares of common stock to the Company's employees which will vest upon the achievement of certain specific, predetermined milestones related to the Company's 2019 operations. Since these options relate exclusively to the achievement of 2019 milestones, no charge for these options has been recorded in the consolidated statements of operations for the year ended December 31, 2018. The Company will assess the likelihood of meeting these milestones throughout 2019 and will record stock option expense as appropriate.

Awards of Stock Options:

On March 15, 2018, the Board of Directors granted options to purchase 531,900 shares of common stock to the Company's management. On April 23, 2018, the Board of Directors granted options to purchase 668,550 shares of common stock to the Company's employees. These grants, which total 1,200,450 shares of common stock, will vest upon the achievement of certain specific, predetermined milestones related to the Company's 2018 operations. The grant date fair value of these unvested options amounted to approximately $5,636,000. On February 19, 2019, Board of Directors determined that the Company has met 60% of these milestones, and accordingly we have recorded approximately $3,381,000 of stock option expense related to these options for the year ended December 31, 2018.

On February 24, 2017, the Board of Directors granted options to purchase 953,200 shares of common stock to the Company's employees which will vest upon the achievement of certain specific, predetermined milestones related to the Company's 2017 operations. The grant date fair value of these unvested options amounted to approximately $3,284,000. On February 15, 2018, based upon the finalization of its review of the Company's progress to meeting the predetermined milestones for 2017, the Board of Directors determined that 810,220 of these options would immediately vest. Accordingly, a charge of approximately $2,791,000 related to these options has been recorded in the consolidated statements of operations for the year ended December 31, 2017.

On June 7, 2016, the Board of Directors granted options to purchase 900,100 shares of common stock to the Company's employees which will vest upon the achievement of certain specific, predetermined milestones related to the Company's 2016 operations. The grant date fair value of these unvested options amounted to approximately $2,437,000. On January 30, 2017, based upon the finalization of its review of the Company's progress to meeting the predetermined milestones for 2016, the Board of Directors determined that 716,480 of these options would immediately vest. Accordingly, a $1,940,000 charge related to these options has been recorded in the consolidated statements of operations for the year ended December 31, 2016.

Change in Control-Based Awards of Restricted Stock Units:

The Board of Directors has granted restricted stock units to members of the Board of Directors, to the Company's executive officers, and to employees of the Company. These restricted stock units will only vest upon a Change in Control of the Company, as defined in the Company's 2014 Long-Term Incentive Plan.

The following table is a summary of these restricted stock units:

	Board of Directors	Executive Management	Other Employees	Total	Intrinsic Value
December 31, 2016	240,000	523,000	744,500	1,507,500	
Granted 2017	24,000	152,300	95,200	271,500	
Forfeited 2017	-	-	(24,000)	(24,000)	
December 31, 2017	264,000	675,300	815,700	1,755,000	$ 11,407,500
Granted 2018	13,200	49,200	256,350	318,750	
Forfeited 2018	-		(69,750)	(69,750)	
December 31, 2018	277,200	724,500	1,002,300	2,004,000	$ 16,192,320

Performance Based Stock Awards:

Pursuant to a review of the compensation of the senior management of the Company, on June 7, 2016, the Board of Directors granted 80,000 restricted stock units to certain senior managers of the Company. These awards were valued at $375,200 at the date of issuance, based upon the market price of the Company's common stock at the date of the grant, and vest one third on the date of the grant, one third on the first anniversary of the date of the grant, and one third on the second anniversary of the date of the grant. These awards are charged to expense over the period which they vest. For the years ended December 31, 2018 and 2017, the Company recorded a charge of approximately $240,000 and $108,000, respectively related to these restricted stock unit awards.

Pursuant to a review of the compensation of the senior management of the Company and managements' performance in 2016, on February 24, 2017, the Board of Directors granted 125,000 restricted stock units to certain senior managers of the Company in order to settle bonuses accrued as of December 31, 2016. These awards were valued at approximately $700,000 on the date of issuance, based upon the market price of the Company's common stock at the date of the grant, and vest one third on the date of the grant, one third on the first anniversary of the grant, and one third on the second anniversary of the date of the grant. For the years ended December 31, 2018 and 2017, the Company recorded a charge of approximately $329,000 and $201,000 related to these restricted stock unit awards.

Pursuant to a review of the compensation of the senior management of the Company and managements' performance in 2017, on February 28, 2018, the Board of Directors granted 146,200 restricted stock units to certain senior managers of the Company in order to settle bonuses accrued as of December 31, 2017. These awards were valued at approximately $1,148,000 at the date of issuance, based upon the market price of the Company's common stock at the date of the grant, and vest one third on the date of the grant one third on the first anniversary of the grant, and one third on the second anniversary of the date of the grant. For the years ended December 31, 2018 and 2017, the Company recorded a charge of approximately $319,000 and $383,000 related to these restricted stock unit awards.

The following table outlines the restricted stock unit activity for the year ended December 31, 2018:

	Shares	Weighted Average Grant Date Fair Value
Non-vested, January 1, 2018	110,003	$ 5.38
Granted	146,200	$ 7.85
Vested	(117,065)	$ 6.33
Non-vested, December 31, 2018	139,138	$ 7.18

Warrants:

As of December 31, 2018, 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
48,960	$ 7.500	March 11, 2019
351,398	$ 4.500	March 11, 2019
30,000	$ 9.900	January 14, 2020
430,358		

In connection with its March 11, 2014 offering, the Company issued warrants to purchase 816,000 shares of common stock. As of December 31, 2018, 351,398 of these warrants remain outstanding. These 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, which is currently $4.50 over the life of the warrants, excluding certain exempt issuances.

11. NET LOSS PER SHARE

Basic earnings per share and diluted earnings per share for the years ended December 31, 2018, 2017 and 2016 have been computed by dividing the net loss attributable to common shareholders for each respective period by the weighted average number of shares outstanding during that period. All outstanding warrants and options and restricted stock awards representing approximately 4,228,000, 4,571,000, and 5,433,000 incremental shares at December 31, 2018, 2017 and 2016, 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 $43,600, $41,700 and $35,900 for the years ended December 31, 2018, 2017 and 2016, respectively.

13. SUBSEQUENT EVENT

In January 2019, the Company entered into an Eighteenth Amendment to Lease with the landlord of its U.S. operating facility which became effective February 1, 2019. This amendment expands the Company's space to 19,920 square feet and extends the term of the lease to May 2020. The amendment also includes a one year renewal option. The Company's new base rent will be approximately $34,000 per month and monthly operating expenses of approximately $29,000 per month.

Pursuant to a review of the compensation of the senior management of the Company and managements' performance in 2018, on March 4, 2018, the Board of Directors granted 22,220 restricted stock units to certain senior managers of the Company in order to settle bonuses accrued as of December 31, 2018. These awards were valued at approximately $179,000 at the date of issuance, based upon the market price of the Company's common stock at the date of the grant, and vest one third on the date of the grant, one third on the first anniversary of the grant, and one third on the second anniversary of the date of the grant. For the year ended December 31, 2018, the Company recorded a charge of approximately $60,000 related to these restricted stock unit awards.

14. QUARTERLY FINANCIAL RESULTS (UNAUDITED)

Summarized quarterly data for 2018, 2017 and 2016 are as follows:

	For the Quarters Ended			
	March 31	June 30	September 30	December 31
2018:				
Total revenue	$4,924,651	5,755,438	5,742,975	6,080,844
Gross margin	3,357,006	3,969,584	3,690,278	3,997,640
Loss from operations	(3,101,167)	(4,187,875)	(2,710,620)	(5,585,266)
Net loss attributable to common stockholders	(2,982,035)	(5,821,202)	(3,004,764)	(5,403,178)
Net loss per share, basic and diluted	$(0.10)	(0.19)	(0.10)	(0.17)
2017:				
Total revenue	$3,113,518	3,566,226	3,824,299	4,646,711
Gross margin	1,859,035	2,084,216	2,307,435	3,381,708
Loss from operations	(1,557,478)	(2,330,908)	(2,149,045)	(3,805,167)
Net loss attributable to common stockholders	(1,524,873)	(2,070,359)	(2,054,279)	(3,147,019)
Net loss per share, basic and diluted	(0.06)	(0.07)	(0.07)	(0.12)
2016:				
Total revenue	$1,810,182	$2,222,338	$2,411,708	$3,083,615
Gross margin	990,683	1,349,072	1,447,827	1,786,536
Loss from operations	(2,090,094)	(2,687,371)	(2,144,212)	(4,570,448)
Net loss attributable to common stockholders	(1,854,596)	(2,814,730)	(2,188,119)	(4,906,011)
Net loss per share, basic and diluted	(0.07)	(0.11)	(0.09)	(0.19)